Dan doktorata
Sveučilište u Zagrebu
Medicinski fakultet

University of Zagreb
School of Medicine
PhD Day

# DAN

KNJIGA SAŽETAKA

# DOKTORATA

## PhD DAY

ABSTRACT BOOK

## 2016.

Sveučilište u Zagrebu, Medicinski fakultet / University of Zagreb, School of Medicine

Dan doktorata 2016 / PhD Day 2016
Knjiga sažetaka / Abstract Book

Sveučilište u Zagrebu, Medicinski fakultet / University of Zagreb, School of Medicine

Dan doktorata 2016 / PhD Day 2016
Knjiga sažetaka / Abstract Book

# Dan doktorata 2016

# PhD Day 2016

## Knjiga sažetaka

## Abstract Book



Sveučilište u Zagrebu – Medicinski fakultet

Zagreb, 2016.

# Table of contents

# Preface

PhD Day (Dan doktorata) started in 2012 and this year it became an annual event of PhD students of both PhD programs (I-Biomedicine and Health Science, and II-Neuroscience) at the School of Medicine University of Zagreb. PhD Day is one day symposium which consists of a presentation of ongoing research of PhD students in a form of published abstracts, posters and selected oral presentations and it is mandatory for all the 2nd-year and 3rd-year students. This symposium is an opportunity for PhD students (for some students this is the first chance to give an oral presentation in front of an audience) and their mentors to exchange ideas among themselves, to present their data to their teachers and experts and get either positive or negative feedback about their scientific work. Thus, this kind of gathering of PhD students, mentors and distinguished internationally recognized scientists provides a great opportunity to share experiences and ideas in specific research field as well as in science generally.

We hope that PhD Day will become a traditional day at our institution which celebrates science, research, co-operation and scientific friendship.

*Marijan Klarica*

# 1. RESEARCH ABSTRACTS

# 1.1.
## RESEARCH ABSTRACTS
## Basic Medical Sciences

## Poster Title: EFFECTS OF BONE MORPHOGENETIC PROTEIN 2 AND 7 ON BONE METABOLISM IN RATS WITH REMOVED THYROID AND PARATHYROID GLANDS

**PhD candidate:** Ivo Dumić Čule, MD

**Thesis proposal:** Effects of bone morphogenetic protein 2 and 7 on bone metabolism in rats with removed thyroid and parathyroid glands

**Mentor/s:** Professor Lovorka Grgurević, MD, PhD

**Affiliation:** Department of Anatomy, School of Medicine, University of Zagreb

**Introduction:** BMP2 and 7 are used locally in FDA approved indications including complicated long bone fractures, non-unions, and spinal fusions. It is unknown whether their systemic release following a local implantation might impact the bone metabolism. Furthermore, it is unknown whether systemic BMP effects on bone are direct or mediated by calciotropic hormones. To answer these questions we examined effects of systemically administered BMP2 and 7 on bone in a rat model with a low level of calciotropic hormones.

**Materials and methods:** Removal of thyroid and parathyroid glands (TPTx) in rats resulted in the decreased level of calciotropic hormones and a subsequent bone loss assessed by microCT and measurement of serum bone formation and resorption markers. BMP2 and 7 were tested in vitro to estimate their influence on osteoblast and osteoclast activity. The administered doses have been calculated according to published bioavailability data from BMP2 and 7 studies.

**Results:** TPTx resulted in bone loss which was restored by systemic administration of 10-70 $\mu$g/kg of BMP2 and all doses of BMP7. BMP2 showed a higher capacity for enhancing trabecular microarchitecture, by increasing trabecular number and diminishing trabecular spacing. In contrast, BMP7 augmented trabecular thickness. In vitro experiments revealed that BMP2 and 7, when uncoupled, increased the number and activity of both osteoblasts and osteoclasts. Collectively, BMP2 and 7 showed ability to increase bone volume in an in vivo environment of low calciotropic hormones.

**Discussion:** These results surprisingly suggest that small amounts of BMP2 and 7 eventually entering the circulation following therapy of bone injuries will not stimulate generalized bone loss. However, osteolysis and heterotopic ossification as major side-effects of BMP2 and 7 devices at local sites of implantation have not been fully elucidated. The osteoblast-osteoclast interaction is probably responsible for orthotopic site osteolysis after BMP device implantation due to initial overbalance of resorption over osteoinductive ability. Dissemination of BMP agglomerates in the adjacent tissue stimulates heterotopic ossification. There is a great medical need for a more effective and safe treatment option in bone defect regeneration, which will include biocompatible carrier with possibility to reduce amount of incorporated BMP.

**Acknowledgments:** -

**MeSH/Keywords:** bone morphogenetic protein 2, bone morphogenetic protein 7, microCT, bone volume

**Poster code:** R-A-2-9

## Poster Title: THE ROLE OF PENTADECAPEPTIDE BPC 157 ON INCISIONAL VENTRAL HERNIA PREVENTION AND WOUND TENSILE STRENGTH IMPACT

**PhD candidate:** Alen Pajtak

**Thesis proposal:** The Role of Pentadecapeptide BPC 157 and NO-system on Incisional Ventral Hernia Prevention and Wound Tensile Strength Impact

**Mentor/s:** 1.Prof Predrag Sikirić, PhD, 2.Prof Janoš Kodvanj, PhD

**Affiliation:** 1.University of Zagreb, School of Medicine, 2.University of Zagreb, Faculty of Mechanical Engineering and Naval Architecture

**Introduction:** Pentadecapeptide BPC 157 has proven positive effect on skin wounds and muscle-tendon damage healing, but its effect on laparotomy wounds, incisional hernia prevention as well as wound tensile strength impact has not yet been studied.

**Materials and methods:** Ingrained method (described by Dubay, 2004.) of early wound failure induction (satisfactory hernia incidence) was performed on Wistar rats. According to experiment protocol rats in experimental groups (BPC157mcg2w, BPC157mcg3w and BPC157mcg4w) were treated with BPC 157 (10mcg/kg, 0.16mcg/mL, 12mL/day/rat, per os in drinking water), while control group received drinking water only. Rats in BPC157mcg2w group were sacrificed 14 days, BPC157mcg3w in 21 days, and BPC157mcg4w group 28 days after initial operation Incisional hernia presence was monitored. 5mm broad samples (no thickness difference, p= 0.875) were taken from the proximal part of laparotomy for tensile strength measurement and analyzed on Beta 50-5 (Messphysik, Austria) Testing Machine. Cutaneous wound healing quality and intraabdominal adhesions were rated (our ordinary scales used).

**Results:** In Control group 73.3% of rats developed hernia while 20% of rats in all experimental groups showed hernia presence. Hernia width in BPC157mcg2w group and BPC157mcg3w group was not significantly different from hernia width in Control group (p=0.126, p=0.072), while hernia width in BPC157mcg4w was significantly smaller (p=0.049). BPC157mcg2w and BPC157mcg3w groups tensile strength was not significantly different (p=0.679, p=0.734) while BPC157mcg4w tensile strength showed significant difference to Control group (p=0.073, p value 0.1 taken significant because of few non-correctable factors). There was a significant difference in cutaneous wound healing (p=0.024) and adhesions presence (P=0.031) between Control group and BPC 157 treated animals.

**Discussion:** Pentadecapeptide BPC 157 has evident hernia prevention, cutaneous wound healing and intraabdominal adhesions prevention effect. No hernia size difference in groups monitored for 14 and 21 days versus significant hernia size difference in 28 days monitored animals pinpoints over time hernia growth prevented by BPC 157. Tensile strength significant difference in 28 days monitored group also implies prolonged BPC 157 healing impact, through all three wound healing phases.

**Acknowledgments:** I would like to express my gratitude to my mentors, for their support and help.

**MeSH/Keywords:** Incisional hernia, BPC 157, Early wound failure, Tensile strength

**Poster code:** R-A-4-23

## Poster Title: EFFECTS OF PENTADECAPEPTIDE BPC 157, L-NAME AND L-ARGININE ON SERIAL RIB FRACTURE IN THE RATS

**PhD candidate:** Goran Zukanović, MD

**Thesis proposal:** Effects of pentadecapeptide BPC 157, L-NAME and L-arginine on serial rib fracture in the rats

**Mentor/s:** Prof. Dinko Stančić-Rokotov, MD, PhD

**Affiliation:** Department of Pharmacology, Medical Faculty, University of Zagreb, Zagreb, Croatia

**Introduction:** Numerous studies have shown the beneficial effects of pentadecapeptide BPC 157 application in tissue healing. The hypothesis of this study was that the use of BPC 157 accelerates and improves healing of surgically induced serial rib fracture in rats. The objectives of this study were to analyze the effects of BPC 157 in healing of surgically induced injury in rats, on the level of clinical and functional outcomes and morphological changes in the examination of the macroscopic characteristics with the help of X-ray, computed tomography (CT) and biomehanical testing.

**Materials and methods:** We used male Albino Wistar rats, 400 g body weight, kept under normal conditions, 5 rats at least per each experimental group and period, randomly assigned for all of the experiments, approved by our Local Ethics Committee. The method we used in causing serial rib fracture was the one described by Hashimoto et al. (1989). In anaesthetized rats, an incision was made on the right lateral aspect of the trunk between the eight and tenth rib. Previously mentioned ribs were located and fractured 2 cm from the vertebral column using a pair of fine scissors. Postoperatively the experimental animals were divided into thirteen groups according to the mode of substance application. The animals were sacrificed according to the study protocol on twentieth and on the sixtieth day after surgical rib fractures. After the sacrifice of the animals, macroscopic evaluation and further verification of the results by X-ray, CT and biomehanical testing was made.

**Results:** In animals treated with BPC 157 bridging occurs earlier in fracture crack, no overproduction of callus and creation of pseudoarthroses was found in later course of the healing process. We also found that the pleural adhesions in control group were significant unlike the treated group were we found no adhesions.

**Discussion:** The present macroscopic and radiological examinations results confirm our hypothesis but the biochemical (serum levels of calcium, phosphate and acid-base status) and histopathological analysis is still in progress.

**Acknowledgments:** I would like to thank my mentor for making this experiment possible.

**MeSH/Keywords:** pentadecapeptide BPC 157, L-NAME, L-arginine, serial rib fracture, rats

**Poster code:** R-A-4-25

## Poster Title: THE EFFECT OF PENTADECAPEPTIDE BPC 157 ON CHRONIC DEEP VEIN THROMBOSIS

**PhD candidate:** Marko Siroglavić, MD

**Thesis proposal:** The effect of pentadecapeptide BPC 157 on chronic deep vein thrombosis

**Mentor/s:** Prof. Martina Lovrić-Benčić, MD, PhD, Prof. Predrag Sikirić, MD, PhD

**Affiliation:** University Hospital Centre Zagreb, University of Zagreb School of Medicine

**Introduction:** Deep vein thrombosis, with incidence of 1 on 1000 in adult population, presents a major health issue and large financial burden on health system. Previous research has shown the effect of BPC 157 on acute deep vein thrombosis and on blood vessels, but its effect on chronic deep vein thrombosis was not investigated. This research would determine the effect of BPC 157 on chronic deep vein thrombosis using an inferior vena cava ligation model for deep vein thrombosis.

**Materials and methods:** In this study female Wistar rats (200g) underwent an inferior vena cava ligation just above the right ovarian vein. Immediately after, control group received 1 ml of saline bath, while the BPC 157 $\mu$g group received 1 ml of BPC 157 (10 $\mu$g/kg) bath and BPC 157 ng group received 1 ml of BPC 157 (10 ng/kg) bath respectively. The thrombi from the vein were evaluated macroscopically after extraction, weighed on a microgram weighing scale on the 4th and 7th day, and the platelet count was assessed on the 7th day.

**Results:** Control group on the 4th day had the thrombi length of 1.93±0.43 cm and the thrombi mass of 0.096±0.005 g, and the control group on the 7th day had length of 1.74 ± 0.35 cm and mass of 0.064 ± 0.002 g, with platelet count of 874 ± 63 10Č9/L on the 7th day. BPC 157 ng treated group on the 4th day had the thrombi length of 1.35 ± 0.16 cm and the mass of 0.063 ± 0.009 g, and the BPC 157 ng group on the 7th day had length of 1.17 ± 0.08cm and mass of 0.049 ± 0.005g. BPC 157 $\mu$g treated group on the 4th day had the thrombi length of 1.05 ± 0.14 cm and the mass of 0.043 ± 0.004 g, and the BPC 157 $\mu$g group on the 7th day had length of 0.87 ± 0.07cm and mass of 0.032 ± 0.003g, with platelet count of 1508 ± 103 10Č9/L on the 7th day.

**Discussion:** This study has shown a significant beneficial effect of pentadecapeptide BPC 157 in both decrease in thrombi size and mass as well as reduction of thrombocytopenia after a thrombotic incident.

**MeSH/Keywords:** venous thrombosis, chronic disease, BPC 157

**Poster code:** R-A-4-38

## Poster Title: THE EFFECT OF PENTADECAPEPTIDE BPC 157 ON A TOXIC DOSE OF LITHIUM IN RATS

**PhD candidate:** Sanja Štrbe, MD

**Thesis proposal:** The effect of pentadecapeptide BPC157, L-NAME and L-arginine on the toxic dose of lithium on rats

**Mentor/s:** Assistant Professor Igor Filipčić MD, PHD

**Affiliation:** University of Zagreb School of Medicine, Department of Pharmacology, Zagreb, Croatia Psychiatry Hospital „Sveti Ivan"

**Introduction:** Li-salts treat bipolar affective disorder presenting, however, muscle weakness, heart failure, brain damages. While is not known antidote we suggest stable gastric pentadecapeptide BPC 157.Li is acting through complex competitive interaction with Na, K, Mg, Ca, second messenger system, 5-HT, DA, AcH,and GABA-ergic system, and we suggest an interaction with NO-system. BPC 157 modulates NO-system, and interferes with the effects of both L-NAME and L-arginine.Illustratively, BPC 157 counteracts lethal outcome in severe hyperkalemia, arrhythmia, hypertension and muscle weakness. Likewise, since Mg concentration directly affects the K concentration, and Li has a proven effect on Mg,while BPC 157 alleviates adverse effect of hypermagnesiemia in rats, BPC 157 would counteract Li-side effects.In particular, BPC 157 would counteract muscle, heart and brain damage and NO-agents, L-NAME and L-arginine, effects.

**Materials and methods:** Rats were randomly selected and treated once daily intraperitoneally (ip) throughout three subsequent days with Li500 mg/kg. Medication (/kg ip, immediately after Li) includes BPC 157 (10 ug, 10 ng), L-NAME (5mg), L-arginine (100 mg) given alone and/or combined while controls received saline (5 ml). Muscle weakness was scored (1-5) after the administration of substance and each rat will be observed and recorded at the vertical grids during the period of 8 minutes. In inhalation anesthetized rats EKG was assessed as described (Barisic et al., 2012). Brain and striated muscle was assessed microscopically as described (Ilic et al., 2009).

**Results:** In general, controls showed more muscle weakness and early fall with the grid unlike animals treated with BPC 157. These were exaggerated with L-NAME, L-arginine and with the combination of L-NAME and L-arginine. By adding BPC 157 to L-NAME and L- arginine, and also to their combination, treated animals once again showed much better results compared to the controls. Illustratively, ECG results showed myocardial damage and ST elevation in the controls with values between 0.6 and 0.7 mV, while treated animals had ST elevation between 0.2 mV(ug BPC's) to 0.3 mV (ng BPC's) over a period of 3 days of consecutive measurements. Histological evaluation of the changes in the brain of control animals indicates hypoxic neurons damaged with the clear cytoplasmic eosinophilia (red neurons) and brain edema unlike BPC 157 treated presenting with undamaged neurons.

**Discussion:** BPC 157 could be used as a therapy for Li side effects

**Acknowledgments:** I would like to thank my previous and present mentor for making this experiment possible.

**MeSH/Keywords:** Pentadecapeptide BPC 157, L-NAME, L-arginine, lithium toxicity

**Poster code:** R-A-4-59

## Poster Title: THE EFFECTS OF SIMVASTATIN AND FENOFIBRATE ON BRAIN GLUTATHIONE AND MALONDIALDEHYDE IN HYPERLIPIDEMIC RATS

**PhD candidate:** Antonija Vukšić

**Thesis proposal:** The effects of antilipid drugs on cholinesterase and oxidative stress parameters in biological material of normolipemic and hyperlipemic rats

**Mentor/s:** Prof. Jasna Lovrić, MD, PhD

**Affiliation:** School of Medicine, University of Zagreb, Department of Pharmacology, Zagreb, Croatia / School of Medicine, University of Zagreb, Department of Medical Chemistry, Biochemistry and Clinical Chemistry,

**Introduction:** Our previous results showed that simvastatin (SIMV) and fenofibrate (FENO) express antioxidative effect by increasing glutathione (GSH) and decreasing malondialdehyde (MDA) levels in brain of normolipidemic rats. We have decided to investigate the influence of SIMV and FENO on GSH and MDA levels in brain of hyperlipidemic rats.

**Materials and methods:** Twenty one male Wistar Zucker rats were divided in one control group (saline) and two experimental groups. One experimental group was on SIMV treatment (50 mg/kg/day) and one experimental group was on FENO treatment (30 mg/kg/day). Agents and saline were given orally for the period of 3 weeks. Animals were sacrificed with ether 24 hours after last dose. Samples were rinsed with saline and stored in a freezer at -70°C until measurement. Concentration of GSH (μg/ml) was measured using Ellman's method (1958), while MDA levels (μmol/l) were measured by HPLC-MS method (Drury JA et al, 1997). Data were analyzed using ANOVA and Dunnett's test. Results were considered as significant with $p < 0.05$. Results are expressed as the means and SDs.

**Results:** SIMV and FENO caused significant decrease ($p < 0.05$) of GSH level (SIMV vs. control: 33.0±24.0 vs. 59.4±22.0 and FENO vs. control: 12.2±5.98 vs. 33.0±24.0). SIMV decreased while FENO significantly increased levels of MDA (SIMV vs. control: 8.59±2.42 vs. 9.74±1.67 and FENO vs. control: 14.6±3.16 vs. 9.74±1.67).

**Discussion:** Our results have shown that simvastatin and fenofibrate decrease GSH levels and fenofibrate significantly increased MDA levels in brain of hyperlipidemic rats. According to these results we have suggested that antioxidative effect of simvastatin and fenofibrate in brain of hyperlipidemic rats is weaker than in normolipidemic rats.

**Acknowledgments:**

**MeSH/Keywords:** simvastatin, fenofibrate, glutathione, malondialdehyde, hyperlipidemic rats

**Poster code:** R-A-4-89

## Poster Title: THE EFFECTS OF PENTADECAPEPTIDE BPC157 ON THE OPENING OF PRESENT COLLATERAL BLOOD VESSELS AFTER LIGATION OF ANTERIOR PANCREATICODUODENAL VEIN IN RATS

**PhD candidate:** Fedor Amić, MD

**Thesis proposal:** The effects of pentadecapeptide BPC157 on the opening of preexisting collaterals and on the healing of duodenal mucose after ligation of anterior pancreaticoduodenal vein in rats

**Mentor/s:** Professor Ante Tvrdeić, MD, PhD, Assist. Prof. Mario Zovak, MD,PhD

**Affiliation:** University of Zagreb School of Medicine

**Introduction:** There is a certain number of inactive blood vessels in various tissues, which do not participate actively in blood distribution and are activated in case of blood stasis. We hypotesize that pentadecapeptide 157 might induce activation of those blood vessels, increase their number and speed up their activation.

**Materials and methods:** The experiment will be conducted on female Wistar albino rats. Ligation of anterior pancreaticoduodenal vein is performed in both control and BPC treated animals at 1 cm below duodenum. BPC 157 will be applied locally on duodenum. We will observe the speed of opening and number of collateral blood vessels 5 minutes, 30 minutes and 24 hours after ligation. Length of observed duodenal segment is determined from the pylorus to the last congested blood vessel. Collaterals will be counted between the congested main blood vessels using a microcamera and the number of those vessels will then be compared. After recording, animals will be sacrificed, their duodenums extirpated and sent to patohystologycal analysis.

**Results:** Duodenums of animals were recorded under microcamera (40x magnification) during 5 minutes. Video image was transformed in digital picture in order to count collaterals. We observed 5 control group animals and 5 animals treated with BPC 157 and counted collateral blood vessels on their duodenums 5 minutes after ligation of anterior pancreaticoduodenal vein. Average number of blood vessels in control animals was 108 while in treated animals it was 217. There were two times more counted collateral blood vessels in treated animals, opposed to control ones. Standard deviation was 11.1 for control groups and 21 for treated groups, with coefficient of variation of 10.2 for control groups and 9.9 for BPC157 treated ones. In 60% of control animals we observed duodenal ulcers while we observed the same in 40% of treated animals.

**Discussion:** Bearing in mind these are preliminary results, although they show promising data, they must be expanded and subjected to more detailed statistical analysis in order to have a definitive conclusion.

**Acknowledgments:**

**MeSH/Keywords:** BPC 157

**Poster code:** R-A-4-158

## Poster Title: ACUTE CHANGES OF BRAIN ACETYLCHOLINESTERASE ACTIVITY IN THE MOUSE AND RAT MODEL OF SPORADIC ALZHEIMER'S DISEASE

**PhD candidate:** Andrija Lončar, MD

**Thesis proposal:** Early changes in the brain induced by central administration of streptozotocin in the experimental model of sporadic Alzheimer's disease

**Mentor/s:** Professor Melita Šalković-Petrišić, MD, PhD

**Affiliation:** Department of Pharmacology,School of Medicine,University of Zagreb, Croatia /Department of Neurology, General Hospital Karlovac, Karlovac, Croatia

**Introduction:** Intracerebroventricular (icv) administration of streptozotocin (STZ) generates a rodent model of sporadic Alzheimer's disease (sAD). Long-term effects of STZ-icv treatment have been well documented but the acute neurochemical impairment has not been investigated thoroughly enough. We aimed to explore and compare the appearance and acute development of impairment in cholinergic transmission in the mouse and rat brain within 24 hours after the STZ-icv treatment.

**Materials and methods:** Adult male mice (strain C57Bl/6) and adult male rat (Wistar) were injected icv with STZ (1.5 mg/kg) or vehicle-citrate buffer (controls). The animals were sacrificed 15 min, and 1, 6 and 24 hours following the STZ-icv treatment. Acetylcholinesterase (AChE) activity in hippocampus (HPC) and parietal cortex (PC) was measured spectrophotometrically by Ellman's method. Data were analysed by Mann-Whitney U test ($p < 0.05$).

**Results:** The AChE activity in mouse PC was unchanged after 15 min and 1 hour, increased 6 (10%) and 24 hours (15.5%) following the STZ-icv injection. In rat PC the activity of AChE was significantly increased after 15 min (35%), unchanged after 1 hour, decreased after 6 hours (-18%) and again increased 24 hours (17%) after STZ-icv treatement. AChE activity in mouse and rat HPC remained generally unchanged.

**Discussion:** STZ-icv administration triggers early changes in cholinergic transmission in the mouse and rat brain, which demonstrate post-treatment time- and brain region-specificity in both species, with some species-dependent difference in their direction in first 6 hours post-treatment.

**MeSH/Keywords:**

**Poster code:** R-A-4-157

## Poster Title: THE ROLE OF AUTOPHAGY IN DIFFERENTIATION AND SURVIVAL OF LEUKEMIA CELL LINES

**PhD candidate:** Vilma Dembitz

**Thesis proposal:** Autophagy and metabolic changes in differentiation of acute myeloid leukemia cell lines

**Mentor/s:** Professor Dora Višnjić, MD, PhD

**Affiliation:** Department of Physiology and Croatian Institute for Brain Research, School of Medicine, University of Zagreb

**Introduction:** Autophagy has been shown to contribute to differentiation of leukemia cells in various experimental settings. Our recent study showed that 5-aminoimidazole-4-carboxamide ribonucleotide (AICAR), a commonly used AMP-kinase (AMPK) modulator, induced differentiation of U937 cells in an AMPK-independent manner. In the present study, we tested for the possible role of autophagy in AICAR-mediated effects.

**Materials and methods:** U937, HL60 and SH-SY5Y cells were treated with AICAR, A76996, metformin, all-trans retinoic acid (ATRA), phorbol 12-myristate 13-acetate (PMA) and 3-methyl-adenine (3-MA). The expression of differentiation markers and cell viability were analyzed by flow cytometry. Cell morphology was determined by phase contrast microscopy and LC3B localization by confocal microscopy. siRNA transfections were done by electroporation. The levels of LC3BII, Beclin-1, PI3KC3 and actin were determined by Western blot.

**Results:** AICAR-mediated increase in CD11b and CD64 was not mimicked by direct AMPK activator A76996 corroborating our previous findings that differentiative effects of AICAR are AMPK-independent. AICAR increased the level of autophagy marker LC3BII in U937 cells after 48 h, but no increase was observed in the presence of metformin, an AMPK modulator without differentiative properties. AICAR-mediated increase in LC3BII correlated with cell-type specific differentiation since no increase in the level of either LC3B or morphological signs of differentiation were observed in neuroblastoma SH-SY5Y cell line, although ATRA and PMA increased autophagy and differentiation in both U937 and SH-SY5Y cells. PI3KC3 inhibitor 3-MA inhibited the agonist-mediated increase in the expression of differentiation markers and decreased the number of viable cells in U937 cell line. However, treatment with 3-MA increased the levels of LC3BII, even though it reduced the levels of PI(3)P. siRNA-mediated decrease in the level of Beclin-1 and PI3KC3 did not abolish the differentiative effects of ATRA and PMA, but had some effects on AICAR-mediated increase in CD64 and metformin-mediated decrease in cell viability.

**Discussion:** Results of the present study show that AICAR induces autophagy during monocytic differentiation of U937 cells. Our data suggest that 3-MA cannot be used as a specific pharmacological inhibitor of autophagy. Preliminary data suggest that the presence of normal levels of Beclin-1 and PI3KC3 may be of importance for AICAR-mediated differentiation and metformin-mediated decrease in cell viability.

**MeSH/Keywords:** acute myeloid leukemia, differentiation, autophagy

**Poster code:** R-A-5-134

## Poster Title: CALMODULIN KINASE II BINDS AND INHIBITS BRUSH BORDER SODIUM-HYDROGEN EXCHANGER 3 BY A NHERF 2 PROTEIN-DEPENDENT PROCESS

**PhD candidate:** Dorotea Bartoniček, MD

**Thesis proposal:** Calmodulin kinase II binds and inhibits brush border sodium -hydrogen exchanger 3 by a NHERF 2 protein – dependent process

**Mentor/s:** Professor Mirza Žižak, MD, PhD

**Affiliation:** University of Zagreb, School of Medicine, University Hospital Centre Zagreb

**Introduction:** Sodium Hydrogen Exchanger 3 (NHE3) is one of nine NHE isoforms, present in brush border (BB) of intestinal Na absorptive cells and in renal proximal tubule cells where it accounts for majority of gastrointestinal and renal sodium absorption. It is made of N-terminal transmembrane domain and C- terminal cytoplasmic domain. Transmembrane domain mediates Na/H exchange, while cytoplasmic domain regulates NHE activity and interacts with other proteins. NHE3 is one of most regulated transport proteins. It is rapidly stimulated and inhibited as part of normal digestive physiology. NHE Regulating Factor 2 (NHERF 2) is protein that regulates NHE3 surface expression and by that its activity. NHERF family members are involved in Ca inhibition of NHE3. Ca/calmodulin-dependent protein kinase II (CaMKII) is present in ileal and renal proximal tubule BB where it regulates neutral NaCl absorption by still unknown mechanism.

**Materials and methods:** Studies were performed using PS120 fibroblasts stably transfected with rabbit NHE3 tagged at C terminus (NHE3V). Some PS120 NHE3V cells were co-transfected with human NHERF2. High levels of NHE3 expression were maintained by acid loading. Pulldown Assay using four His6-tagged fusion proteins of NHE3 C-terminus was used to identify which fragment binds CaMKII in presence or absence of calcium. Na/H activity was measured fluorometrically using intracellular pH-sensitive fluorescent dye BCECF. Stably transfected PS120 cells were studied with/without presence of CaMKII inhibitors KN-62 or KN-93. NHE activity was calculated as HČ efflux rate. The nonlinear regression data analysis (Microcal Origin software) was used to analyze data. Statistical significance was determined by Student's t test.

**Results:** CaMKII directly binds NHE3 under basal conditions and this binding is calcium dependent. CaMKII inhibits Na /H exchange activity under basal condition. CaMKII inhibition of basal NHE3 activity is NHERF2-dependent.

**Discussion:** Our study revealed that under basal condition CaMKII directly binds to NHE3 as novel NHE3 binding protein. CaMKII inhibits basal NHE3 activity and this inhibition is mediated by NHERF 2. CaMKII binding and reducing NHE3 activity is part of physiological regulation of NHE3 that occurs in fibroblast as in BB of intestinal cells.

**Acknowledgments:**

**MeSH/Keywords:** Sodium- Hydrogen Exchanger 3, NHE Regulating Factor, Ca /Calmodulin-dependent Protein Kinase II

**Poster code:** R-A-5-159

## Poster Title: GENETIC MECHANISMS OF LYSOSOMAL DYSFUNCTION IN PARKINSON'S DISEASE

**PhD candidate:** Antonela Blažeković, MD

**Thesis proposal:** Genetic mechanisms of lysosomal dysfunction in Parkinson's disease

**Mentor/s:** Associate Professor Fran Borovečki, MD, PhD, Professor Maja Relja, MD, PhD

**Affiliation:** Department for Functional Genomics, Centre for Translational and Clinical Research, University of Zagreb School of Medicine, University Hospital Centre – Zagreb

**Introduction:** Several rare monogenic disorders caused by mutations in lysosomal genes show parkinsonian-like symptoms and alpha-synuclein accumulation, which is a key molecule that accrues in the brain of patients with Parkinson's disease (PD). Research on rare forms of PD which are caused by mutations in the alpha-synuclein gene (A53T, A30P, E46K) indicates impairment of alpha-synuclein lysosomal removal. The familial cases are rare, comprising only 5% of all PD cases. The aim of this study is to investigate and characterize the underlying genetic mechanisms leading to autophagy-lysosomal pathway (ALP) dysfunction in PD patients by applying a novel genomic panel consisting of 440 genes associated with lysosomal pathways, neurodegeneration and alpha-synucleinopathies.

**Materials and methods:** The study included patients suffering from PD. DNA was extracted from whole blood samples using commercially available DNA extraction kits. We developed the LYSOGENE, a targeted next-generation sequencing (NGS) panel, which allowed us to obtain a uniform and accurate coding sequence coverage of a comprehensive set of 440 autophagy-lysosomal pathway genes based on the Human Lysosome Gene Database (hLGDB). We also included genes associated with PD.

**Results:** We detected around 1000 variants per sample (622-1884) with an average of 13 category 1 variants per sample (10-16). A total number of 25 genes was represented in category I variants. Myosin VIIA (MYO7A), Serglycin (SRGN),Vacular Protein Sorting 11 (VPS11) were present in at least 80% of samples. Glucocerebrosidase variants were present in 36% of samples, mostly in intronic regions. Alpha-synuclein variants were present in 100% of samples, mostly in 3' UTR regions. Presenilin 2 variants were present in 82% of samples, mostly in intronic regions, but also as silent mutations (synonymous coding), rarely in 3' UTR regions.

**Discussion:** Preliminary data suggests that there is a significant number of gene variants present in autophagy-lysosomal pathway in PD patients. Our results confirmed the important role of alpha-synuclein in PD. Further analyses on a larger patient cohort are warranted. The underlying mechanisms of autophagy-lysosomal pathway dysfunction still have to be fully elucidated.

**MeSH/Keywords:** Parkinson disease, Lewy bodies, lysosomes, genomics, alpha-Synuclein

**Poster code:** R-A-6-20

## Poster Title: INCREASED SPECIFIC IMMUNOGLOBULIN G4 ANTIBODIES INDUCED BY NATURAL EXPOSURE TO AMBROSIA POLLEN IN PATIENTS WITH ALLERGY

**PhD candidate:** Vedran Ostojić

**Thesis proposal:** Changes in specific immunoglobuline isotype levels in atopic and healthy subjects, prior and after natural exposure to Ambrosia elatior pollen

**Mentor/s:** Asja Stipić Marković

**Affiliation:** University Hospital

**Introduction:** Induction of specific immunoglobulin G4 (sIgG4) response (so-called blocking antibodies) in patients who receive specific immunotherapy (SIT) has been observed for many years. Although many other mechanisms have been identified as key regulators of immunologic processes in peripheral tolerance to allergens, the rise of sIgG4 during immunotherapy is still believed to be one of the most important mechanisms through which SIT reaches its clinical efficacy. The aim of this prospective study was to measure levels of IgG4 and sIgE in healthy subjects and subjects allergic to Ambrosia elatior pollen, before and during natural exposure.

**Materials and methods:** Twenty-four patients with allergic diseases of the respiratory tract and 24 healthy controls entered the study. The sIgG4 and sIgE levels were measured in serum by using the ELISA, before and during A. elatior pollination season.

**Results:** A significant increase of the sIgG4 level in subjects with allergy during natural exposure to an allergen (0.676 increased to 0.937, $p < 0.05$) was shown. An increase in sIgE levels was also observed. Healthy subjects had comparable levels of sIgG4 as in subjects with allergy before the pollination season and no change in sigG4 and slgE levels during the pollination season.

**Discussion:** Natural allergen exposure, and not just the application of desensitization, led to a significant increase of sIgG4 levels in patients with allergy thus indicating that increase in the sIgG4 level during desensitization is an unlikely immune mechanism that leads to improvement. This data supported the clinical findings of other investigators, which found clinical improvement in patients who received SIT before the increase in the sIgG4 level and even in patients who showed no increase in the sIgG4 level (1).
As expected, the levels of sigE in the study group were high. After a natural allergen exposure, further rise was shown in a study group, which was consistent with other studies (2). Healthy individuals did not show a significant increase in sIgE nor sIgG4 levels, although they have low basal levels of sIgE and thus the memory IgE B cells, which was shown earlier (3,4). The reasons may be numerous: sustained intact epithelial barrier permeability, differences in caveolar transport of allergenic molecules, more efficient local antigen clearence by mucosal slgA and slgG and, more recently, IL-10 B lymphocytes. Some investigators concluded that the induction of tolerance by IL-10 is the most likely mechanism.

**MeSH/Keywords:** Allergens, Ambrosia, Pollen, Blocking Antibodies, Immunoglobulin E, Immunoglobulin G

**Poster code:** R-A-7-73

## Poster Title: INDUCTION OF JOINT-ASSOCIATED MYELOID LINEAGE CELLS BY CHRONIC INFLAMMATION IN COLLAGEN INDUCED ARTHRITIS

**PhD candidate:** Darja Flegar, MD

**Thesis proposal:** Characterization of osteoclast progenitor responses and increased osteoresorption in mouse model of rheumatoid arthritis

**Mentor/s:** Professor Danka Grčević, MD, PhD

**Affiliation:** Laboratory for Molecular Immunology, Croatian Institute for Brain Research, Zagreb, Croatia, Department of Physiology and Immunology, University of Zagreb School of Medicine, Zagreb, Croatia

**Introduction:** Collagen induced arthritis (CIA) is a mouse model for human rheumatoid arthritis characterized by chronic inflammatory response and enhanced osteoresorption. We aimed to dissect systemic and local changes of immune cell populations, which could subsequently mediate increased osteoclast recruitment, differentiation and activity.

**Materials and methods:** C57BL/6 mice were immunized with chicken type II collagen emulsified in complete Freund's adjuvant, followed by a booster dose. Development of arthritis was confirmed by detection of anti-collagen antibodies (IgG1 and IgG2a) and clinical scoring up to 70 days. Spleen, periarticular bone marrow and tarsometatarseal part of hind paws were analyzed by a series of hematopoietic markers (CD3, CD4, CD8, B220, NK1.1, CD11b, CD115, Gr1) to determine changes in lymphoid and myeloid populations as well as osteoclast progenitor (OCP) phenotype using flow-cytometry.

**Results:** Immunized mice developed arthritis with incidence of 60 to 70% (maximum score 14/16). Flow-cytometry showed highly induced myeloid lineage populations in local arthritis-affected sites, particularly lymphoid-negative CD11b /Gr-1 subset that comprised 49±12.7% of cells in CIA compared to 24±4.1% in controls. In contrast, peripheral hematopoietic lineages were not significantly affected by arthritis. Frequency of OCPs (CD3-B220-NK1.1-CD11b CD115 ) was also increased in local arthritis-affected sites (1.18±0.48% in controls, 2.97±0.80% in CIA). OCPs were further characterized by the expression of CCR2 and RANK.

**Discussion:** Our results indicate that the myeloid lineage is induced in joint-associated areas by CIA, with no significant changes at the systemic level. This increase possibly contributes to the higher production of proresorptive mediators and enhanced osteoclast recruitment and activity in arthritis.

**MeSH/Keywords:** arthritis, myeloid progenitor cells, inflammation

**Poster code:** R-A-7-154

## Poster Title: THE EFFECT OF BPC 157 ON ISCHEMIC/REPERFUSION INJURIES IN RAT BRAIN

**PhD candidate:** Jakša Vukojević

**Thesis proposal:** The effect of BPC 157 on ischemic/reperfusion injuries in rat brain

**Mentor/s:** Prof. Predrag Sikirć, MD, PhD, Assist. Prof. Gorana Aralica, MD, PhD

**Affiliation:** Department of Pharmacology, School of Medicine, University of Zagreb, Department of Pathology, School of Medicine, University of Zagreb

**Introduction:** Ischemic/reperfusion injuries are elementary pathophysiological findings in stroke, thereby making it the third most common cause of death in the modern world and the first cause of long-term disability. Pentadecapeptide BPC 157, has already been proven to have an effect on vessel integrity, it is a mediator of Robert's cytoprotection and interacts with the NO system, all of which, make it a promising agent when it comes to cerebral ischemic/reperfusion injuries.

**Materials and methods:** In this experiment, ischemic/reperfusion injuries are induced using bilateral carotid artery occlusion (BCAO). The effect of BPC 157 on ischemic/reperfusion injuries was investigated in male Wistar Albino rats. After an occlusion of 20 min, the rats were randomly divided into groups. The treated group received BPC 157 ($10\mu g$/kg, 10ng/kg, I.P.) right after surgery, while the control group received saline (1ml, I.P.) immediately after surgery. After a reperfusion period of 24 or 72 hours, the neurological assessment was performed and samples were gathered for further examination. Neurological assessment was conducted using the Morrison water maze test (MWMT) and beam walk test (BWT).

**Results:** In the MWMT the control animals had far greater memory loss and spatial orientation loss, while the BPC 157 treated group had almost no loss in the MWMT. The control group lost 10.3 seconds, while the BPC 157 treated group gained 1 second in comparison to the training results. In the beam walk test, we also observed substantial differences between the control and treated group, where the control group walked far worse and scored 1, while the BPC 157 treated group walked much better and scored 4. The pathology findings concurred with the results obtained in the neurological assessment.

**Discussion:** Pentadecapeptide BPC 157 showed that it counteracts ischemic/reperfusion injuries, saving the rats from memory and orientation loss, as well as maintaining their motor capabilities. The results we present here are promising and prove that BPC 157 has potential as a neuroprotective agent in cerebral ischemic/reperfusion injuries, although further investigations should be conducted to further confirm the full effects of BPC 157.

**Acknowledgments:**

**MeSH/Keywords:** BPC 157, BCAO, Neuroprotection, Stroke

**Poster code:** R-A-9-7

## Poster Title: THE ROLE OF ALTERED CHOLESTEROL METABOLISM ON RETROMER (DYS)FUNCTION IN NEURODEGENERATIVE DISORDERS

**PhD candidate:** Kristina Dominko, BSc, MSc in Molecular Biology

**Thesis proposal:** Molecular link(s) between membrane trafficking, cholesterol homeostasis and Alzheimer's disease

**Mentor/s:** Associate Professor Nataša Jovanov Milošević, PhD and Senior Research Associate Silva Katušić Hećimović, PhD

**Affiliation:** Laboratory for Neurodegenerative Disease Research, Division of Molecular Medicine, Ruđer Bošković Institute, Zagreb, Croatia

**Introduction:** Retromer is a protein complex that plays a major role in recycling of transmembrane receptors from endosomes to the trans-Golgi network and thus, maintaining function of proteins within the endo/lysosomal pathway. Retromer dysfunction has been linked to a growing number of neurological disorders. It is an early pathological feature in Alzheimer's disease (AD). However, the molecular triggers of retromer dysfunction in AD are still unknown. In this work we tested hypothesis that membrane cholesterol levels may modulate trafficking within the endo/lysosomal pathway and thus, may modulate function of retromer. To test this, we used an innovative model of a rare childhood neurodegenerative disorder Niemann-Pick type C (NPC) that is caused by mutations in cholesterol transport genes NPC1 or NPC2. Interestingly, recent studies, also from our group, have established several links between NPC and AD, indicating that the two neurodegenerative disorders may share a common pathological pathway(s).

**Materials and methods:** To determine the effect of cholesterol levels on retromer function we used cellular and mouse models of NPC disease. For that purpose, we analyzed Chinese hamster ovary cells (CHOwt) and CHO NPC1-null cells in which NPC1 gene has been deleted. We also confirmed our results in mouse primary neurons and in NPC1-deficient mouse brains (Jackson laboratory, USA). Protein levels and co-localization of retromer components and the Alzheimer's $\beta$-amyloid precursor protein (APP) were determined by Western blot and immunocytochemistry, respectively.

**Results:** The levels of retromer components (Vps26 and Vps35) between CHOwt and CHO NPC1-null cells were not different. However, their cellular localization was changed. In CHO NPC1-null cells, in contrast to CHOwt cells, retromer was retained in early endosomes where it co-localized with APP. Using cholesterol depletion treatments we were able to rescue retromer mistrafficking in CHO NPC1-null cells. In CHOwt cells cholesterol loading caused a similar defect of retromer localization as seen in CHO NPC1-null cells.

**Discussion:** Our results indicate that retromer (dys)function is dependent on cholesterol levels. Together with the recent finding of a therapeutic potential of small molecule(s) that enhances stability/function of retromer, our results propose that cholesterol reducing compounds may be considered in protecting/reverting the retromer function both in NPC and AD, as well as in other neurodegenerative diseases.

**MeSH/Keywords:** Alzheimer's disease, APP, cholesterol, neurodegeneration, Niemann-Pick type C disease, NPC1, retromer

**Poster code:** R-A-9-133

## Poster Title: EFFECTS OF GUANYLIN PEPTIDES IN THE BRAIN

**PhD candidate:** Nikola Habek, MD

**Thesis proposal:** Expression and effects of uroguanylin in the mouse brain

**Mentor/s:** Prof. Aleksandra Sindic, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, Croatian Institute for Brain Research, Laboratory for Cell Neurophysiology

**Introduction:** Guanylin peptides (GP), guanylin (GN) and uroguanylin (UGN) are proposed to be intestinal natriuretic peptides, produced in the intestine after high salt meal causing electrolyte and water secretion by the kidneys. GP activate guanylate cyclase C (GC-C) and increase cGMP concentration. Presence of GP in the brain was never confirmed. However, GC-C was reported in dopaminergic neurons of Substantia nigra pars compacta and Ventral tegmental area where GP neuromodulate neuron activity and GC-C knock-out mice were suggested as new model for ADHD. GC-C was also reported in Hypothalamus where it plays role in feeding and satiation.

**Materials and methods:** Expression analysis of mRNA for UGN, GN and GC-C was tested by PCR. Primary astrocyte culture was isolated by MACS (Magnetic activated cell separation) method. Effect of UGN, GN and cell permeable cGMP on membrane potential was recorded by whole cell patch clamp electrophysiology configuration. Effect of UGN on intracellular calcium concentration was tested by microfluorescent method.

**Results:** Expression analysis showed presence of mRNA for UGN and GC-C, but not for GN, in different brain regions after feeding. Recordings of membrane voltage showed that UGN and GN hyperpolarize astrocytes which is opposite to depolarization by membrane permeable cGMP suggesting that GC-C is not receptor for UGN in astrocytes. In the same type of the cells UGN increase intracellular calcium.

**Discussion:** We showed for the first time presence of UGN in the brain. This is of great importance because its expression is depending on feeding status. As we know that UGN can modulate neuronal firing rate and is connected with browning of white fat tissue by activation of sympathetic nervous system presence of UGN in the brain can be of great importance for brain control of energy balance. In astrocytes, we also discovered new cGMP/GC-C independent but calcium dependent signalling pathway for UGN which could be specific for brain cells.

**MeSH/Keywords:** guanylin, uroguanylin, cGMP, intracellular calcium signalling, astrocytes, brain slices, electrophysiology

**Poster code:** R-A-9-143

## Poster Title: TLR2 IS INVOLVED IN THE ACUTE REACTION TO INTERMITTENT HYPOXIA

**PhD candidate:** Dora Polšek

**Thesis proposal:** Features of neuroinflammation during chronic intermittent hypoxia as the mouse model of obstructive sleep apnea

**Mentor/s:** Prof. Srećko Gajović, MD, PhD, Ivana Rosenzweig, MD, PhD

**Affiliation:** Department of Hystology and Embriology, University of Zagreb School of Medicine / Sleep and Brain Plasticity Centre, Department of Neuroimaging IoPPN, King's and Imperial Colleges London Sleep Disord

**Introduction:** Obstructive sleep apnea (OSA) is a prevalent chronic multisystem disease characterized by brief upper airway occlusions, hypoxia, hypo/hypercarbia and sleep fragmentation. OSA has recently been linked to early cognitive decline and Alzheimer's disease (AD). Even though the pathogenic mechanism behind this association is not clear, neuroinflammatory process has been suggested to play the role. Neuroinflammation is increasingly recognized as one of the important possible precipitants of neurodegeneration, such as occurs in the AD. In this study we set to investigate the presence of neuroinflammation in the animal model of OSA using in vivo imaging of the TLR2 signal.

**Materials and methods:** A customized set-up for exposing mice to intermittent hypoxia was designed. Transgenic TLR2-luc mice underwent 8 h daily of 90s periods of 5,7% of oxygen and room air during 3 weeks, while the controls were kept near the setup to account for the stress of handling. All mice were regularly imaged after exposure throughout the period using a prolonged imaging protocol for more precise signal acquisition. The 3D source of the bioluminescent signal was also reconstructed using diffuse light imaging tomography. A group of mice underwent ex vivo imaging. After the protocol, the mice were sacrificed and the brains stained for microglial marker Iba1 as well as for luciferase.

**Results:** The mice (N=20) that underwent chronic intermittent hypoxia showed a significant upregulation of TLR2 signal following the first day of exposure, after which the signal remained elevated throughout the protocol. The diffuse light imaging tomography showed the signal to be located in the frontal region of the brain, but also in a second locus possibly relating to the hippocampus. Luciferase was co-localised with the Iba1 marker showing TLR2 expression primarily located in microglia. Finally, quantification of Iba1 cells in the hippocampus, olfactory bulb and anterior olfactory nucleus showed microglial hyperplasia in mice that had been exposed to intermittent hypoxia.

**Discussion:** Our results suggest that TLR2 might play an acute and chronic role in mediating the neuroinflammatory response to intermittent hypoxia.

**MeSH/Keywords:** Intermittent hypoxia, obstructive sleep apnea, microglia, neuroinflammation

**Poster code:** R-A-9-63

## Poster Title: PSYCHOLOGICAL OUTCOMES IN PRETERM CHILDREN WITH STRUCTURAL BRAIN CHANGES

**PhD candidate:** Branka Bartolić Spajić, mag.psych.

**Thesis proposal:** Psychological outcomes in preterm children with structural brain changes

**Mentor/s:** Prof. Neven Henigsberg, MD, PhD

**Affiliation:** School of Medicine, University of Zagreb

**Introduction:** The development of neonatal pediatric care has significantly increased the survival rate in premature born children, who are at higher risk of early brain lesions that lead to various neurodevelopmental difficulties. Some recent studies show that cognitive difficulties are the most common disabilities caused by the early brain lesions. MR studies can clearly show various brain structures and potential correlates of the psychological outcomes in these children. This study tries to light up these connections, with the main goal of the future development of early neuroprotective strategies and therapies for preborn children.

**Materials and methods:** The study includes two groups of premature children scanned at MR device twice, at the age of 0 and 2 years. The first group includes children with structural lesion related to perinatal pathology and evident neurological disorders of different levels. The second group will include prematurely born babies who have no signs of neurological disorders and have normal brain morphology. Psychological assessment of these children is at age 3-7 years and it includes assessment of general and specific cognitive functions (Wechsler Preschool and Primary Scale of Intelligence – WPPSI-III), executive functions (tasks of EF) and behavioral outcome (CBCL, ADHDT).

**Results:** We expect that preschool children with perinatal brain injury will show general cognitive impairment, impairment of executive functions, behavioral difficulties and structural brain changes. We also expect that all the variables of psychological outcome will correlate positively between themselves and negatively with the variables of structural brain changes (with possible regional differences).

**Discussion:** Cognitive impairment is one of the most common neurodevelopmental outcome in preterm children with perinatal brain injury. Structural brain changes are the basis of many long term neurodevelopmental difficulties. Children with perinatal brain injury show many difficulties on various fields: perceptive, visuo-motor, constructive, verbal, learning and memory, attention, executive functions. It is also shown that children with perinatal brain injury more often have some of the psychiatric disorders. Modern studies show that neonatal MR in preterm children is a good predictor of future developmental outcome.

**Acknowledgments:** prof.dr.sc. Neven Henigsberg, academic Ivica Kostović, Petra Kalember, dr.med., Policlinic Neuron

**MeSH/Keywords:** executive functions, cognitive functions, pretermn birth, perinatal brain injury, MRI, structural brain changes, children

**Poster code:** R-A-9-156

## Poster Title: EXPRESSION OF MOLECULES INVOLVED IN MUCIN EXOCYTOSIS AND DISCHARGE REGULATION IN HUMAN AND MOUSE ENDOCERVICAL TISSUE

**PhD candidate:** Marta Skelin, MD.

**Thesis proposal:** Molecular mechanisms of secretion activity regulation in human endocervical glandular epithelium

**Mentor/s:** Assist. Prof. Marija Ćurlin, MD, PhD.

**Affiliation:** Department of Histology and Embryology, School of Medicine

**Introduction:** Endocervical secretory epithelium produces cervical mucus, a glycoprotein gel that accepts, filters, prepares, stores and releases sperm for transport to the oviduct for fertilization, as well as provides a barrier to the infection. The mechanisms of mucus secretion in the cervix are poorly investigated. We propose a new model of regulation of mucus secretion that involves action potential independent activity of GABAA receptors. This research will investigate the role of GABAA receptors in non-genomic mucus secretion regulation, as well as examine a pathway operating via acetylcholine. Besides researching secretion stimulation, the pathway of bicarbonate ion production, which is crucial for discharge of mucin aggregates and formation of mucus with proper rheological properties, will be investigated.

**Materials and methods:** To test our hypothesis, using immunohistochemistry and PCR, we analyzed mouse and human endocervical tissue for the presence of GABA receptors, VGAT, GAD, ACII, AChR and CFTR.

**Results:** The results showed that GABAAR is present in the endocervical tissue of both human and mouse. Human tissue also expressed VGAT, and GAD which are a part of GABA signalling pathway, elements of AChR signalling pathway (AChR and ACII) and CFTR, which is necessary for $HCO_3^-$ secretion. These results strongly support our hypothesis and the proposed model which is necessary for $HCO_3^-$ secretion.

**Discussion:** The detection of these proteins in the endocervical tissue of fertile females was the prerequisite for further steps in investigation of molecular mechanisms of estrogen regulated mucin exocytosis and discharge. In order to perform necessary further experiments, a 3D endocervical cell culture should be established. This way the effect of different conditions, such as variations of estrogen level, pH, GABAAR activation and inhibition, can be evaluated by immunohistochemical and electron microscopy analysis.

**Acknowledgments:**

**MeSH/Keywords:** endocervical, mucus, secretion, GABA, cell culture

**Poster code:** R-A-9-101

# Poster Title: HIPPOCAMPAL EXPRESSION OF NEUROPLASTIN IN ALZHEIMER'S DISEASE

**PhD candidate:** Katarina Ilić, MD

**Thesis proposal:** Association of ganglioside composition and neuroplastin expression in neurodegeneration

**Mentor/s:** Professor Svjetlana Kalanj Bognar, MD, PhD

**Affiliation:** Croatian Institute for Brain Research, School of Medicine, University of Zagreb

**Introduction:** Neuroplastin (Np) is a transmembrane glycoprotein acting as cell adhesion molecule (CAM). Evidenced physiological effects of Np in brain include promoting neurite outgrowth, regulation of structure and function of synapses and involvement in synaptic plasticity. Np is implicated in molecular mechanisms of learning and memory. Most recent data show that ablation of Np in adult mice causes retrograde amnesia of associative memories, which clearly confirms a crucial role of neuroplastin in associative learning. Specific Np distribution has been described in mouse and rat hippocampus, but there is lack of data on Np localization in human brain. Since there is a demonstrated upregulation of CAMs in neurodegeneration, and Np is shown to be involved in learning and memory, the aim of this study is to determine neuroplastin expression in neurodegeneration. In addition, Np immunolocalization in normal adult human brain will be analyzed.

**Materials and methods:** Immunohistochemical analysis of Np expression was performed in 12 formalin-fixed paraffin-embedded human hippocampal sections from individuals with diagnosed Alzheimer's disease (AD) and 12 age- and gender-matched controls. Sections were analyzed by optical microscope and semiquantitative estimation of Np immunoreactivity was performed.

**Results:** This study is the first to report systematic data on Np expression in normal adult human hippocampus and hippocampus affected by AD. Increased immunoreactivity of Np was observed in hippocampi affected by neurodegeneration, markedly in the inner and external molecular layer of the dentate gyrus. Also, a disturbed organization of immunoreactive fibers of the CA1 radial layer was demonstrated.

**Discussion:** Our preliminary results show changed Np expression in hippocampi affected by AD, suggesting a potential role of Np in pathophysiology of neurodegeneration. Increased Np expression in the hippocampus in AD, resembling the changes of other CAMs such as polysialylated neural cell adhesion molecule, indicates possible tissue compensatory response mechanism to neurodegeneration.
We suggest that neuroplastin may serve as a plasticity marker, due to its higher expression during reorganization and plasticity reactivation in neurodegeneration.

**MeSH/Keywords:** Neuroplastin, Alzheimer's disease, hippocampus

**Poster code:** R-A-9-102

## Poster Title: VOLUMETRIC ANALYSIS OF CORTICOPONTINE SYSTEM IN THE HUMAN PRETERM INFANTS

**PhD candidate:** Marina Raguž, MD

**Thesis proposal:** Impact of hypoxic-ischemic encephalopathy on projection pathways of the premature infant brainstem

**Mentor/s:** Associate Professor Milan Radoš, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, Department of Anatomy and Clinical Anatomy and Croatian Institute for Brain Research

**Introduction:** Perinatal hypoxic-ischemic encephalopathy (HIE) is a major cause of white matter injury and long-term neurological deficits in children. Motor corticospinal as well as cortico-pontine pathways are frequent targets of injury since they pass through vulnerable periventricular space and crossroads. In this study we analyzed cerebral volumes as indicator of white matter injury and compared with recipient areas in pons and cerebellum in order to find possible selective vulnerability of corticopontine system.

**Materials and methods:** Study involved 10 normal term infants, 10 normotypic premature infants without lesions and 10 premature infants who have lesions associated with perinatal HIE. All groups were scanned by MRI device twice, first at the corrected term age and second at the age of two years. All volumes were measured on 3T MR images utilizing semi-automated (MNI toolbox) and manual segmentation methods (Analyze 8.1).

**Results:** Unlike growth observed in normal group, normotypic group showed decreased volume of pons and cerebellum at term age, which compensate till the age of 2 years. Group with HIE lesions shows volume reduction during both scanning.

**Discussion:** It seems that both origin and trajectory - termination areas of the motor pathways are reduced in HIE. We have found that corticopontine pathways are regularly damaged in HIE brain as a part of general white matter pathology. Our finding is in the agreement with hypothesis that periventricular crossroads and periventricular fiber system are vulnerable in HIE.

**MeSH/Keywords:** brainsteam, MRI, perinatal hypoxic-ischemic encephalopathy, premature infant

**Poster code:** R-A-9-104

## Poster Title: VOLUMETRIC PARAMETERS OF THALAMOCORTICAL DEVELOPMENT IN TERM AND PRETERM CHILDREN

**PhD candidate:** Valentina Galkowski, MD

**Thesis proposal:** The perinatal hypoxic-ischemic encephalopathy impact on the premature infant thalamus and cortex

**Mentor/s:** Associate Professor Milan Radoš, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, Croatian Institute for Brain research

**Introduction:** The development of paediatric care significantly increased the survival rate in premature born children, but preterm birth is still leading cause of cognitive impairment in childhood and is associated with cortical and deep gray matter abnormalities. Impairment of thalamic development is an important component of preterm brain injury and is often associated with cortical alterations. Measurements of thalamic and cortical volumetric parameters in term and preterm children can advance our understanding of normal perinatal brain development and also mechanisms of perinatal brain injury. In this study, we analyzed correlation of thalamus volume with cortical thickness, area and volume in different lobes

**Materials and methods:** All volumes were measured from 3T MR images using semi-automated and manual segmentation methods (MNI toolbox, Analyze 8.1).The study included premature children scanned at MR device twice, first at the corrected term age and then at the age of two years. As a control we used MRI scans of healthy children of the same age

**Results:** Volumetric analysis showed difference between preterm and term children, and also between preterm children with neurological and mental aberrations and preterm children without neurological symptoms.

**Discussion:** Normal growth of thalamus and cortex is essential for normal development of premature children and early detection of growth disturbance increases the possibility of timely interventions in order to reduce subsequent neurological and psychological disorders.

**MeSH/Keywords:** thalamus, MRI, premature infant

**Poster code:** R-A-9-132

# Poster Title: RELIABILITY OF PARAMETERS FREQUENTLY USED FOR THE EVALUATION OF ARM MOTOR FUNCTION

**PhD candidate:** Tatjana Trošt Bobić, prof.cin.

**Thesis proposal:** Ipsilateral and contralateral effects of kinesitherapy on hand function after stroke

**Mentor/s:** Assistant professor Iris Zavoreo, MD, PhD, Professor Goran Šimić, MD, PhD

**Affiliation:** University of Zagreb, School of Kinesiology, University Hospital Centre Sestre milosrdnice

**Introduction:** A wide number of stroke survivors never fully recover the function of the affected arm. The use of objective kinetic measures to quantify hand function may facilitate the clinical adoption of behavioral interventions for stroke, such as constraint-induced movement therapy and other bimanual task practice-based interventions. The aim of this study was to evaluate the intra- and inter-session reliability of numerous dynamometric parameters that are frequently used for the evaluation of arm motor function.

**Materials and methods:** A new custom-made measurement system was designed and built. One hundred fifty healthy active individuals ($20.5\pm1.7$ years) where included in the validation study. They were asked to perform three maximal voluntary wrist flexion and extension stressing explosive force production. Signals were recorded by means of load cells and electrogoniometers. Altogether sixteen parameters, which are frequently used to evaluate arm motor function where computed from the recorded signals. Three components of reliability were calculated: systematic bias, within-individual variation, and retest correlation.

**Results:** Intra-session reliability - Within individual variation (coefficient of variance - CV) varied from 13.8% to 19.2% for almost all the parameters (i.e. max. average force, rate of force development) established in the time intervals of 30 and 50 ms. When the same parameters where extracted for 100 and 200 ms CV remained in the range of 6.4-11.9%. The majority of parameters had a high intra-session reliability (intraclass correlation coefficient – ICC=0.84-0.91). Inter-session reliability - CV ranged 4.8%-17.5%. High ICC were obtained for almost all the parameters (ICC=0.81-0.9).

**Discussion:** The main finding of this study is that the extracted variables had better inter- and intra-session reliability when calculated for the time interval of 100 and 200 ms of maximal voluntary contraction (MVC), rather than for 30 and 50 ms respectively. Such data suggests that the indices of arm motor function should be calculated in wider time windows of MVC. The obtained results will be implemented in the upcoming investigation of the doctoral thesis, which is about the effectiveness of different exercise therapy modalities on hand motor function recovery after stroke. Using the most reliable variables will allow greater security in drawing conclusions on the fact that an eventually registered motor recovery is due to the implemented therapy, rather than just an accidental error of measurement.

**Acknowledgments:** I would like to thank my mentors for guidance and support.

**MeSH/Keywords:** upper extremity motor function, dynamometry, reliability, stroke recovery

**Poster code:** R-A-9-142

# 1.2.
## RESEARCH ABSTRACTS
## Clinical Medical Sciences

## Poster Title: PULMONARY VASCULAR PERMEABILITY INDEX AND EXTRAVASCULAR LUNG WATER IN PATIENTS WITH SEPSIS SYNDROME

**PhD candidate:** Željko Drvar, MD

**Thesis proposal:** Pulmonary vascular permeability index and extravascular lung water in patients with sepsis syndrome

**Mentor/s:** Professor Dinko Tonković, MD, PhD

**Affiliation:** Department of Anesthesiology, Reanimatology and Intensive care, University Hospital Center Zagreb – Croatia

**Introduction:** Early detection of mild acute respiratory distress syndrome (ARDS) is very important since there are few early signs suggesting it. Pulmonary vascular permeability index (PVPI) and extravascular lung water (EVLW) are becoming interesting as indicators of mild ARDS. It is possible to measure both parametars with PiCCO (Pulse-induced Contour Cardiac Output) monitoring.

**Materials and methods:** Aims: To investigate PVPI and EVLW values and dynamics of pulmonary oedema in patients with sepsis by volumetric PiCCO plus monitoring (Drager infinity R PiCCO smart pod TM). Methods: Prospective observational study. Investigated group included 50 patients, of both sexes, after urgent abdominal surgery, with mild ARDS. Control group included 50 patients of both sexes, after urgent vascular surgery, without mild ARDS. Age: 18-60 years of age. Diagnosis of sepsis was clinically and laboratory confirmed, mild ARDS as defined by Berlin definition. PVPI and EVLW measurements were taken in both study groups three times a day in 8-hour intervals. All measured or calculated data were statistically processed using the Smirnov-Kolmogorovljev and independent t-test. Values of $P<0,05$ were considered statistically significant.

**Results:** Analysis of variance for repeated measurements showed statically significant difference in PVPI and EVLW dynamics between investigated and control group in 7-day interval of time. PVPI1-arithmetic mean (a.m.) 2,84/1,58, SD 0,48/0,23, t 16,86, df 98,00, $P<0,001$. PVPI3-a.m. 3,47/1,70, SD 0,44/0,25, t 24,60, df 98,00, $P<0,001$. PVPI7-a.m. 3,93/1,90, SD 0,72/0,38, df 75,00, $P<0,001$. EVLW1-a.m. 990,10/347,00, SD 125,38/101,34, t 28,21, df 98,00 $P<0,001$. EVLW3-a.m. 1037,64/357,14, SD 140,35/102,04, t 27,79, df 98,00 $P<0,001$. EVLW7-a.m. 1023,66/321,20, SD 182,49/58,43, t 80,00, df 80,00 $P<0,001$.

**Discussion:** The results of this study show that PVPI and EVLW can be used in the early diagnosis and dynamics of mild ARDS in surgical patients with sepsis. The initially measured PVPI and EVLW values in the investigated patient group were higher than in the control group, but still within the reference interval spread. Significant increase in PVPI and EVLW values in the investigated patients group were recorded on the 3rd day and maximum values were achieved on the 7th day of measurement. Other studies also indicated that PVPI and EVLW could be used as reliable indicators for early detection of patients with mild ARDS.

**Acknowledgments:**

**MeSH/Keywords:** Pulmonary vascular permeability index, extravascular lung water, mild ARDS, sepsis, PiCCO

**Poster code:** R-B-1-16

## Poster Title: EFFECT OF ACUTE POSTOPERATIVE PAIN TREATMENT ON THE BODY'S STRESS RESPONSE

**PhD candidate:** Vilka Bekavac Mišak, MD

**Thesis proposal:** Effect of acute postoperative pain treatment on the body's stress response

**Mentor/s:** Professor Dinko Tonković, MD, PhD

**Affiliation:** Department of Anesthesiology, Reanimatology and Intensive care, University Hospital Center Zagreb-Croatia

**Introduction:** Strong nociceptic somatic and visceral pain in immediate postoperative period is considered the most relevant factor in the development of endocrine and neurohumoral disorders. In the stimulation phase of severe pain, the stress hormone concentrations are increased and may serve as biomarkers of uncontrolled pain. The main purpose of this study was to evaluate the effects of three different postoperative pain management modalities on pain intensity and cortisol, prolactin, adrenalin and noradrenalin serum concentrations in patients undergoing open renal surgery by lumbotomy approach.

**Materials and methods:** The prospective, monocenter, randomized controlled open-label study included 63 patients randomly assigned the day before surgery to one of three groups:a study group receiving continuous intravenous analgesia(CIA)with sufentanil and ketamine (n=22), a study group receiving continuous epidural analgesia(CEA)with levobupivacaine and sufentanil(n=20), and a control group receiving intravenous analgesia(IV) with tramadol, metamizol, and non-steroid antirheumatic drug(n=21). Serum hormone levels were determined before the surgery and 3, 24, and 48 hours after the onset of analgesia. The intensity and characteristics of pain were evaluated in all patients using visual analogue scale (VAS).

**Results:** Three hours postoperatively, the reported pain intensity in the CEA group was lower by almost 50% in comparison with the CIA and control groups. Serum cortisol in the CIA and control groups showed a 2.8- and 2.5-fold increase at 3 hours postoperatively in comparison with preoperative values, whereas the increase in the CEA group was only 38%. Prolactin levels significantly increased in all groups at 3 hours postoperatively in comparison with preoperative values. At 24 and 48 hours postoperatively, prolactin levels were similar in the CEA and CIA groups and significantly lower than in the control group. Adrenaline levels increased 10-fold in all three groups at 3 hours postoperatively and then decreased to values twice higher than the preoperative ones. Noradrenalin levels were the highest 3 hours postoperatively, showing similar values in all three groups.

**Discussion:** Although CEA was significantly more effective in providing pain relief than the CIA and control IV analgesia, all three postoperative pain management modalities resulted in satisfactory pain reduction. However, the endocrine response to trauma and pain cannot be completely blocked by any analgesia.

**Acknowledgments:**

**MeSH/Keywords:** pain, postoperative pain management, endocrine response

**Poster code:** R-B-1-29

## Poster Title: RISK FACTORS ASSOCIATED WITH ADVERSE CARDIOVASCULAR EVENTS DURING ORTHOTOPIC LIVER TRANSPLANTATION AND EARLY POST TRANSPLANTATION PERIOD

**PhD candidate:** Nataša Višković Filipčić, MD

**Thesis proposal:** Estimating donor and recipient's risk factors for adverse cardiovascular events during orthotopic liver transplantation and early post transplantation period

**Mentor/s:** Assistant Professor Tajana Filipec Kanižaj, MD, PhD

**Affiliation:** University Hospital Merkur, Zagreb, Croatia

**Introduction:** Liver transplantation is a curative method for end-stage liver disease. The procedure itself poses a great stress for recipient's cardiovascular system and adverse events are not unusual. These can vary from mild (benign arrhythmias, transient hypotension) to serious (pulmonary embolism, malign arrhythmias, hearth failure, myocardial infarction and cardiac arrest). Risk factors for these events are due to donor and recipient's characteristics. It is the aim of this study to find the incidence of these adverse events and design simple scoring and prognostic scales for their occurrence in this subgroup of transplant patients.

**Materials and methods:** Medical records from patients with liver transplantation conducted at the University Hospital Merkur during 2013-2015 are being analysed. Exclusion criteria are: split-liver, living donor, combined organ transplantation, re transplantation, acute hepatic insufficiency and patients <18 years. Donor factors are collected from Eurotransplant donor reports. Recipient characteristics (age, sex, weight, hight, BMI, lab work, previous disease history) are obtained from medical charts. Intraoperative and postoperative occurrence of adverse cardiovascular events as well as use of vasopressors, time of mechanical ventilation, dialysis and ICU stay is noted. Adverse events are stratified as mild and serious. Their incidence will be calculated. Multivariable statistical analysis will be performed. Risk factors for adverse cardiovascular events will be investigated. Simple grading scale and prognostic scale for the occurrence of these events will be designed at the end of the study.

**Results:** Data collection is still in progress (expected to end in June 2016). At the moment, preliminary results are being statistically analysed and there are not any preliminary results available.

**Discussion:** The results of this study should give us an overview of the liver transplantation in University Hospital Merkur, emphasizing the incidence of adverse cardiovascular events during the orthotropic liver transplantation and in early post transplantation time. Furthermore, establishing these factors might contribute to better donor-recipient matching. Simple scoring and prognostic scales arising from this study, if implemented as part of the routine screening, might furthermore reduce adverse cardiovascular events in this vulnerable group of patients.

**MeSH/Keywords:** liver transplantation, donors, transplant recipients, risk factors, cardiovascular complications

**Poster code:** R-B-1-81

## Poster Title: RANDOMISED COMPARISON OF D-BLADE TO C-MAC AND DIRECT LARYNGOSCOPY

**PhD candidate:** Vedran Hostić, MD

**Thesis proposal:** The impact of blade curvature on intubation characteristics in videolaryngoscopy in patients with predicted difficult airways

**Mentor/s:** Associate Professor Vladimir Bedeković, MD, PhD

**Affiliation:** University Hospital Centre Sestre milosrdnice

**Introduction:** Videolaryngoscopes are increasingly being used in clinical practice. C-Mac D-Blade is recently introduced extension to the existing C-MAC videolaryngoscope system. We could find no studies evaluating the two videolaryngoscope blades against direct laryngoscopy (DL). We performed randomised comparison of the C-MAC D-Blade, C-MAC and DL using seven point intubation difficulty scores (IDS) as our primary outcome measure in a planned total of 180 patients.

**Materials and methods:** Following approval of the University Medical Centre ethics commitee, patients undergoing general anesthesia with tracheal intubation were invited to take part in the study. We recorded success rate, POGO score, total time to intubation and seven point IDS. Failure of the procedure was declared if intubation was not successfull after 120s. We used SPSS v 20 to analyse the data: one-way ANOVA for continuous data and Kruskall-Wallis for ordinal data.

**Results:** So far, 140 patients (48 D-blade, 52 C-MAC and 40 DL) were included with mean (SD) age 58 (17) years, BMI 27 (4) kg/m_2 and male to female ratio of 79:61 over a period of nine months. Total time to intubation (s) was similar in all groups with mean (SD) 18,5 (6,8) in D-blade, 16,6 (5,7) in C-MAC and 18,3 (8,1) in DL group (p=0.34). The view obtained during laryngoscopy was best in D-blade group with mean (SD) POGO score (%) of 98 (7) in comparison to 74 (35) in C-MAC and 59 (45) in DL group (p<0,001). Overall there was a significant effect of laryngoscope used on the IDS (p=0,015). From the pairwise comparisons, there was a significant difference between D-blade and DL, but not between the other pairs of devices. Two failures were recorded: one with C-MAC blade and one in DL group. In both cases intubation was unsuccessful after multiple attempts requiring longer than 120s. D-blade was used successfully as a rescue device in both cases (p=0,93).

**Discussion:** The results of our study suggest that despite statistical differences regarding intubation difficulty and quality of laryngeal view obtained during laryngoscopy, there is little clinical benefit that the D-Blade or C-Mac blades provide over conventional direct laryngoscopy in patients with normal airways. Success of the D-blade as a rescue device in our study suggests that D-blade could be benefitial in patients with difficult airways.

**Acknowledgments:**

**MeSH/Keywords:** videolaryngoscopy, intubation, difficult airway, C-MAC, D-blade

**Poster code:** R-B-1-70

## Poster Title: BIOLOGICAL PROPERTIES OF T-CELL LYMPHOMA (Mycosis fungoides) IN CORRELATION WITH THE CLINICAL PICTURE, STAGE AND PATIENT OUTCOME IN CROATIA – TEN-YEAR FOLLOW-UP

**PhD candidate:** Sandra Jerković Gulin, MD

**Thesis proposal:** Biological properties of T-cell lymphoma (Mycosis fungoides) in correlation with the clinical picture, stage and patient outcome in Croatia – ten-year follow-up

**Mentor/s:** Assoc. Prof. Romana Ceovic, MD

**Affiliation:** [1]General Hospital Šibenik, [2]University of Zagreb School of Medicine University Hospital Centre Zagreb

**Introduction:** Recent studies suggest that the following factors in patients with early-stage MF (IA-IIA) were associated with reduced survival and increased risk of disease progression (DP): plaques, advanced clinical stage, increased age, male sex, increased lactate dehydrogenase, large cell transformation, presence of large Pautrier microabscesses and lymphocytes with hyperchromatic or vesicular nuclei in the dermal infiltrate and less than 20% CD8 cells in the dermal infiltrate. Aim of this study is to identify predictors of DP and death in patients with early stage MF in a ten-year period.

**Materials and methods:** 83 patients diagnosed with early-stage MF at the Departments of Dermatovenerology and Pathology, UHC Zagreb between 01/2003 and 12/2012 and with complete clinical data and enough stored samples of the initial biopsy for further analysis were included in this retrospective study. Following were analysed: clinical picture, response to therapy, DP, lichenoid dermal infiltrate (LDI) of lymphocytes, lymphocytes keepers (LK), atypical lymphocytes (AL) and loss of surface markers of T lymphocytes CD2, CD3, CD5 and / or CD7. Statistical analysis of the impact of each of the observed variables on DP and the death was performed.

**Results:** Disease progression was significantly associated with 1) the initial stage (IS) of the disease IIa, 2) clinically enlarged lymph nodes, 3) therapy without response and 4) > 50% AL (p <0.05). Patients with complete response to therapy and scarce LDI often does not progress (p <0.05). The IS of the disease IIa increases the risk for DP 363% compared to patients with lower initial stages (p<0.05). Complete response to therapy reduces the risk for DP for 86% and scarce LDI reduces that risk for 71% reduce this risk (p<0.05). Death was significantly associated with 1)the IS of the disease IIa, 2) plaques, 3) clinically enlarged lymph nodes, 4) DP, 5) therapy without response, 6) dense LDI, and 7) higher number of LK (p<0.05). IS Ia, patches without plaques and normal lymph nodes, are often not associated with death (p <0.05). The risk of death is increased in patients with 1) the IS of the disease IIa 9.83 times, 2) increased lymph nodes 5.80 times, 3), therapy with no response 288 times, dense LDI 14.25 times, and increased number of LK 1.06 times (p<0.05). Loss of surface markers of T lymphocytes CD2, CD3, CD5 and/or CD7 was not statistically significant.

**Discussion:** This study has identified new prognostic factors for early stage MF.

**Acknowledgments:**

**MeSH/Keywords:** early stage mycosis fungoides, histological features, prognostic factors

**Poster code:** R-B-2-62

## Poster Title: ITCHY AND PAINFUL DERMATOSES CARRY THE HIGHEST PSYCHOLOGICAL BURDEN AMONG DERMATOVENEROLOGICAL PATIENTS

**PhD candidate:** Iva Dediol, MD

**Thesis proposal:** Itchy and painful dermatoses carry the highest psychological burden among dermatovenerological patients

**Mentor/s:** Veljko Dordevic, Mirna Situm

**Affiliation:** Department of Psychiatry University Hospital Center Zagreb, Department of dermatovenereology University Hospital Center Sestre milosrdnice

**Introduction:** Skin diseases are mostly chronic and lifelong with recurrences. Severity of the disease does not always correlate with the influence of the disease on the patient's life. The most aggravating fact for the patients is that the skin diseases are „public". Reactions of other people, will change patient's perception of her/himself and influence patient's self-confidence with consequences on her/his behavior pattern and habits. Quality of life is also influenced by physical symptoms of the skin diseases, like itch and pain. Development of psychiatric comorbidity in patients with some skin diseases is already established. Little is known about psychological comorbidity ande quality of life bewtween common skin diseases and venereological diseases.

**Materials and methods:** Two hundred and ninty participants were divided into three groups: first group of participants were those with itchy/painfull dermatoses like psoriasis, atopic dermatitis and venous ulcer, second group of participants were with non-itchy/non-painfull dermatoses like vitiligo, alopecia and acne and third group of participants involved venereological patients with diagnose of HPV, Herpes simplex and balanopostitis.

**Results:** Participants with itchy and painfull dermatoses had the highest influence of the disease on their quality of life. Only psychological dimension of quality of life was not influneced by skin or venereological disease. 4,1% of the participants had a high depression scores, 11,5% of participants had high and very high anxiety symptoms as state and 15,6% as trait. There was no statistically significant difference between depressive symptoms in all study groups. Significant differences in anxiety symptoms were registered between patients with venereological disease and other two study groups. Patients with more severe skin lesions were more depressed but patients with always exposed lesions were more anxious.

**Discussion:** Patients with pruritic and painful dermatoses have the most influence of skin disease on their quality of life.

**Acknowledgments:**

**MeSH/Keywords:** skin diseases, venereal diseases, quality of life, depression, anxiety

**Poster code:** R-B-2-99

**Poster Title: ASSOCIATION OF SERUM CONCENTRATIONS OF INTERLEUKINS IL-18, IL-19, IL-21 AND IL-22 WITH THE ETIOPATHOGENESIS AND ASSESSMENT OF CLINICAL ACTIVITY OF NONSEGMENTAL FORM OF VITILIGO**

**PhD candidate:** Maja Kovačević, MD

**Thesis proposal:** association of serum concentrations of interleukins IL-18, IL-19, IL-21 and IL-22 with the etiopathogenesis and assessment of clinical activity of nonsegmental form of vitiligo

**Mentor/s:** Assistant professor Vesna Lukinović Škudar[1], MD, PhD; Professor Andrija Stanimirović, MD, PhD [2]

**Affiliation:** [1]Department of Physiology and Immunology, Zagreb School of Medicine, Šalata 3, Zagreb, Croatia, [2]Naftalan Special Hospital for Medical Rehabilitation, Omladinska 23a, Ivanić Grad, Croatia

**Introduction:** Vitiligo is a pigmentary disorder characterized by appearance of depigmentation macules on skin and mucosa. The autoimmune factors have an important role in disease development. Present studies about the role of IL-18, IL-19, IL-21 and IL-22 in etiopathogenesis of vitiligo and clinical activity are limited, but those cytokines in autoimmune diseases related to vitiligo provoke inflammation and aggravate the disease.

**Materials and methods:** 75 participants aged 18-65 (50 patiens with NSV aged 18-65 and 25 age-and sex-adjusted healthy volunteers as controls) will be included in the cross-sectional study. A detailed patient history will be taken, in addition with specially designed questionnaire. Clinical examination of the patient under the visible and UV light will be performed as well as determination of VASI and VIDA score. Skin lesions will be photographed with Canon Eos 5D MkII camera. Peripheral venous blood samples (5 mL) will be collected and serum concentrations of IL-18, IL-19, IL-21 and IL-22 in patients with NSV and control group will be determined with ELISA method, using commercial kits (MBLI for IL-18 and R and D Systems, Minneapolis, USA, for IL-19, IL-21 and IL-22). The differences in the indicated parameters between patients with NSV and the control group will be observed as well as the differences in the indicated parameters between patients with NSV depending on clinical findings (VASI score), activity of the disease (VIDA score) and disease duration. Statistical significance will be considered to be achieved when $P<0,05$.

**Results:** We expect that our results would expand the lacking knowledge about the role of cytokines IL-18, IL-19, IL-21, IL-22 in the complex pathogenesis of vitiligo.

**Discussion:** The obtained new data could be used for the assessment of clinical activity and prognosis of the disease and may be useful for the development of targeted biologic therapy of NSV.

**Acknowledgments:**

**MeSH/Keywords:** itiligo, autoimmunity, IL-18, IL-19, IL-21, IL-22

**Poster code:** R-B-2-137

## Poster Title: PREDICTION OF RADIOGRAPHIC PROGRESSION AND BONE MINERAL DENSITY IN PATIENT WITH ANKYLOSING SPONDYLITIS

**PhD candidate:** Iva Žagar

**Thesis proposal:** Prediction of radiographic progression and lower mineral density in patient with ankylosing spondylitis

**Mentor/s:** Assistent Professor Nadica Laktašić-Žerjavić, MD, PhD

**Affiliation:** University Hospital Center Zagreb, University of Zagreb School of Medicine

**Introduction:** The inflammatory process in the ankylosing spondylitis (AS) causes intense bone re-modeling and new bone formation. Syndesmophytes arising from the creation of new bone are the main feature of the AS. In addition to syndesmophytes formation and ankylosis, in AS we observe the process of accelerated bone resorption, such as osteoporosis and erosion.

**Materials and methods:** 168 patients with a diagnosis of AS will be included during 2015. and 2016. upon arrival at the regular check-up. During the visit we analyzed: erithrocyte sedimentation rate, C-reactive protein, calcium, phosphate, alkaline phosphatase, vitamin D. BMD was measured by standard DXA, and the radiographs of thoracic and lumbar spine. On standard radiographs the presence and extent of syndesmophytes was determined (new bone formation). The outcome measure instruments used in this research were divided into those related to the clinical assessment (BASMI index, BASFI index, BASDAI index) and those related to the assessment of the impact of the disease on the physical and the emotional components of life (Short Form 36, FACIT index). Information on the values of the independent variables in the period from 2008 to 2011 were collected from the patient medical history.

**Results:** So far, we included 130 participants, 93 male and 37 female patients, median age 48 years, and mean disease duration of 6 years. Median of radiographic progresion was 12 (0-36), and the mean value of vitamin D was 59. BASDAI median was 4.1, BASMI median was 4.9, BASFI median was 3.4. Since there was relatively large number of predictors compared to number of patients, forward selection regression procedure was used and level of statistical significance for predictor to enter into predictive model was set to $p=0.250$.

**Discussion:** Preliminary results are showing that the statistically significant predictors of radiographic progression and faster bone loss in patients with AS are: the patients age at time of diagnosis, peripheral arthritis, positive family anamnesis, alkaline phosphatase level, results on BASMI and BASFI questionnaires, Shober-test results, lower baseline breathing index. Influence on risk factors at the right time could slow down the irreversible structural changes and loss of bone mass leading to vertebral fractures, and impaired quality of life in patients.

**Acknowledgments:**

**MeSH/Keywords:** ankylosing spondylitis, radiographic progression, bone mineral densitiy

**Poster code:** R-B-3-45

## Poster Title: SPORT INJURIES, TREATMENT METHODS, RECOVERY PREDICTORS AND OVERALL SATISFACTION AMONG PROFESSIONAL ICE HOCKEY PLAYERS: A 6 YEAR RETROSPECTIVE – PROSPECTIVE STUDY

**PhD candidate:** Marko Mance, MD

**Thesis proposal: S**port injuries, treatment methods, recovery predictors and overall satisfaction among professional ice hockey players: a 6 year retrospective –prospective study

**Mentor/s:** Assist. Prof. Milan Milošević, MD, PhD; Assist. Prof. Igor Borić, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, School of Public Health "Andrija Štampar"; University of Split School of Medicine

**Introduction:** Hockey is the fastest team sport with players reaching 70 km/h and the puck being shot at up to 160 km/h. Aggressive contact between players, rigid obstacles (boards, posts), and solid ice surfaces can result in high energy trauma and severe injuries, despite the protective equipment they wear. Professional athletes are exposed to many different types of trauma and injuries during their professional career and some are never fully rehabilitated, which significantly affects the players physical and mental health. It is important to standardize the methods of treatment for all types of hockey injuries ensuring the best possible outcome and chance of return for the player.

**Materials and methods:** Our goal is to conduct research on the types of injury and disease rates in professional hockey Ebel (Austrian / Slovenian / Czech Republic) and the KHL (Russia / Finland / Croatia / Czech Republic / Belarus / Kazakhstan / Lithuania / Latvia) leagues over the last 6 seasons.

**Results:** We documented the mechanism of injury, degree of injury, time away from playing, success of treatment and re injuring rates. The results are still not complete.

**Discussion:** Aggressive contact between players, rigid obstacles (boards, posts), and solid ice surfaces can result in high energy trauma and severe injuries, despite the protective equipment they wear. Professional athletes are exposed to many different types of trauma and injuries during their professional career and some are never fully rehabilitated, which significantly affects the players' physical and mental health. It is important to standardize the methods of treatment for all types of hockey injuries ensuring the best possible outcome and increase the chance of return to play for the player. At the professional level, standardized methods of treating hockey injuries is non existent in Europe and should be defined and implemented, assuring the best treatment for the player continent wide.

**Acknowledgments:**

**MeSH/Keywords:** hockey injuries

**Poster code:** R-B-3-136

## Poster Title: COMPARISON BETWEEN GnRH AGONIST VERSUS hCG AS OVULATION TRIGGER IN THE MILD STIMULATED IVF CYCLES

**PhD candidate:** Fatos Muhaxhiri MD

**Thesis proposal:** Comparison between GnRH agonist versus hCG as ovulation trigger in the mild stimulated IVF cycles

**Mentor/s:** Prof.dr.sc. Dinka Pavičić-Baldani, Prof.assoc. Zeqir Dervishi

**Affiliation:** School of Medicine, University of Zagreb, Department of Gynecology and Obstetrics – University Clinical Center of Prishtina

**Introduction:** First in vitro fertilization (IVF) baby in the world born on 1978 was conceived on natural cycle IVF which in late 1970s was replaced by controlled ovarian stimulation aiming higher success. International Society for Mild Approaches in Assisted Reproduction (ISMAAR) has described the mild stimulated IVF where the low dose medications are used. This method has increased the cumulative success rates of IVF. It has lower costs compared to conventional stimulated cycle. There is no risk of ovarian hyper stimulation syndrome (OHSS), and the risk of a multiple pregnancy is low. In the mild stimulated IVF the ovulation triggering beside the hCG can also be performed by GnRH agonist, which before the modification of luteal support has been related to low pregnancy rate. Until now there are no data published related to the use of GnRH agonist as ovulation trigger in the mild stimulated IVF cycle.

**Materials and methods:** The 150 infertile woman randomized in two groups of 75 will undergo mild stimulated IVF. Controlled follicle growth will start on d5MC with 150IU Menotropine. GnRH-antagonist will be co-administered at follicle of 14mm. At follicle d17-18mm and E2≈200pg/dl per follicle, ovulation will be triggered in the standard group with GnRH agonist compared to the control group triggered by hCG. The luteal support includes Estradiol valerate, progesterone and micronized progesterone on daily basis. The standard group will also be given 1500IU of hCG on OPU and OPU 5 days to rescue the luteolysis. Pregnancy rate/ET, clinical pregnancy and OHSS rate will be compared.

**Results:** Currently the study is on the patients' recruitment phase and data collection. Until now, 16 patients in total have undergone the study 10 from the standard group and 6 from the control group. So far no cases of OHSS have been reported.

**Discussion:** Study will help us understand the impact of GnRH agonist ovulation triggering on the final oocyte maturation, pregnancy rate/ET and OHSS in the mild stimulated IVF compared to hCG. Furthermore it will help us compile gold standard protocols as safer, cost-effective and more familiar approaches to high risk OHSS patients and those who can't effort the costly standard ovarian stimulation protocols.

**Acknowledgments:** Special Hospital for Gynecology, Infertility and Endocrinology FATI IM

**MeSH/Keywords:** ovarian hyper stimulation syndrome, hCG beta, GnRH analog, ovulation induction

**Poster code:** R-B-5-95

## Poster Title: RELATIONSHIP BETWEEN SERUM DPP-4 ACTIVITY, INSULIN RESISTANCE AND MICROVASCULAR COMPLICATIONS IN TYPE 1 DIABETIC PATIENTS

**PhD candidate:** Kristina Blaslov

**Thesis proposal:** Relationship between serum DPP-4 activity, insulin resistance and microvascular complications in type 1 diabetic patients

**Mentor/s:** Lea Smirčić Duvnjak

**Affiliation:** Vuk Vrhovac University Clinic, University hospital Merkur

**Introduction:** Dipeptidyl peptidase-4 (DPP4) is a ubiquitous serine protease recently proposed as a novel adipokine linked to insulin resistance (IR). We investigated the relationship between fasting serum DPP4 activity, IR and hepatic markers of IR, estimated glomerular filtration rate (eGFR) and retinopathy in type 1 diabetic (T1DM) patients.

**Materials and methods:** A cross-sectional study comprised 44 T1DM patients aged >18 and <65 years. Insulin sensitivity was calculated using the equation derived from euglycemic-hyper-insulinemic clamp studies-estimated glucose disposal rate (eGDR). DPP4 serum activity was determined spectrophotometrically as a rate of cleavage of 7-Amino-4-Methyl Coumarin (AMC) from H-Gly-Pro-AMC.

**Results:** Patients were divided according to mean DPP4 serum activity (31.42 U/L). The group with higher compared to the group with lower mean fasting serum DPP4 activity showed lower eGDR (p=0.003), higher alanine aminotransferase (ALT) (p=0.001) and aspartate aminotransferase (AST) level (p=0.002), lower estimated glomerular filtration rate (eGFR) and higher prevalence of retinopathy (p<0.005). The linear regression analysis showed that eGDR decreases for 0.155 mgkg-1min-1; eGFR decreases for 1,371 ml/min/1,73m2 while ALT increases for 1.216 U/L by each increase of serum DPP4 activity of 1 U/L ((p=0.007, p=0,014, p=0.025 respectively) after adjustment for possible confounders: age, gender, disease duration, HbA1c, use of antihypertensives and statins. Multivariate multinominal regression analysis found that fasting serum DPP4 activity was positively associated with the prevalence of proliferative (OR 1.571 (1.159-2.131)) and non-proliferative (OR 1.338 (1.090-1.643)) retinopathy after adjustment for age, gender, disease duration and HbA1c level.

**Discussion:** Serum DPP4 activity is associated with IR, its hepatic markers, eGFR as well as with the prevalence of retinopathy in T1DM patients. The possible role of DPP-4 enzyme in the pathophysiology of insulin resistance and its relation with the development of microvascular complications merits to be further investigated.

**Acknowledgments:** I acknowledge Professor Lea Smirčić Duvnjak for intellectual and moral support and guidance through this research

**MeSH/Keywords:**

**Poster code:** R-B-9-6

## Poster Title: EVALUATION OF METABOLIC FEATURES AND HYPOTHALAMIC-PITUITARY-ADRENAL FUNCTION IN PATIENTS WITH SUBCLINICAL CUSHING'S SYNDROME

**PhD candidate:** Arita Haxhiu, MD, PhD Candidate

**Thesis proposal:** Evaluation of metabolic features and Hypothalamic-Pituitary-Adrenal function in patients with subclinical Cushing's syndrome

**Mentor/s:** Prof. Darko Kaštelan, MD, PhD

**Affiliation:** University of Zagreb, School of Medicine, University Hospital Centre Zagreb

**Introduction:** Subclinical Cushing's syndrome (SCS) is defined as corticotrophin (ACTH) independent cortisol secretion by adrenal adenoma,in the absence of classical stigmata of overt hypercortisolemia.An increased frequency of components of metabolic syndrome has been described in patients with SCS.The most appropriate management of SCS is controversial,either adrenalectomy or close follow-up being recommended for their treatment.

**Materials and methods:** It is a prospective randomized study that includes 24 patients with SCS, 15 with pheocromocytoma (Pheo) and 20 with non-functional adrenal tumor (NFA). Over a period of one year 7 of 24 patients with SCS (4 female/3 male, median age 65) were randomly selected to undergo surgery (n=3) or conservative management (n=4). A control group of 9 patients with Pheo (8 female/1 male, median age 57) and 9 with NFA (5 female/4 male, median age 53) following unilateral adrenalectomy, were also observed during this period.All surgical procedures were laparoscopic. All patients were followed up for a period of 6 months, clinically and biochemically, particularly monitoring for diabetes mellitus (DM), arterial hypertension, dyslipidemia and obesity. Hormone evaluation was also performed, particularly monitoring for recovery of Hypothalamic-pituitary-adrenal (HPA) axis following surgery.

**Results:** The prevalence of metabolic syndrome was observed in 57.1% (4 of 7) of patients with SCS compared to 33.3% (6 of 18) of other types of adrenal tumors. In SCS following surgery,DM normalized or improved in 66% of patients (2 of 3), hypertension in 66% (2 of 3), hyperlipidemia in 33.3% (1 of 3), and obesity in 33.3% (1 of 3). On the other hand, no improvement of DM, hypertension, and hyperlipidemia was noted in conservatively-managed patients. One of the patients with SCS developed adrenocortical insufficiency following unilateral adrenalectomy which lasted for more than 6 months. In patients with Pheo and NFA following surgery the need for hormonal replacement therapy during stress (acute illness) was observed in 11.1% (2 of 18) which lasted for about 1 month.

**Discussion:** Based on the preliminary results hypertension, DM, and obesity were more common in patients with SCS.The findings of our study wich were compatible with the results of other studies shows that the laparoscopic unilateral adrenalectomy appears to be more beneficial than conservative management for SCS in a term of improvement of metabolic profile. However in our study group, the relative insufficiency of HPA axis following surgery was observed not only in SCS patients.

**MeSH/Keywords:** Subclinical Cushing's syndrome, unilateral adrenalectomy, metabolic syndrome, pheochromocytoma, nonfunctional adrenal tumours, Hypothalamic-pituitary-adrenal axis.

**Poster code:** R-B-9-17

## Poster Title: EFFECTIVENESS OF LONG TERM DOPAMINE AGONISTS THERAPY IN PATIENTS WITH PROLACTINOMA

**PhD candidate:** Arta Haxhiu, MD, PhD Candidate

**Thesis proposal:** Effectiveness of long term dopamine agonists therapy in patients with prolactinoma

**Mentor/s:** Associate Professor Tina Dušek, MD, PhD

**Affiliation:** University of Zagreb ,School of Medicine, University Hospital Centre Zagreb

**Introduction:** Given the remarkable success of dopamine agonists (DA) therapy in lowering prolactine (PRL) levels, decreasing tumor size, and restoring gonadal function, medical therapy has become the mainstay of treatment for both micro-and macroprolactinomas. Current challenges related to the management of prolactinomas remain in the recurrence of the disease after dose reduction or withdrawal of DA, unknown optimal duration of treatment and the treatment of prolactinoma in pregnancy

**Materials and methods:** We included 35 patients (pts) with prolactinoma (25 female/10 male, age 50 /-27years) diagnosed and treated in Division of Endocrinology at University Hospital Centre Zagreb between 2008 and 2014. In all pts we evaluate long term effects of DA and in some of them who received DA treatment for at least 2 years and showed normalization of PRL levels and tumor disappearance or shrinkage, we evaluate DA dose reduction or withdrawal, the current recurrence rate of hyperprolactinemia, and possible factors that predict recurrence.

**Results:** At the time of the diagnosis 51% were macro and 49% microprolactinomas. The mean PRL levels at presentation were 1687 ug/L. Hypopituitarism, other than hypogonadism, was present in 14%. All pts were treated initially with bromocriptine and switched to carbegoline when sideeffects occured. 88% of micro and 50% of macroprolactinoma entered the remission. Additional transsphenoidal surgery was necessary in 2 pts due to DA resistance. We also evaluated DA dose reduction and withdrawal in 42.8% of pts selected according to certain criteria. The remission rate was 42%. The maximum tumor diameter and baseline PRL levels were significantly higher in the recurrence group (p=0.001). The mean duration of DA therapy was longer in the remission group (36 ± 8 months). The mean time to recurrence was 6.3 ± 3.2 months. The mean PRL levels at recurrence time were lower than baseline PRL levels.

**Discussion:** DA are effective in normalizing PRL values, and inducing tumor shrinkage. The remission rate in our study group was lower compared to other studies, which was thought to be associated with the shorter duration of DA treatment. The findings of our study wich were compatible with the results of other studies shows that the cessation or dose reduction of long-term DA therapy leads to recurrence of symptoms and hyperprolactinaemia, which most likely occur in the year after drug withdrawal, and the most important predictors of recurrence were maximum tumor diameter and baseline PRL levels

**Acknowledgments:** University Hospital Centre Zagreb, Department of Endocrinology

**MeSH/Keywords:** Prolactinoma, Dopamine agonist withdrawal, Cabergoline, Bromocriptine Recurrence

**Poster code:** R-B-9-18

## Poster Title: BIOMARKERS OF PROXIMAL TUBULE INJURY IN ENDEMIC NEPHROPATHY

**PhD candidate:** Jelena Kos, MD

**Thesis proposal:** Biomarkers of proximal tubule injury in endemic nephropathy

**Mentor/s:** Prof. Bojan Jelaković, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre Zagreb, Department of nephrology, arterial hypertension, dialysis and transplantation

**Introduction:** Endemic nephropathy (EN) is a chronic tubulointertsitial kidney disease that affects rural population west of Slavonski Brod along the Sava river. Recent data have shown that EN is caused by aristolochic acid. Considering that proximal tubules are the main site of kidney damage in EN, more sensitive biomarkers of tubular impairment are extensively studied. Among them are kidney injury molecule 1 (KIM-1), hepatocyte growth factor (HGF) and interferon inducible protein 10 (IP-10) which have already proven their role in acute kidney injury. The aim of this study is to determine the role of these biomarkers (KIM-1, HGF, IP-10) in EN and to determine prognostic value of these biomarkers in chronic kidney disease (CKD).

**Materials and methods:** In this cross-sectional study 1351 participants from 3 endemic villages and 2 non-endemic villages were enrolled. Participants were classified in 5 subgroups: "EN diseased", "EN suspects", "EN at risk", "EN others", non-EN controls. Participants, who gave informed consent, were included in follow up visit after 7 years. All participants fulfilled extensive questionnaire, underwent physical examination, their blood was drawn and urine sample collected. Serum creatinine was determined, eGFR calculated and urinary KIM-1, HGF and IP-10 were determined.

**Results:** According to our preliminary results there are statistically significant difference between „EN suspects" and „others" in KIM-1 Š366.97 (202.78-760.42) vs 271.70 (140.63-532.63), p 0.005Ć and HGF Š419.63 (218.14-791.59) vs 323.16(197.74-565.77), p 0.01Ć. There is no significant difference in IP-10 between these two subgroups. In these subgroups, we found no correlation between KIM-1, HGF and IP-10 and glomerular filtration rate and serum creatinine. We found positive correlation between biomarkers (KIM-1 and HGF) and urinary albumin/creatinine ratio (r=0.134, p 0.03/ r=0.114, p 0.11 respectively).

**Discussion:** Our preliminary results have shown significantly higher levels of KIM-1 and HGF in „EN suspects" in comparison to „others". This might imply that there is still some ongoing kidney damage in „EN suspects". So far we analyse these two subgroups among EN groups. Further evaluation is needed to compare all EN subgroups, as well as EN to non-EN group. Renal function and biomarkers would be evaluated across the whole group. After all statistical analysis is done we'll be able to more precisely draw the conclusions about the role of urinary biomarkers in EN as well as in CKD.

**Acknowledgments:**

**MeSH/Keywords:** endemic nephropathy, proximal tubule injury, urinary biomarkers, KIM-1, HGF, IP-10

**Poster code:** R-B-9-19

## Poster Title: LOW CONCENTRATION OF THE IRON AND FREQUENCY RLS IN THE PATIENTS ON THE HAEMODIALYSIS

**PhD candidate:** Sonja Hodžić, MD, MSc

**Thesis proposal:** Low concentration of the iron and frequency RLS in the patients on the haemodialysis

**Mentor/s:** Prof. Petar Kes, MD, PhD

**Affiliation:** HDNDT

**Introduction:** Restless leg syndrome (RLS) is a neurological disorder with disturbing sensations in the legs with tendency to move them threw the night. In this study I shall explore the influence of the low concentration of the iron in the 100 adults patients on the haemodialysis. Control group will be 100 adult patients on the haemodialysis without the RLS symptoms.

**Materials and methods:** All patients would be divided in the groups according to the gender, age, BM, duration of the haemodialysis, concentration of Fe, Ca, P, feritin, TSAT, urea, creatinin, PTH. Objective metods like EMNG would be doing according to opinion of the neurolog specialist

**Results:** For now in the last two months I do not have significant results for my thesis that low concentration of the iron is significant for greater occurence RLS in patients on the haemodialysis.

**Discussion:** In this study I shall prove / or not that low concentration of the iron is significant for occurence RLS in the patients on the haemodialysis. Also, Ill show how much influence have long of HD and their adequacy. In the same time it will show influence of the doses of the dialysis, drugs and other factors ( obesity, alchocol, cigarettes, low wight, inflammation).

**Acknowledgments:** Prof.dr.sci. Petar Kes

**MeSH/Keywords:** iron, restless leg syndrome, haemodialysis

**Poster code:** R-B-9-113

## Poster Title: ONE-YEAR FOLLOW-UP AFTER IRRIGATED MULTI-ELECTRODE RADIOFREQUENCY ABLATION OF PERSISTENT ATRIAL FIBRILLATION

**PhD candidate:** Nikola Pavlović

**Thesis proposal:** Comparison of Irrigated Multi-Electrode Radiofrequency Ablation and point-by-point ablation for Pulmonary Vein Isolation in Patients with Persistent Atrial Fibrillation

**Mentor/s:** Prof Diana Delić Brkljačić, MD,PhD; Prof Christian Sticherling, MD, PhD

**Affiliation:** University Hospital Centre Sestre milosrdnice, Zagreb; University Hospital Basel, Switzerland

**Introduction:** Irrigated multi-electrode ablation (IMEA) is a novel tool to perform pulmonary vein isolation (PVI). The aim was to compare IMEA with point-by-point radiofrequency (RF) ablation in patients with persistent atrial fibrillation (AF) undergoing PVI.

**Materials and methods:** Forty-nine patients (age 60 9 years, 82% male) were studied. In 24 patients, the IMEA catheter was used in conjunction with an electroanatomic mapping system. Twenty-five patients undergoing RF point-by-point ablation (RF-PVI) served as a control group. Validation of PVI based on the IMEA catheter was performed using a standard circular mapping catheter.

**Results:** Ninety-two of 94 pulmonary veins (PVs) (98%)were isolated using IMEA alone. Procedure time was $125\pm23$ min in the IMEA group and $127\pm31$ min in the RF-PVI group (P=0.79). Fluoroscopy time was 12.2(11–16.1) min with IMEA compared with 5.2 (4.1–9.3) min in the RF-PVI group (P=0.001). Net ablation time was 11.8 (10.2–15.4) min in the IMEA group compared with 33.6 (30.3–40.1) min in the RF-PVI group (P=0.001). Of 94 PVs presumed to be isolated after IMEA ablation, validation using a standard circular mapping catheter showed persistent PV potentials in 33 PVs (35%), requiring additional IMEA ablation. At 12 months, 16 of 24 patients (67%) in the IMEA group compared with 17 of 25 patients (68%) in RF-PVI group were free from AF (P=0.99).

**Discussion:** The main findings of our study are: (1) Acute PVI can be achieved in almost all patients and PVs using solely the IMEA catheter. However, the recordings from the IMEA catheter were not sufficient to confirm isolation in 35% of PVs (requiring additional IMEA ablation in these PVs to achieve isolation). (2) Procedure duration is similar between ablation using the IMEA catheter and standard point-by-point ablation, while fluoroscopy times and radiation doses are higher in the IMEA-PVI group. (3) There was no significant difference in freedom from AF after a follow-up of 1 year.

**Acknowledgments:**

**MeSH/Keywords:** Atrial fibrillation, Pulmonary vein isolation, Radiofrequency ablation

**Poster code:** R-B-9-40

# Poster Title: PREDICTION OF MAJOR ADVERSE CARDIAC EVENTS BY APELIN LEVEL FOLLOWING ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

**PhD candidate:** Xhevdet Krasniqi

**Thesis proposal:** The influence of apelin level on the incidence of major adverse cardiac events after ST-segment elevation myocardial infarction

**Mentor/s:** Josip Vincelj, Masar Gashi

**Affiliation:** University Dubrava Hospital, University Clinical Center of Kosova

**Introduction:** Apelin regulates cardiac contractility, protects against ischemia reperfusion injury and promotes cardiomyocyte survival by inhibiting apoptosis. However, it's still unclear whether apelin has impact to troponin and brain natriuretic peptide (BNP) in major adverse cardiac events (MACE) in ST-segment elevation myocardial infarction (STEMI). We hypothesized that normalized or elevated values of apelin are expected to be related with decrease rate of MACE. Our objective is to evaluate the impact of apelin level related to accurance of MACE following STEMI.

**Materials and methods:** We enrolled a total of 22 randomized patients as a subgroup of 100 patients with acute STEMI who underwent reperfusion therapy- fibrinolysis. Serum apelin was detected and after therapy, all patients were followed for 12 months. The follow-up end-point was the occurrence of myocardial infarction, unstable angina, stent thrombosis, stroke and heart failure in the group of MACE. The subgroup of patiens was devided further in two groups based on the level of apelin-12 at a threshold of 1.7ng/ml on the seventh day on admission.

**Results:** Kaplan–Meier analysis revealed that the MACE-free rate was significantly lower correlating with lower serum levels of apelin (P= 0.0002, log rank test) so this was significantly associated with the incidence of MACE. The multivariate Cox proportional hazard analysis adjusted with the clinical and angiographic characteristic reveals that the serum low apelin is a predictor for MACE incidence (hazard ratio 0.1382, 95% confidence interval).

**Discussion:** We can conclude that the high serum level of apelin can predict the MACE in patients with STEMI following reperfusion therapy.

**Acknowledgments:**

**MeSH/Keywords:** Apelin, STEMI, MACE.

**Poster code:** R-B-9-36

## Poster Title: USE OF DRUG-ELUTING BALLOON IN THE SIDE BRANCH OF BIFURCATION CORONARY ARTERY LESIONS

**PhD candidate:** Dario Gulin, MD

**Thesis proposal:** Use of drug-eluting balloon in the side branch of bifurcation coronary artery lesions

**Mentor/s:** Assistant Professor Jozica Šikić, MD, PhD; Associate Professor Roman Urek, MD, PhD

**Affiliation:** University Hospital Sveti Duh, Department of Cardiovascular diseases, Internal Clinic; University of Zagreb School of Medicine

**Introduction:** Interventions on bifurcation lesions (BL), with prevalence of nearly 20% of coronary artery lesions, belong to the most complex procedures in interventional cardiology. True bifurcation lesion, affecting both side branch (SB) and main branch (MB) are less frequent. In recent years, among bare metal stent (BMS) and drug-eluting stent (DES), drug-eluting balloon (DEB) was introduced. It is commonly used to treat restenosis in BMS. Based on several well-defined studies (108 patients enrolled in PACCOCATH ISR I trial and 106 in PEPCAD II trial), DEB was suggested in the guidelines for percutaneous coronary interventions (PCI) of the European Society of Cardiology, but only for treatment of in-stent restenosis (ISR) in the BMS. Recently, indications for DEB are the subject of numerous studies and include ISR in the DES, BL (PEPCAD V study in only 28 patients), and "de novo" lesions of large and small coronary arteries. Using DEB in the SB of BL simplifies the complexity of the PCI and reduces the amount of metals in the blood vessels which can reduce the most common adverse effect, restenosis and stent thrombosis.

**Materials and methods:** This prospective research, with six-month follow-up, included eleven patients with true bifurcation lesions. Ten patients were in the investigated group (DES in MB, DEB in SB), and one patient in control group (DES in MB, DES in SB). Six-month follow-up coronary angiography was performed in three patients from investigated group.

**Results:** Patient age was from 50 to 80 years with mean age of $63.37 \pm 10.67$. 73% were men and 27% were women. From cardiovascular risk factors smoking was present in 45%, hyperlipidaemia and arterial hypertension in 91%, previous PCI in 73% and previous myocardial infarction in 36%, while only 18% were physically active. There were no patients with diabetes. Culprit lesion was LAD/D1 in 54%, ACx/OM1 in 36%, RCA/ventricular artery in 9%. All patients from investigated group showed better control angiographic results (2.29 vs. 1.94 mm). All patients were free from target lesion revascularisation, hospitalization due to chest pain or major adverse cardiac events.

**Discussion:** Although in small proportion of patients control coronary angiography was performed, significant angiographic improvement was noticed in both SB and MB. Immediate result after DEB in SB could not be fully assessed as nominal healthy lumen, but six-month follow-up results confirm the active DEB function.

**Acknowledgments:**

**MeSH/Keywords:** coronary artery disease, percutaneous coronary intervention, drug-eluting stents, coronary balloon

**Poster code:** R-B-9-48

## Poster Title: COMPARISON OF CLINICAL CHARACTERISTICS AND OUTCOMES IN PATIENTS WITH ST-ELEVATION MYOCARDIAL INFRACTION IN KOSOVO AND CROATIA

**PhD candidate:** Rreze Koshi, MD

**Thesis proposal:** Comparison of Clinical Characteristics and outcomes in patients with ST-elevation myocardial infraction in Kosovo and Croatia

**Mentor/s:** Prof. Maja Strozzi, MD, PhD

**Affiliation:** UCC Zagreb, University of Zagreb School of Medicine

**Introduction:** The differences of clinical characteristics, risk factors and treatment in coronary heart diseases in patients from different areas or countries still remain a challenge for investigators. The aim of the proposed investigation is to compare clinical characteristics, risk factors treatment modalities and prognosis in STEMI patients in two different countries such as Croatia and Kosova. Beside the acute phase, the follow-up after 6 months will be performed to analyze clinical outcomes and quality of secondary prevention.

**Materials and methods:** The study will include 60 patients with STEMI network treatment of the UCC Rebro in Zagreb Croatia and 60 STEMI patients treated in Regional Hospital Gjakova - Kosova. Standard laboratory test will be performed in both study groups treatment modalities will be compared according to the ESC Guidelines. PCI or/and standard medical therapy as well as clinical outcomes during in -hospital stay. Follow up will be done after 30 days and 6 months post MI regarding major adverse events (MACE): death, reinfarction, stroke or reintervention, particularly stent thrombosis.

**Results:** In both groups we have mached an important differences between age and gender (T=0.738,P=0.464). Dyslipidaemia between the patients from both groups is without significant difference($x^2$=0.343,P 0.577,P>0.05). Diabetes mellitus in both groups of patients we mached a significant differences ($x^2$=6.96,P=0.008,P<0.01) DBT between patients included in both groups were with no significant differences(U'=1009.5,P=0.809). DES was implanted in 3.5% of patients and 84.2% BMS in patients from the UCC Rebro Zagreb comparing with the patients from Gjakova Hospital, was implanted 29.1% DES and 25.5 BMS, in both groups were significant statistic differences ($x^2$test=13.5,P=0.0002,P<0.01), With the Mann-Whitney test we have an important significant difference between the average value of the glycaemia in both hospitals (U'=1530.5, P=0.013).The cardiac enzymes troponin, LDH, CRP, Ac uric, cholesterol, triglyceride and also smoking, hypertension and anamnesis family were no significant differences between two groups.

**Discussion:** We compared the clinical and demographical characteristics, gender differences, treatment strategies, health insurance system, cultural background and quality of the secondary prevention in STEMI from Kosova and Croatia.

**Acknowledgments:** No financial support

**MeSH/Keywords:** STEMI, DBT, DES, BMS patient.

**Poster code:** R-B-9-71

## Poster Title: DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF TWO COHORTS OF CHRONIC GRAFT-VERSUS-HOST DISEASE PATIENTS UNDERGOING IMMUNOGLOBULIN G N-GLYCOSYLATION ANALYSIS

**PhD candidate:** Ema Prenc

**Thesis proposal:** N-glycosylation of immunoglobulin G in chronic Graft-versus-Host disease after allogeneic hematopoietic stem cell transplantation

**Mentor/s:** Steven Z. Pavletić, Drazen Pulanić

**Affiliation:** Croatian cooperative group for hematologic diseases, Zagreb, Croatia

**Introduction:** Chronic graft-versus-host disease (cGVHD) is a systemic alloimmune and autoimmune disorder and major late complication after allogeneic hematopoietic stem cell transplantation (alloHSCT). The disease is characterized by an altered homeostasis of the humoral immune response and the production of allo- and autoantibodies. Immunoglobulin G (IgG) glycoprotein is the main effector molecule of the humoral immune response. Changes in IgG glycosylation are associated with a number of autoimmune diseases. This research will analyze IgG glycosylation in cGVHD patients and determine associations of different IgG glycoforms with demographic and clinical characteristics of cGVHD.

**Materials and methods:** Patients were included as part of two cross-sectional cGVHD natural history studies (National Institutes of Health (NIH), USA, 2004-2014. and Clinical Hospital Center Zagreb, Croatia, 2013-2015.). They have been diagnosed with cGVHD according to the established NIH criteria. Extensive demographic and clinical data, as well as plasma samples, were collected. Descriptive statistical analysis was performed using Excel software (Microsoft Office 2013.). Subsequent glycan composition analysis of plasma samples will be done by high-resolution biochemical methods (liquid chromatography and mass spectrometry).

**Results:** The NIH study included 253 cGVHD patients and 10 control subjects (patients after alloHSCT, without cGVHD). Median age of the patient cohort was 46 (range 5-71) and 59% of patients were male. In 32% of patients cGVHD onset was defined as de novo, in 38% progressive and in 30% quiescent. Disease was scored as severe in 75% and considered to be active in 86% of patients. The Croatian cohort included 32 patients and 32 controls, matched by age and gender. Median age was 43 (range 9-60) and 50% of patients were male. Ten patients (31%) had de novo cGVHD, twelve (38%) progressive and ten (31%) quiescent. The disease was scored as mild in 9%, moderate in 41% and severe in 50% of the cases. It was considered to be active in 50% of patients. A detailed review of all patient characteristics is given in Table 1.

**Discussion:** The cohorts are well characterized, comparable and suitable for analysis of immunoglobulin G glycan composition. We hypothesize that N-glycosylation of plasma IgG of cGVHD patients will be associated with clinical manifestations of cGVHD, and could lead to development of potential diagnostic or prognostic biomarkers of cGVHD.

**MeSH/Keywords:** allogeneic hematopoietic stem cell transplantation, chronic Graft versus Host Disease, immunoglobulin G, N-glycosylation

**Poster code:** R-B-9-152

**Poster Title: CORRELATION OF ESTROGEN RECEPTOR ALFA AND INTERLEUKIN 6 POLYMORPHISM WITH ENDOTHELIAL FUNCTION IN ASYMTOMATIC DESCENDANTS OF PATIENTS WITH EARLY CORONARY DISEASE AND ACUTE CORONARY SYNDROME – EARLY RESULTS**

**PhD candidate:** Zoran Miovski MD

**Thesis proposal:** Correlation of estrogen receptor alfa and Interleukin 6 polymorphism with endothelial function in asymtomatic descendants of patients with early coronary disease and acute coronary syndrome

**Mentor/s:** Ljiljana Banfić MD., PhD

**Affiliation:** University Hospital Centre Zagreb, Department of cardiovascular diseases

**Introduction:** The key moment in the development of coronary artery disease is the dysfunction of endothelial cells. It is believed that hereditary factors have a strong influence. Described hereditary factors for coronary heart disease are ER$\alpha$ receptor polymorphism (ER$\alpha$p) and IL6 polymorphism (IL6p). Studies showed strong correlation between endothelial dysfunction and coronary disease.Gold standard for testing endothelial (dis)function is FMD.

**Materials and methods:** First phase will include at least 50 patients (M ≤45 y., F ≤55 y.) with CAD who will develop acute coronary syndrome. Coronary angiography (or percutaneous coronary intervention) will be performed to patient with ACS using transfemoral or transradial approach. Using PCR method, TA length of estrogen receptor alfa will be analysed. According to the length of TA sequence, patient will be divided to those who have short length TA polymorphisms (<18 „S") and those who have long length TA polymorphisms (≥18 "L" ).According to the literature , allelic forms that are connected to CAD are LL and SL. IL6 -174 G>C genotipisation will be done using PCR method. Allelic forms that are connected to CAD are CC and CG. Second phase will include asymptomatic descendants of patients with early coronary disease and acute coronary syndrome who have estrogen receptor alfa/interleukin 6 polymorphism. FMD will be performed on right brachial artery using Aloka alfa 10 according to the FMD guidelines from 2002.

**Results:** In the first phase of research we enroled 40 patient with early presentation of acute coronary syndrome. After confirming coronary artery disease by coronary angiography, we analysed IL6p and ER$\alpha$Rp. IL 6p : 17 patients had GC polymorphism (44%), 4 patients had CC polymorphism (10%), 17 patient didn't have IL6p (44%). Two patients didn't have adequate samples. ER$\alpha$p: 22 patients had SL polymorphism (61%), 8 patients had LL polymorphism (22%), 6 didn't have Er$\alpha$Rp. Four patients didn't have adequate samples. In summary, 18 patients had both polymorphisms (50%), and only 3 patients did not have either mutations.

**Discussion:** According to literature IL6p in offspring's of CAD patients is about 56%, in CAD patient 64%, and in general population about 43% (1). In our research in this early stage we got 54%. ER$\alpha$p in literature is described in 65% (2), and in our research in this early stage in about 83%. These results encourage us for second phase of research.

**Acknowledgments:**

**MeSH/Keywords:** CAD, IL6 , ERalfa, young

**Poster code:** R-B-9-79

## Poster Title: COMPARISON OF STEERABLE VERSUS NON-STEERABLE TRANSSEPTAL SHEATHS DURING CATHETER ABLATION FOR ATRIAL FIBRILLATION - CONTACT FORCE ASSESSMENT

**PhD candidate:** Ante Anić, MD

**Thesis proposal:** Comparison of steerable versus non-steerable transseptal sheaths during catheter ablation for atrial fibrillation - contact force assessment

**Mentor/s:** Anton Šmalcelj, MD, PhD and Laszlo Geller, MD, PhD

**Affiliation:** Medical School, University of Zagreb and Semmelweis University, Budapest, Hungary

**Introduction:** Atrial fibrillation (AF) is the most common cardiac arrhythmia and left atrial tissue serves as a substrate for its initiation and maintenance in most patients. Left atrial tissue ablation with intention of making circumferential pulmonary veins (PV) isolation via percutaneous catheter ablation can cure this arrhythmia. Traditionally, access to left atrium via femoral vein was accomplished using preshaped, non-steerable transseptal sheath. Recently, a newer technology of transseptal sheaths was developed with having steering mechanism that allows for changing the shape of the sheath that presumably could result in more reliable catheter tissue contact.

**Materials and methods:** In 14 patients undergoing left atrial ablation (circumferential pulmonary vein isolation) for AF we recorded catheter-tissue contact force at all left atrial sites where radiofrequency ablation was applied. Lesion sites were designated to prespecified quadrants around each pair of pulmonary veins thus creating 8 regions for which obtained mean contact force in grams was compared. In 7 patients, steerable sheath technology (Agilis NxT, SJM) was used for left atrial access and ablation, while in rest non-steerable were used.

**Results:** Overall, 672 ablation points with corresponding mean catheter-tissue contact force were taken for analysis. Usage of steerable sheaths resulted in higher catheter-tissue contact in 2 quadrants, both around right PV, superior-posterior and inferior anterior (p=0,03 and 0,001 respectively). At all other quadrants there was no significant difference in obtained contact.

**Discussion:** These results are in alignment with clinical observations that point to a better ablation success when steerable sheaths are used for left atrial access for PV isolation. Higher contact force during ablation around right PV might result in durable electrical isolation, while ablation done with less contact force predisposes for tissue recovery and electrical reconnection of the veins that leads to AF recurrence.

**Acknowledgments:** I thank the staff of General Hospitalžs Zadar electrophysiology lab for helping in acquiring the intraprocedural data.

**MeSH/Keywords:** Catheter ablation

**Poster code:** R-B-9-80

## Poster Title: INFLUENCE OF ADIPONECTIN AND GLYCATED HEMOGLOBIN IN PREDICTION OF MAJOR ADVERSE CARDIAC EVENTS IN NON-DIABETIC PATIENTS AFTER ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

**PhD candidate:** Blerim Berisha MD

**Thesis proposal:** This study is part of the PhD Thesis

**Mentor/s:** Prof.dr. Josip Vincelj, Prof dr. Masar Gashi

**Affiliation:** Internal Medicine, Cardiology

**Introduction:** Adiponectin is a protein secreted by adipose cells that may be responsible for metabolic, antiatherogenic and proangiogenic effects. However, it is still unclear whether adiponectin has any clinical significance for risk stratification of coronary disease. We hypothesised that low levels of adiponectin might be responsible for microvascular damage and poor clinical outcome. Hipoadiponectinemia and hyperglicemia could lead to major adverse cardiac events (cardiac death, re infarction, angina pectoris, stroke and congestive heart failure), because by extending infarct size and accelerating heart failure. Therefore, the objective of this study is to evaluate the correlation between adiponectin levels, glycated hemoglobin (HbA1C) and major adverse cardiac events (MACE) in non-diabetic patients after ST-segment elevation myocardial infarction.

**Materials and methods:** Patients who experienced ST-segment elevation myocardial infarction were involved. We measured adiponectin, and glycated hemoglobin (HbA1C) in all patients. Patients with Diabetes mellitus and patients who had a history of previous percutaneous coronary intervention were excluded from the Study. All patients were divided in two groups: Group I patients with elevated HbA1C and group II patients with normal levels of HbA1C. In one-year follow-up, the study subjects were observed for MACE (cardiac death, re-infarction, angina pectoris, stroke and congestive heart failure).

**Results:** Adiponectin correlate significantly with MACE and with body mass index BMI (P<0.01) but not with glycated hemoglobin (HbA1C) levels or left ventricular ejection fraction(LVEF).

**Discussion:** This study showed that adiponectin is not responsible for pre-infarct glucometabolic dysregulation in non-diabetic patients who survived acute myocardial Infarction but other mechanisms of hipoadiponectinemia may be responsible for cardiovascular damages.

**MeSH/Keywords:** adiponectin, glycated hemoglobin, STEMI, major adverse cardiac events

**Poster code:** R-B-9-84

## Poster Title: CORRELATION OF GHRELIN AND GHRELIN RECEPTOR WITH THE GRADE OF DYSPLASIA IN COLONIC ADENOMAS – PRELIMINARY RESULTS

**PhD candidate:** Sanja Stojsavljević, MD

**Thesis proposal:** Correlation of ghrelin and ghrelin receptor with the grade of dysplasia in colonic adenomas

**Mentor/s:** Professor Marko Duvnjak, MD PhD, Assistant professor Davor Tomas, MD PhD

**Affiliation:** University Hospital Centre Sestre milosrdnice, Zagreb, Croatia

**Introduction:** Obesity, as well as malignant diseases have become epidemics of the modern age. Obesity can change the relationship of concentrations of circulating ghrelin levels, lead to a relative surplus of acyl-ghrelin and deficit of des-acyl ghrelin, which could account to insulin resistance in metabolic syndrome. Prevalence of colonic adenomas, considered as precancerous lesions, accompanies the prevalence of colonic adenocarcinomas. Consummation of food with high percentage of unsaturated fat, alcohol, obesity, smoking and poor physical activity are considered as risk factors for developing colonic carcinoma.

**Materials and methods:** We included up till now 65 out of estimated 90 patients, with endoscopically proven colonic adenomas. After the patients agreed to participate in the study, a complete medical history was obtained, blood tests and physical examinations connected with the presence of metabolic syndrome were performed. Serum samples for determination of acyl-ghrelin and des-acyl ghrelin concentrations with ELISA were stored for further testing. Pathohystological analysis of the colonic adenoma and a part of the healthy tissue will be performed, as well as immunohistochemical staining using polyclonal antibodies for ghrelin receptor and ghrelin after all the specimens are collected.

**Results:** We report of results obtained up to this point. From the 65 enrolled patients 48 were men (73.85%) and mean age of the studied population was 65,6 ± 7,5. The mean BMI was 30,05 ± 5,3, with 44 % of obese and 27 % of overweight patients. Of all patients enrolled 43/65 (67%) had a known arterial hypertension and almost 46 % of them poorly regulated blood pressure. Hyperlipidemia was also noticed in a high percentage of patients, almost 50% had a total cholesterol level higher that 6 mmol/L and triglyceride level higher that 1,7 mmol/L. About 70% of patients had a tubular adenoma, and 35% of the patient had an adenoma with a high grade dysplasia.

**Discussion:** Our data up till now concur with the data presented from other developed countries and point out to the conclusion that an increased body mass index (BMI) is associated with an increased risk of colorectal adenomas. These patients also had a noticably high incidence of high arterial blood pressure and a poorly regulated one for that matter, as well as hyperlipidemia.

**MeSH/Keywords:** acyl-ghrelin, des-acyl ghrelin, ghrelin receptor, obesity, metabolic syndrome, colonic adenomas, dysplasia in colonic adenoma

**Poster code:** R-B-9-85

**Poster Title: THE ROLE OF MARKERS OF ENDOTHELIAL DYSFUNCTION: ASYMMETRIC DIMETHYLARGININE AND NITRIC OXIDE IN THE ASSESSMENT OF CARDIOVASCULAR RISK AFTER LIVER TRANSPLANTATION – PRELIMINARY RESULTS**

**PhD candidate:** Maro Dragičević, MD

**Thesis proposal:** The Role of Markers of Endothelial Dysfunction: Asymmetric Dimethylarginine and Nitric Oxide in the Assessment of Cardiovascular Risk after Liver Transplantation

**Mentor/s:** Anna Mrzljak, MD, PhD, Marijana Vučić Lovrenčić, PhD

**Affiliation:** University Hospital Merkur

**Introduction:** Cardiovascular diseases are the leading cause of mortality in patients with stable liver graft function. Endothelial dysfunction is the first step in the development of atherosclerosis, which is the main feature of CV diseases. Asymmetric dimethylarginine (ADMA) and nitric oxide (NO) have an important role in the development of endothelial dysfunction and they can be seen as indicators of early CV risk.

**Materials and methods:** 34 patients with end stage liver disease matching the inclusion criteria, so far, were prospectively followed up to 6 months after liver transplantion (LT). ADMA levels were determined before and 6 months post LT. ADMA concentration was measured using validated competitive enzyme-immunoassay procedure.

**Results:** The differences between ADMA levels before and 6 months after liver transplantation did not reach a statistical significance, however post transplant ADMA values show an increasing trend.

**Discussion:** Asymmetric dimethylarginine (ADMA) is an endogenous inhibitor of nitric oxide NO, which plays an important role in circulatory abnormalities. Elevated ADMA plasma levels are associated with impaired endothelium-dependent vasodilatation. Our preliminary results of pre LT- and 6 months after LT-ADMA levels on 34 cases have not reached a statistical significance (p=0,15), however they demonstrate an increasing ADMA trend after LT which may reflect early development of metabolic and subsequent cardiovascular complications. We intend to extend our study by recruiting more patients with longer follow up in order to investigate the ADMA/NO pattern after LT and their significance in the context of cardiovascular risk in transplant population.

**Acknowledgments:** Many thanks to my mentors for all of their support.

**MeSH/Keywords:** ADMA, NO, cardiovascular diseases, endothelial dysfunction, end stage liver disease, liver transplantion

**Poster code:** R-B-9-139

## Poster Title: CIRCULATING NEUREGULIN-1B LEVELS AS A PREDICTOR OF PATHOLOGICAL VENTRICULAR REMODELING IN PATIENTS WITH ACUTE ST ELEVATION MYOCARDIAL INFARCTION – PRELIMINARY RESULTS

**PhD candidate:** Ozren Vinter, M.D.

**Thesis proposal:** Circulating Neuregulin-1β levels as a predictor of pathological ventricular remodeling in patients with acute ST elevation myocardial infarction

**Mentor/s:** Assist. Prof. Matias Trbušić, MD, PhD

**Affiliation:** University Hospital Centre Sestre Milosrdnice

**Introduction:** The signalling complex consisting of the growth factor neuregulin-1 (NRG1) and its tyrosine kinase receptors ErbB2 and ErbB4 has a critical role in cardiac development and homeostasis of the structure and function of the adult heart. Research has so far shown a correlation between circulating neuregulin 1β and prognosis in patients with ischemic cardiomyopathy and in patients with congestive heart failure with NYHA III/IV functional stadium. In other study inverse correlation between circulating neuregulin 1 β levels and severity of CAD was shown. In this study we aim to investigate neuregulin 1 β as a potential biomarker for pathological ventricular remodeling after acute myocardial infarction with ST elevation (STEMI).

**Materials and methods:** In this prospective, observational study on patients with acute STEMI levels of circulating plasma neuregulin 1 β in acute phase will be determined using an ELISA method. Cardiac remodeling is defined with echocardiography parameters and will be assessed 6 months after the MI. In every patient the concentration of NT-proBNP as a marker of congestive heart failure will be determined. Other than to determine wether neuregulin 1 β can be used as a biomarker for pathological ventricular remodeling we intend to compare it to other known factors that contribute to pathological ventricular remodelling such as age, sex, BMI, presence of diabetes, levels of creatinine kinaze and troponin, NTproBNP-a levels, localisation of myocardial infarction, „pain to door" and „ door to baloon" times using multivariat logistical analysis

**Results:** We aim to include 154 patients in our study based on power calculation. So far we have included only 10 patients, none of whom have finished follow up period (6 months) so we don't have any primary endpoints. Patients included so far are predominantly male (70%) with mean age 63 years whereas female mean age was 71. Out of 10 patients 4 had diabetes (40%). Predominant coronary lession was ACD (50% in all patients, 66% in female sex subgroup) while LAD and Acx were responsible for 40% and 10% of myocardial infarctions respectively.

**Discussion:** Due to the lack of primary endpoints in the study so far, it is not possible to write the discussion.

**Acknowledgments:**

**MeSH/Keywords:** neuregulin 1 β, pathological ventricular remodeling, STEMI

**Poster code:** R-B-9-103

# Poster Title: PREVLENCE AND RISK FACTORS FOR UROLITHIASIS IN PATIENTS WITH HEMOPHILIA

**PhD candidate:** Marijo Vodanović

**Thesis proposal:** Prevlence and risk factors for urolithiasis in patients with hemophilia

**Mentor/s:** Professor Silva Zupančić Šalek, MD, PhD

**Affiliation:** University Hospital Center Zagreb, Department of Internal Medicine, Division of Haematology

**Introduction:** Hemophilia is an inherited coagulation disorder, manifested by increased bleeding tendency due to lack of FVIII (hemophilia A) or FIX (hemophilia B) activity. Due to improved treatment patients with hemophilia have more age-related diseases such as hypertension, diabetes, thromboembolic incidents, renal disease, urolithiasis. Urolithiasis is the appearance of stones in the urinary tract with the incidence of 4,5/10,000 in the group younger than 40 years. The aim of study is to show prevalence of urolithiasis and determination of risk factors for urolithiasis.

**Materials and methods:** It was included almost one third of patients (33 patients with hemophilia A and 2 with hemophilia B), after one year study. 23 patients were with severe hemophilia, 12 patients with mild hemophilia. The median age of patients was 43 years (range 19-67), median age of hemophilia diagnosis was 2 years (range 0,5 - 60). 17 patients receive prophylaxis therapy, 16 patients on demand. Two patients with mild hemophilia have not yet received any hemostatic treatment. 17 patients with hemophilia are treated with recombinant factor, while 16 patients with plasma derived factor. Five patients (14%) have hemophilia with FVIII inhibitors, and they are treated with FVIII bypassing agent (recombinant FVIIa, or FEIBA).

**Results:** Twenty patients with hemophilia (58%) have suffered from any urinary tract disease based on medical history. The prevalence among patients with severe hemophilia was 61% (14/23), while 50% patients (6/12) with mild hemophilia had any disease of urinary tract. The prevalence of urinary infection was 23%, fourteen patients had gross hematuria (40%), 10 patients with severe hemophilia (43%), and 4 patients with mild hemophilia (33%). 20% of patients had urolithiasis in their medical history. During this investigation, about one year, four patients had gross-macrohematuria (11%), two with severe and two patients with mild hemophilia, while two patients (6%) had urolithiasis, both on recombinant factor, noted on ultrasound and CT. One of them was treated with endoscopic lithotripsy successfully.

**Discussion:** There is significant difference regarding the number of patients with mild and severe hemophilia. There is a tendency higher incidence of renal diseases in the whole group patients with hemophilia compared with normal population. It is necessary to include more patients, and both groups should be approximately equal according to the number of patients.

**Acknowledgments:** University Hospital Center, National Hemophilia Center, Division of Hematology

**MeSH/Keywords:** hemophilia, coagulation factor, renal stone, urolithiasis

**Poster code:** R-B-9-90

## Poster Title: EVALUATION OF NUTRITIONAL STATUS AND PHYSICAL PERFORMANCE IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

**PhD candidate:** Zinka Matković

**Thesis proposal:** Evaluation of nutritional status and physical performance in patients with chronic obstructive pulmonary disease

**Mentor/s:** Professor Neven Tudorić, MD, PhD, Marc Miravitlles, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, Dubrava University Hospital, Zagreb, Croatia

**Introduction:** Chronic obstructive pulmonary disease (COPD) is characterised by chronic bronchial inflammation, airflow limitation and chronic respiratory symptoms – cough, expectoration and dyspnea. Although respiratory symptoms predominate in clinical presentation, extrapulmonary manifestations are recently being recognised as important determinants of the disease severity and prognosis. Physical inactivity and nutritional status abnormalities are frequent findings in patients with COPD. The aim of this study was to compare disease severity, daily physical activity, nutritional and psychological status in COPD patients with normal and poor exercise capacity (EC).

**Materials and methods:** A cross-sectional study was conducted in patients with moderate to very severe COPD, clinically stable and free of other diseases that might influence physical activity / nutritional status. EC was measured by the six-minute walk distance (6MWD): <350m was defined as poor, and ≥350m as normal EC. Severity of COPD was assessed by the spirometry, COPD Assessment Test (CAT), and modified Medical Research Council (mMRC) dyspnea scale. Nutritional status was evaluated by the body mass index (BMI), dual energy X-ray absorptiometry, and Mini Nutritional Assessment (MNA). In the psychological evaluation Hospital Anxiety and Depression Scale (HADS) was used. Daily physical activity was measured by the ankle-worn accelerometer StepWatch Activity Monitor®. Bivariate and multivariate analyses were performed.

**Results:** Study population included 91 patients (65 men), all smokers/ex-smokers, mean ± standard deviation (SD) age 66.9 ± 7.6 years, with mean forced expiratory volume in 1 sec (FEV1) 49.4 ± 15.0 %pred, mean BMI 27.8 ± 5.7 kg/m2. Fifty-five patients (60%) had good EC, and 36 (40%) poor EC. Patients with poor EC had lower FEV1, higher CAT score, worse dyspnea, lower lean and fat-free mass index, bone mineral content, bone mineral density (BMD), T-score, MNA score, lower daily step count, and higher HADS-Depression score (all comparisons p<0.05). Higher FEV1 (OR=1.073, p=0.012) and BMD (OR=2.866, p=0.039) were independently and significantly associated to better EC. Conversely, older age (OR=0.834, p=0.004) and higher mMRC dyspnea level (OR=0.137, p=0.001) decrease the probability of normal EC.

**Discussion:** COPD patients with poor EC have more severe disease, deficient nutritional status and lower daily physical activity. In the treatment of patients with COPD an effort should be made to improve nutritional status and physical performance.

**MeSH/Keywords:** COPD, physical activity, nutritional status, body composition, musculoskeletal system

**Poster code:** R-B-9-100

## Poster Title: GLUCOCORTICOID RECEPTOR GENE POLYMORPHISMS IN PATIENTS WITH ADRENAL INCIDENTALOMA

**PhD candidate:** Bojana Gardijan

**Thesis proposal:** Glucocorticoid receptor gene polymorphisms and risk of metabolic syndrome in patients with adrenal incidentaloma

**Mentor/s:** Associate Professor Darko Kaštelan, MD, PHD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre Zagreb, University Hospital Merkur

**Introduction:** The effect of glucocorticoids is mediated through binding on the glucocorticoid receptor (GR). Various gene polymorphisms of the GR are associated with modified glucocorticoid sensitivity. Certain single nucleotide polymorphisms (SNP) are associated with increased sensitivity (BclI, N363S). The ER22/23EK polymorphism is associated to a resistance to glucocorticoid action. We aimed to show that GR gene polymorphisms ER22/23EK, BclI and N363S are differently distributed in patients with adrenal incidentaloma (AI) than in the normal population, possibly causing different glucocorticoid sensitivity.

**Materials and methods:** We enrolled 101 patients with AI verified by MSCT or MRI (based on G power analysis, $X^2$ test/exact binominal test, 100 patients, $\alpha=0.05$, $1-\beta=0.95$, $\rho=0.5$). Exclusion criteria included pheocromocytoma, primary hyperaldosteronism, adrenocortical carcinoma, Cushing syndrome, adrenal metastases, use of exogenous glucocorticiods, the inability to consent to the trial or radiological characteristics of a non-adenoma (HU>10). A complete physical examination and medical history were performed. Data on tumor size was collected. Complete laboratory work-up, including plasma ACTH, free urinary cortisol and overnight DST were performed. From venous blood sample, leukocyte DNA was extracted. GR polymorphisms were determined using PCR and pirosequencing. Statistical analysis (descriptive and analytical) was done using Statistica v12.0, Dell, with $p<0.05$. For comparison, we used the previously published data on GR polymorphisms distribution in the normal matching population

**Results:** A total of 101 patients were enrolled .There were 73 female and 28 male pts. Mean age was 60 yrs (ranging from 34 to 85yrs). The frequency of N363S polymorphism was 0,079 (general population 0,03, $p<0,05$). The frequency of BclI polymorphism was 0,594 (general population 0,277, $p<0.001$). The frequency of ER22/23EK was 0,049 (general population 0,013, $p<0,001$).

**Discussion:** The frequency of GR polymorphisms (BclI, N363S, ER22/23EK) in the specific population with AI is significantly different than in the general population, possibly modifying glucocorticoid sensitivity. This data could imply a genetic background of different response to glucocorticoid action. GR polymorphisms could also have a role in the development of AI. Further research planed in the thesis is expected to provide additional information

**Acknowledgments:** I would like to thank Professor Daniela Giachino from the Department of Medical Genetics, University of Torino, Italy for the collaboration and DNA sequencing

**MeSH/Keywords:** glucocorticoid gene receptor polymorphism, adrenal incidentaloma, glucocorticoid sensitivity

**Poster code:** R-B-9-120

## Poster Title: PREDICTORS OF BIOLOGICAL BEHAVIOUR OF PITUITARY TUMORS

**PhD candidate:** Mirsala Solak, MD

**Thesis proposal:** Predictors of biological behavior of pituitary tumors

**Mentor/s:** Associate Professor Tina Dušek, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre Zagreb

**Introduction:** Pituitary tumors are benign intracranial tumors, however, from clinical point of view they can vary in terms of aggressiveness. Most of them are well defined adenomas that can be successfully removed, however, significant proportion of them are locally aggressive. Ki-67, transcriptive factor p53 and mitotic activity in pituitary tumors are considered as markers of proliferative activity. Aim of our study was to analyze the expression of Ki-67, p53 and mitotic activity in pituitary tumors and to determine their connection to proliferative activity. Furthermore, we analyzed clinical course of patients with pituitary tumors.

**Materials and methods:** We retrospectively reviewed all patients between 18 and 85 years of age referred to pituitary surgery to the Department of Neurosurgery, University Hospital Center Zagreb due to pituitary tumor since 2004 to 2011. Invasiveness, relapse and progression of the tumor was assessed by MR imaging. Detailed hormonal assessment was performed in all patients prior and after the surgery. Immunohistocemical staining and mitotic activity was determined in all patients, while expression of Ki-67 was determined in most patients. Our further plan is to determine the expression of Ki-67 and p53 in all patients. Data were analyzed using descriptive statistic.

**Results:** In our study 184 patients were included. All patients underwent pituitary surgery, transsphenoidal in 94%, transcranial in 3.8% of patients. Based on MRI 10.9% patients had microadenoma and 88.6% macroadenoma. In 29.9% of patients tumor was noninvasive, while it was invasive in 52.7% (infiltrating sphenoid and/or cavernous sinus). Based on hormone assessment 56.5% patients had nonfunctional tumor, 40.8% had functional tumor, while for 2.7% data are missing. On histology analysis nonfunctional tumor was found in 47.8% patients, somatotropinoma in 22.3%, prolactinoma in 8.7%, corticotropinoma in 7.4%, gonadotropinoma in 7.1% and silent corticotropinoma in 2.2%. Mean age at the time of surgery was 49.86 (range 17-79). Mean time of follow up was 67.45 months (range 1-143.1). 52.7% of patients were male while 47.3% were female. Residua after surgery was present in 31.5% and they were offered second line treatment, while 42.4% did not have residua. Mitotic activity was analyzed in all histology specimens while the expression of Ki-67 was analyzed in most patients.

**Discussion:** This research allows us to better understand specific histologic markers and their role in etiopathogenesis of pituitary tumors.

**Acknowledgments:**

**MeSH/Keywords:** pituitary tumors, proliferation, tumor markers, invasiveness, Ki-67, p53, mitotic activity

**Poster code:** R-B-9-125

**Poster Title: PATHOGENETIC MECHANISMS AND PREDICTORS OF ELEVATED PULMONARY VASCULAR RESISTANCE REVERSIBILITY AND PULMONARY HYPERTENSION IN PATIENTS WITH CHRONIC SYSTOLIC HEART FAILURE**

**PhD candidate:** Marijan Pašalić, MD

**Thesis proposal:** Pathogenetic mechanisms and predictors of elevated pulmonary vascular resistance reversibility and pulmonary hypertension in patients with chronic systolic heart failure

**Mentor/s:** Prof. Davor Miličić, MD, PhD, F.C.A.

**Affiliation:** Department for Cardiovacular Diseases, Zagreb University Hospital Centre, University of Zagreb, School of Medicine

**Introduction:** Chronic heart failure (CHF) is one of the most significant medical issues of the modern society. Pulmonary hypertension (PH) and pulmonary vascular resistance (PVR) play an essential role in pathophysiological sequence of CHF. The aim of this study is to shed light on the pathogenetic mechanisms and to recognize the optimal predictors of outcome in patients with PH due to CHF. Right ventricle systolic function (RVF), pulmonary pulse pressure (PPP), platelet aggregability and renal function are hypothesized as being crucial for the pathophysiology of CHF and the most accurate in predicting the patient outcome.

**Materials and methods:** 250 patients diagnosed with CHF and PH will be included. Initial and follow-up diagnostics comprise of patient history, standard laboratory, platelet aggregometry, functional status evaluation, echocardiography and right heart catheterization. Outcomes include the overall survival, functional status, changes in PH, PVR and cardiac function parameters. Patients are stratified and compared according to the PH severity, PVR reversibility and therapy modalities.

**Results:** 171 patients have been included in the study as of December 2015. The average patient age is 52.8±21.8 years, the majority of patients are male (78,9%) and the two most often diagnoses are dilated (39,2%) and ischemic (28,1%) cardiomyopathy. The overall 2-year survival is 71% and mostly depends on the PH and PVR severity. Although a strong predictor of the PH severity and reversibility (r=0,607, p=0,000), RVF does not correlate with the PVR (r=0,214, p=0,136). PVR seems to be associated with the left ventricular function (r=0,655, p=0,000) and PPP (r=0,606, p=0,000). On the other hand PVR reversibility depends mostly on the PH severity (r=-0,395, p=0,001). Measured platelet function does not correlate with PH nor PVR. Interestingly, although no significant difference was found in PH severity, PVR was significantly higher in women (∆=1,17±0,62 WU).

**Discussion:** Preliminary results show that PH and PVR result from the joint effect of the right and left ventricular dysfunction. PPP is an important parameter that characterizes both the RVF and PVR. Platelet activity was not shown to have a significant role in PVR development. The importance of renal function in PH pathogenesis is currently being evaluated. Further research, encompassing additional analysis and including patient and outcome stratification, is pending.

**Acknowledgments:** I would like to thank my mentor and the Department of cardiovascular diseases at Zagreb University Hospital Centre, for their scientific and professional advice. I would also like to thank my family for their support.

**MeSH/Keywords:** chronic heart failure, pulmonary vascular resistance, right ventricle, pulse pressure, platelet aggregation, sex-differences

**Poster code:** R-B-9-126

## Poster Title: SIGNIFICANCE OF PULMONARY ARTERY TO AORTA RATIO MEASUREMENT IN EVALUATING PULMONARY HYPERTENSION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

**PhD candidate:** Kristina Gašparović, MD

**Thesis proposal:** Pulmonary artery to aorta ratio is an independent indicator of pulmonary hypertension in severe COPD patients

**Mentor/s:** Prof. Miroslav Samaržija, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre – Zagreb

**Introduction:** Pulmonary hypertension is an important contributor to the progression of chronic obstructive pulmonary disease (COPD) which is evident as an increase in the frequency of exacerbations, accompanied bi an increase in mortality. Right heart catheterisation (RHC) is frequently considered to be the gold standard for the quantification of pulmonary hypertension but it is an invasive procedure that harbors potential for various complications. We aim to investigate wheter non-invasive alternatives to RHC can be utilized while maintaining an acceptable diagnostic accuracy.

**Materials and methods:** The study population includes 30 patients with COPD in GOLD D status who underwent pulmonary functional testing, echocardiographic assessment, CT of the chest and right heart catheterisation during of period of stability in a lung pretransplantation assessment. Mean pulmonary artery pressure assessment bi RHC was compared to pulmonary artery to aorta diameter ratio assessed by computed tomography, number of exacerbations, years of smoking, CAT questionnaire, mMRC breathlessness scale, BODE indeks for COPD survival, echocardiographic measurements of the right and left heart systolic function.

**Results:** Patients with more severe COPD do have greater pulmonary artery diameter and greater PA/A diameter ratio, but significance in Pearsons correlation has not met statistical significance (preliminary data, study in progress). The MRC breathlessness scale, BODE index, 6-MWT, the COPD assessment test are good predictors of COPD status, but so far showed no correlation with pulmonary hypertension level nor PA/A diameter ratio. Parameters of right ventricular systolic function assessed by echocardiography showed good correlation with parameters assessed with RHC (Rho Pearsons 0.845, p=0.002, N=20). A score combining PA/A ratio, echocardiographic parameters and COPD assessment tests could be the best predictors of pulmonary hypertension and disease progression.

**Discussion:** Pulmonary to aorta diameter ratio could distinct patients with COPD who are at higher risk for disease progression and combined with echocardiographic markers could offer a precious non invasive tool for selecting patients for right heart catheterisation.

**Acknowledgments:** Special Thanks to my mentor, prof. Samarzija for helping me to understand the complex pulmonary pathology, special Thanks to Prof. Separovic-Hanzevacki for tutoring in beautiful Echocardiographic Science. I would also like to thank Prof. Mažuranić for all the help in Radiology field.

**MeSH/Keywords:** Pulmonary hypertension, COPD, cardiac imaging, pulmonary to aorta ratio

**Poster code:** R-B-9-138

# Poster Title: INCIDENCE OF DIABETIC KETOSIS AND KETOACIDOSIS IN PATIENTS WITH CLINICAL FEATURES OF TYPE 2 DIABETES MELLITUS

**PhD candidate:** Ivan Kruljac, MD

**Thesis proposal:** Hyperglycemic crises in patients with diabetes mellitus in Republic of Croatia

**Mentor/s:** Milan Vrkljan, MD, PhD, Professor of medicine

**Affiliation:** University hospital center Sestre milosrdnice

**Introduction:** Current paradigm suggests that diabetic ketosis (DK) and diabetic ketoacidosis (DKA) occur mostly in patients with type 1 diabetes mellitus (DM). Ketosis-prone diabetes or atypical diabetes is poorly defined subgroup of type 2 DM of unknown pathogenesis, which occurs predominantly in obese middle-aged men of Hispanic and afroamerican ethnicity and in regions of sub-Saharan Africa. The incidence of DK and DKA in adult population is unknown. The main aim of this thesis is to estimate the incidence of DK and DKA in well-defined, predominantly Caucasian population in Croatia.

**Materials and methods:** The study was carried out in Emergency department which supplies emergency care service for a population of 261749 adults. We reviewed electronic charts from all patients with plasma glucose >13.9 mmol/L at admission over 5-year period. DK was defined as plasma glucose > 14 mmol/L, ketonuria >2 and a bicarbonate level >18 mEq/L or pH >7.30, while DKA implied a bicarbonate level <18 mEq/L or pH <7.30. The remaining were defined as non-ketotic hyperglycemia (NKH). Crude incidence rates were calculated, age- and gender-adjusted to the 2013 standard European population and expressed per 100000 person-years.

**Results:** Among 3409 admissions, we observed 630 episodes of DK in 520 patients, 215 episodes of DKA in 165 patients and 2562 episodes of NKH in 2041 patients. Readmission rate was higher in patients with DKA when compared with controls (20.3% vs. 23.3%, P=0.016) and patients with DK (23.3% vs. 17.5%, P=0.03). Patients with DKA and DK were younger than controls, had higher serum glucose levels at admission, higher male predominance, higher rates of newly diagnosed DM and higher hospitalization rates. Incidence of DK and DKA in age band 40-50 was six-times higher in males. Overall annual incidence rate for DK was 48.1 and 17.0 for DKA. When we excluded patients with previously diagnosed T1DM and all patients younger than 40 years of age, the incidence of DK rose to 69.2 (increase by 30.5%) and DKA to 19.3 (increase by 11.9%).

**Discussion:** The results suggest that DK and DKA occur frequently in Caucasian population and that the overall incidence is higher in patients with clinical features of type 2 DM. This can be explained either by higher prevalence of atypical diabetes or mistreatment of patients with undiagnosed type 1 DM. Further analyses will aim to elucidate this issue.

**Acknowledgments:**

**MeSH/Keywords:** ketosis-prone diabetes mellitus, type 2 diabetes mellitus, diabetic ketosis, diabetic ketoacidosis, incidence

**Poster code:** R-B-9-148

# Poster Title: ACOUSTIC FEATURES OF VOICE ANALYSIS FOR ASSESSMENT OF FATIGUE IN PATIENTS WITH MYELOFYBROSIS

**PhD candidate:** Dubravka Čaržavec, MD

**Thesis proposal:** Acoustic features of voice analysis could be used for assessment of fatigue in patients with myelofibrosis

**Mentor/s:** Professor Rajko Kušec, MD, PhD, Professor Krešimir Ćosić, B.Sc.E.E., PhD

**Affiliation:** Clinical Hospital Center Sestre Milosrdnice, Dubrava University Hospital, Faculty of Electrical Engineering and Computing, Zagreb, Croatia.

**Introduction:** Myelofibrosis (MF) is a myeloproliferative neoplasm (MPN) associated with dysregulated JAK/STAT signaling. Typical manifestations of MF are splenomegaly, cytopenias and most commonly fatigue. New drugs (JAK inhibitors) are effective in diminishing the MF symptoms. To stress the most specific symptoms common in MPN the Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score (MPN-SAF TSS) has been developed. MPN-SAF TSS consists of 10 questions that are answered in scale of 0-10. Fatigue related physiological changes indirectly influences acoustic voice features. Voice analysis with standard acoustic feature computation procedures can objectively and in real time assess intensity of fatigue. This method could be complementary to MPN-SAF TSS and use for assessment of patients with MF and their monitoring.

**Materials and methods:** 25 patients with MF will take part in study voluntarily. The control group consists of 25 healthy and rested subjects consistent with the age and sex. Voice recording in patients with MF will be done two times in a span of three months. On the day of voice recording the DIPSS risk group will be determined. All participants will fill out a Croatian version of MPN-SAF TSS questionnaire and TSS will be calculated. The voice recording takes place in a quiet room using high-quality microphone and personal computer. It will be recorded A. basic data-reading always the same text B. vocalization data-pronouncing of vowel "a" with intensity of 80-100 dB. From recorded material relevant acoustic features of voice will be extracted. The results obtained for each patient will be correlated with their TSS and DIPSS risk group. Also, results of patient voice analysis will be correlated with results obtained from control subject.

**Results:** So far we evaluated three patients with MF and three healthy subjects as a control group. Spectrogram (spectral distribution) provides a first insight into possible fatigue-sensitive acoustic features with different waveforms of the same utterance for MF patients and control group. Preliminary results showed that MF patients have lower fundamental frequency (rate of vocal fold vibration) with less variation in frequency. Also, voice energy on the basis of the amplitude in different intervals were higher in control group.

**Discussion:** Acoustic features of voice analysis could be efficacy and sensitive method for evaluation of patients with MF and may be used together with MPN-SAF TSS in clinical drug reasearch and clinical practice.

**Acknowledgments:**

**MeSH/Keywords:** myelofibrosis, fatigue, voice analysis

**Poster code:** R-B-9-151

## Poster Title: VEIN DIAMETER AFTER INTRAOPERATIVE DILATATION WITH VESSEL PROBES AS A PREDICTOR OF SUCCESS OF HEMODIALYSIS ARTERIOVENOUS FISTULAS

**PhD candidate:** Branko Fila, M.D., Prim., Mr

**Thesis proposal:** Vein diameter after intraoperative dilatation as a predictor of success of hemodialysis arteriovenous fistulas

**Mentor/s:** Prof. dr. sc. Zdenko Sonicki, dr med

**Affiliation:** Department of Vascular Surgery, University Hospital Dubrava, Zagreb, Croatia

**Introduction:** The primary objective of this prospective study was to investigate the predictive value of vein diameter after intraoperative dilatation with vessel probes on hemodialysis fistula maturation.

**Materials and methods:** Ninety-three fistulas were performed by a single surgeon from February 1, 2006 to January 31, 2009. Intraoperative vein dilatation with vessel probes was attempted in all fistulas. Measurements of the feeding artery diameter, vein diameter and the increased vein diameter after intraoperative dilatation were performed and immediate failure, early patency, early failure, primary patency, and fistula survival outcomes were recorded during 48-month follow-up.

**Results:** Early failure occurred in 20% of fistulas and 70% matured sufficiently for cannulation. Variables with significant impact on the failure to mature by univariate analysis were: body-mass index (P=0.041), artery diameter (P<0.001), vein diameter (P=0.004), and vein diameter after dilatation (P=0.002). However, multivariate analysis showed that only body-mass index (P=0.038), artery diameter (P=0.001), and the diameter of the vein after dilatation (P=0.018) significantly affected maturation. In a group of 56 (60%) patients with vein diameter before dilatation ≤2 mm, among vessel characteristics found by multivariate analysis, only vein diameter after dilatation (P=0.004) significantly affected function.

**Discussion:** Artery diameter and vein diameter after intraoperative dilatation with vessel probes were the main predictors of fistula function. Careful intraoperative exploration and dilatation of the vein with vessel probes could be useful adjunct procedure which helps the surgeon to estimate vein patency and distensibility. This information could be crucial in the decision of using an explored vein, especially of borderline size or in the lack of valid preoperative duplex ultrasonography.

**Acknowledgments:** Special thanks to all patients who participated in the study.

**MeSH/Keywords:** Arteriovenous fistula, hemodialysis, intraoperative vein dilatation, vascular probe

**Poster code:** R-B-10-15

**Poster Title: PROGNOSTIC SIGNIFICANCE OF PREOPERATIVE ANEMIA ON OCCURRENCES OF REGIONAL METASTASES AND SECOND PRIMARY TUMORS IN PATIENTS WITH EARLY STAGE ORAL SQUAMOUS CELL CARCINOMA**

**PhD candidate:** Enis Gllareva, DMD

**Thesis proposal:** Preliminary results show an impact of microcytic/macrocytic anemia and low hemoglobin level as an independent predictor in regional metastasis

**Mentor/s:** Ass. Prof. Ivica Lukšić, MD, PhD

**Affiliation:** University of Zagreb, School of Medicine

**Introduction:** Squamous cell carcinoma (SCC) is the most common type of oral cancers, accounting for 90% of all oral cancers. The etiology appears to be multifactorial and strongly related to lifestyle, mostly habits and diet (particularly tobacco and alcohol usage). Low hemoglobin level (anemia) is associated with an increased level of vascular endothelial growth factor (VEGF) in cancer patients, which may therefore be an indicator for the angiogenic potential and biological aggressiveness of a tumor.

**Materials and methods:** This is a retrospective cohort study. Candidates for inclusion are consecutive patients with OSCC, in period between 1 January 2000 and 31 December 2010, meeting the following criteria: Verified T1-T2N0M0 stage and anemia (severity and type of anemia). Evaluation of patient records are performed by the end of 2015, and they are assessed for occurrence of regional metastases/second primary tumors.

**Results:** Using Cox proportional hazards regression to investigate the effect of "anemia", significant data (microcytic/macrocytic anaemia and low hemoglobin level) about impact of anemia in regional metastases were detected (100 cases evaluated from 400 in total).

**Discussion:** Preliminary results show an impact of microcytic/macrocytic anemia and low hemoglobin level as an independent predictor in regional metastasis but not in second primary tumors. There are 300 more cases to evaluate and results can be change.

**Acknowledgments:** My mentors, Dental clinic – ProfessionalDent.

**MeSH/Keywords:** Anemia, regional metastases/second primary tumors, OSCC

**Poster code:** R-B-10-130

## Poster Title: IMPACT OF ANTIPLATELET THERAPY AND CARDIOPULMONARY BYPASS ON PLATELET FUNCTION IN PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFTING USING MULTIPLE ELECTRODE AGGREGOMETRY

**PhD candidate:** Martina Zrno Mihaljević

**Thesis proposal:** Relationship between level of glycosylated hemoglonin and platelet function in patients undergoing coronary artery bypass grafting

**Mentor/s:** Associate Professor Bojan Biočina, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre – Zagreb, Department of Cardiac Surgery

**Introduction:** Antiplatelet therapy (APT) is known to substantially reduce mortality and rate of ischemic complications after coronary artery bypass grafting (CABG). Rate of perioperative APT resistance varies widely and could be influenced by cardiopulmonary bypass (CPB). The purpose of the study was perioperative assessment of platelet function with respect to administered APT and CPB, and determination of patients with APT resistance who could benefit from more aggressive treatment strategy.

**Materials and methods:** In prospective study we enrolled 192 patients undergoing elective CABG. Patients were divided into 4 groups with respect to their preoperative APT management. All patients received Aspirin (ASA) 300 mg/day postoperatively starting on the day of procedure. Platelet function was assessed prior to surgery and at fourth postoperative day (POD 4) using multiple electrode aggregometry (MEA). Adenosine diphosphate (ADP test) and arachidonic acid (ASPI test) induced platelet aggregation tests were used.

**Results:** Group of patients exposed to ASA preoperatively had lower values of ASPI test ($P<0.001$) comparing to patients not receiving ASA. However, we registered 28.6% ASA resistant patients. Both ASPI ($P<0.001$) and ADP ($P<0.001$) test values increased significantly at POD 4, suggesting postoperative platelet hyperactivity. Postoperatively, we registered 33.3% ASA resistant patients despite higher ASA dosing regimen.

**Discussion:** MEA can recognize patients with ASA resistance during the both the pre- and post-CABG period. Postoperatively, ASA 300 mg did not sufficiently inhibit platelet aggregation in 33.3% patients. In this subgroup, dual antiplatelet therapy with ASA and clopidogrel could be useful for maintaining graft patency, and preventing adverse ischemic events.

**Acknowledgments:**

**MeSH/Keywords:** Coronary artery bypass, Aspirin, Platelet aggregation, Aspirin resistance, Multiple electrode aggregometry

**Poster code:** R-B-10-128

# Poster Title: ASSOCIATION BETWEEN ACE GENE POLYMORPHISMS AND SEVERITY OF SYSTEMIC SCLEROSIS

**PhD candidate:** Boris Karanović, MD

**Thesis proposal:** Association between ACE gene polymorphisms and severity of systemic sclerosis

**Mentor/s:** Professor Branimir Anić, MD, PhD

**Affiliation:** School of Medicine University of Zagreb, Department of Clinical Immunology and Rheumatology, University Hospital Center Zagreb

**Introduction:** Angiotensin-converting enzyme (ACE) is a widely distributed enzyme, with roles in various pathophysiological conditions. It is controlled by an ACE gene on chromosome 17 (17q3). More than 160 polymorphisms of ACE gene were found, with one polymorphism, including insertion (I) or deletion (D) of 287-bp DNA sequence on intron 16 of the ACE-gene that distinguishes subjects with greater activity of ACE (DD) compared to other subjects (II). Systemic sclerosis is characterised by micro and macrovascular changes. It is possible that ACE has a role in susceptibility, as well as severity of clinical presentation of systemic sclerosis. Researches in this field are contradictory and inconclusive.

**Materials and methods:** With the approval of medical ethics committee, 88 patients (with possible extra addition of patients) fulfilling the strict ACR inclusion criteria and under the care of Department of Clinical Immunology and Rheumatology, University Hospital Center Zagreb, enrolled in EULAR Scleroderma Trials and Research group (EUSTAR) project, are being currently investigated. Blood sampling for ACE gene analysis performed in a laboratory in our Institution is currently underway. Also, other data, obtained from patients' medical history and clinical evaluation, is still being collected. Severity of lung interstitial fibrosis was assessed by HRCT, spirometry and CO diffusion, pulmonary hypertension by echocardiography, severity of Raynaud phenomenon and peripheral vasculopathy by Rodnan score and ankle brachial index (ABI) and renal insufficiency by laboratory findings.

**Results:** There are 88 subjects enrolled in the study, 5 of them male and 83 female. Median age of the whole group is 60 (range 33 to 82), for men being 59 (range 35-74) and for women 60 (range 33-82). Blood sampling and analysis of other data is currently underway.

**Discussion:** ACE polymorphisms are associated with different pathophysiological mechanisms that may lead to diabetic nephropathy, Alzheimer's disease, cardiovascular diseases, sarcoidosis, systemic lupus erythematosus, systemic sclerosis and other diseases. Most studies on this association gave contradictory results. This research may contribute to better understanding of systemic sclerosis. The results could be implemented in everyday medical practice by using ACE genotype as a marker for assessment of severity of the disease, thus distinguishing patients in need for more aggressive treatment and more frequent evaluations.

**Acknowledgments:**

**MeSH/Keywords:** systemic sclerosis, ACE, gene polymorphism

**Poster code:** R-B-14-109

## Poster Title: ATROPHY PROGRESSION OF ELLIPSOID ZONE IN DRY FORM OF AGE RELATED MACULAR DEGENERATION

**PhD candidate:** Krešimir Mandić

**Thesis proposal:** Influence of drusen morphology on disruption of photoreceptor layer in age related macular degeneration

**Mentor/s:** Professor Nenad Vukojević, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre – Zagreb

**Introduction:** Senile macular degeneration or age-related macular degeneration (ARMD) is a major cause of significant vision loss and blindness in developed world, in adults over 50 years of age. There are two forms of the disease, non exudative ("dry") and "exudative ("wet") form. The characteristic feature of "dry" ARMD are drusen made of clusters of extracellular material that accumulates between the choroid and retina. Drusen over time may progress and change its morphology, leading to functional disorders of photoreceptors making it a direct cause of the visual function deterioration, either by causing photoreceptor atrophy or converting to „wet" form of ARMD (advanced stages of ARMD). Today's high resolution OCT scans provide plenty information on drusen and retinal layers.

**Materials and methods:** Patients who had been diagnosed of having drusiform form of senile macular degeneration with indirect ophthalmoscopy had been be scanned with optical coherent tomography (OCT) in interval of 2 years. Every drusen scanned with OCT was measured for shape, height, width, homogeneity, reflectivity and ellipsoid zone deterioration. All drusen from 1 eye had been compared with same eye after period of 2 years. Overall 40 eyes had been involved in study.

**Results:** We found that there is statistical difference in drusen number in period of 2 years for both right and left eye. Average patient with drusiform „dry" ARMD had increase of 5 drusen in period of 2 years. Women have statistically significant lower CRT no matter the eye and time of measurement.

**Discussion:** Age related disease study 1 and 2 (AREDS 1, AREDS 2) were very important in terms of finding out morphologic characteriscs of drusen on indirect ophthalmocopy that are more prone to progressing to advanced stages of ARMD. Unfortunately that study did not include OCT scans, which is today most frequently used tool for diagnosing all kinds of macular disease including ARMD. Today's high resolution OCT provide many interesting information about retinal layers and drusen characteristics. Although primary goal of our study was finding out high risk OCT characteristics for photoreceptor atrophy, in part of our study, we came upon interesting statistical data. It turned out that woman with drusiform „dry" ARMD have statistically significant lower central retinal thickness (CRT) than men, as well as the fact that average patient with „dry" form of ARMD gains approximately 5 drusen per eye in period of 2 years.

**Acknowledgments:**

**MeSH/Keywords:** drusen, age related macular degeneration, photoreceptor, OCT

**Poster code:** R-B-18-4

# Poster Title: RETINAL NERVE FIBER LAYER CHANGES IN PATIENTS WITH CHRONIC OPTIC NEURITIS

**PhD candidate:** Danijela Mrazovac

**Thesis proposal:** Combined functional, electrophysiological and structural ophthalmologic investigation in early diagnosis of optic neuritis in multiple sclerosis

**Mentor/s:** Prof. Branimir Cerovski, MD, PhD

**Affiliation:** Department of Ophthalmology, University Hospital Centre Zagreb, Croatia

**Introduction:** Optic neuritis (ON) is an inflammatory, demyelinating condition that causes acute, usually monocular, visual loss and is highly associated with multiple sclerosis (MS). It is the presenting feature of MS in up to one third of patients and occurs in 50% of cases at some time during the course of their illness. Axonal and neuronal degenerations are important features of MS and other neurological disorders that affect the anterior visual pathway. Optical coherence tomography (OCT) is a non-invasive technique that allows imaging of the retinal nerve fiber layers (RNFL). It provides a possibilty to quantify the structural effects in inflammatory and chronic changes of the optic nerve, which can then be compared to functional outcomes.

**Materials and methods:** We have performed a prospective study of 13 patients with chronic optic neuritis, between March 2015 and December 2015. All patients underwent complete standard ophthalmic exam. A spectral domain OCT has been performed in all patients on both eyes in midriasis. Measurements of mean peripapillary retinal nerve fiber layer thickness were performed. We excluded patients with other ophthalmological diseases.

**Results:** Median age was 41,2 years. 15 eyes were diagnosed with chronic optic neuritis and 11 eyes showed no structural and functional changes. 11 patients had a history of acute optic neuritis on one eye. Eyes of the patients with chronic ON and eyes with a history of acute ON had decreased mean RNFL thickness (79.5 mm) compared to healthy eyes (113 mm). There was a statistically significant difference between these two groups (p< 0.001).

**Discussion:** Optical coherence tomography is a simple, non-invasive, reproducible technique that provides us in vivo high-resolution reconstruction and objective measurements of the retinal nerve fiber layer thickness. Our previous studies showed there is a possibility of quantifying axonal loss in chronic optic neuritis using OCT. Our study showed that there is a statistically significant difference in RNFL structure in eyes with chronic optic neuritis compared to healthy eyes.

**Acknowledgments:**

**MeSH/Keywords:** optic neuritis, retinal nerve fiber layer, optical coherence tomography, multiple sclerosis

**Poster code:** R-B-18-12

## Poster Title: COMPARISON BETWEEN STANDARD INVASIVE AND NON- INVASIVE TEAR FILM BREAK-UP TIME TEST RESULTS

**PhD candidate:** Sania Vidas

**Thesis proposal:** The role of non-invasive tear break-up time measurement using hand held instrument for lipid layer examination in tear film stability assessment

**Mentor/s:** Assoc. Prof. Tomislav Jukić, MD, PhD

**Affiliation:** Department of Ophthalmology, Zagreb University Hospital Centre, Zagreb, Croatia

**Introduction:** Standard method for tear film stability assessment is tear film break-up time (TBUT), an invasive method that changes tear film physiology. Non-invasive tear break-up time (NIBUT) enables native tear film function evaluation. NIBUT is usually performed by sophisticated and expensive instruments, unsuitable for clinical practice. In general population TBUT values are significantly shorter than the NIBUT (4-16 s), but almost equal in patients with dry eye. Direct visualization, interferometry, of the tear film surface allows NIBUT assessment. It can be performed by Tearscope or by using more practical and accessible hand held instrument for lipid layer examination since it works on the same physical principle as Tearscope. Aim of this study was to compare standard test with hand held instrument NIBUT assessment in dry eye diagnostics.

**Materials and methods:** Study included 50 adult patients, 31 patients with dry eye symptoms (dry eye group) and 19 patients without dry eye symptoms (control group). First a standardized Schein questionnaire, modified for issues relevant to this research, was performed in order to determine the symptoms of dry eye. Than during the standard slit lamp examination three NIBUT measurements were performed on both eyes to all patients, using handheld instrument, following three TBUT measurements.

**Results:** NIBUT values were significantly shorter in dry eye group than in control group in all three measurements (median 9, 8, 8 s vs 21, 22, 21 s, $p\_1 < 0.001$, $p\_2 < 0.001$, $p\_3 < 0.001$). TBUT values showed no significant difference between the groups in first measurement, but values where significantly shorter in dry eye group in second and third measurement (median 5, 5, 5 s vs 10, 11, 13 s, $p\_1 = 0,053$, $p\_2 = 0,020$, $p\_3 = 0,003$). NIBUT values showed positive correlation compared to TBUT values in all three measurements in both groups ($p\_1 = <0.001$, $p\_2 = <0.001$, $p\_3 = <0.001$). NIBUT values where longer 2-3 s than TBUT values in dry eye group while in control group values showed more dispersion.

**Discussion:** NIBUT measured by hand held instrument correlates with standard test. It indicated more significant difference between two groups than standard test and detected dry eye even with first measurement. Standard test showed no significant difference between the groups in first measurement, questioning the accuracy of first TBUT measurement. NIBUT measured by hand held instrument showed preferable results than standard test in evaluation of dry eye.

**Acknowledgments:**

**MeSH/Keywords:** Cornea, Dry eye syndrome, TBUT, NIBUT

**Poster code:** R-B-18-41

## Poster Title: PROSPECTIVE COMPARISON OF TWO EXCIMER LASER PLATFORMS IN TREATMENT OF HIGH ASTIGMATISM WITH LASER IN SITU KERATOMILEUSIS

**PhD candidate:** Alma Biščević, MD

**Thesis proposal:** Prospective comparison of two excimer laser platforms in treatment of high astigmatism with laser in situ keratomileusis

**Mentor/s:** Professor Iva Dekaris, MD, PhD

**Affiliation:** Specialty Eye Hospital Svjetlost

**Introduction:** Laser in situ keratomileusis (LASIK) is probably the most popular surgical procedure used to correct refractive errors. Predicting the outcome of treating astigmatism is complex because astigmatism involves two figures: power and axis. Thus, astigmatism can be treated as a vector because it has a magnitude and directional quality. We used the Thibos procedure that involves calculation of three figures namely $J_0$, $J_{45}$ and S.

**Materials and methods:** Patients were divided in four groups, depending on the type of astigmatism and laser platform on which they were treated. Astigmatism was between 2 and 7 diopters (D). 135 patients with myopic astigmatism (246 eyes) and 102 patients with mixed astigmatism (172 eyes) underwent unremarkable LASIK correction on Wavelight Allegretto Eye-Q 400Hz and Schwind Amaris 750S laser platform. The preoperative and postoperative sphere, negative cylinder [C] and axis (ø) of manifest refractions were subjected to vector analysis by calculations of the standard J0 (cos $[4\pi(ø-90)/360]$xC/2) and J45 (sin$[4\pi(ø-90)/360]$xC/2).

**Results:** Reporting the keyresults, we found $J_0$ significantly reduced after LASIK in both groups (p<0.001) but not for $J_{45}$. There was no significant association between individual pairs of pre and postoperative $J_0$ & $J_{45}$ values. There was no significant difference between the outcomes of the two platforms.

**Discussion:** Wavelight Allegretto 400Hz and Schwind Amaris 750S showed excellent results for treating patients with astigmatism, regardless whether it is mixed or myopic astigmatism. The $J_{45}$ did not reduce significantly possibly because of low number of eyes with oblique astigmatism. There was no genuine difference post-operatively between groups treated on two different laser platforms according to the vector analyses.

**Acknowledgments:** none

**MeSH/Keywords:** LASIK, astigmatism, vector analysis

**Poster code:** R-B-18-164

# Poster Title: IL-17 IN EARLY INVASIVE BREAST CANCER

**PhD candidate:** Marina Barić, MD

**Thesis proposal:** IL-17 in early invasive breast cancer

**Mentor/s:** Professor Damir Vrbanec, MD, PhD; Senior Research Associate Ana Kulić, PhD

**Affiliation:** Department of Medical Oncology, University Hospital Centre Zagreb

**Introduction:** There is a growing body of evidence supporting the role of immunity and inflammatory responses at different stages of tumor development. Recent studies have shown that there is an increased expression of IL-17 in breast cancer tissue compared to healthy breast tissue. The role of inflammatory response mediated by IL-17 in the development and progression of breast cancer has not yet been clarified. Some studies suggest antitumor activity of IL-17, and others speak in favor of its association with tumor aggressiveness and poorer prognosis.

**Materials and methods:** The study will be conducted in the Clinical Hospital Centre Zagreb. Blood samples and tumor tissue specimens from 120 patients diagnosed with an early invasive breast cancer, and the serum of 60 healthy women, will be analyzed accordingly. Two blood samples will be taken from breast cancer patients, first before surgery, and the other after 3 cycles of chemotherapy, or 3 months of hormone therapy. The serum IL-17 levels will be measured by the enzyme-linked immunoadsorbent assay (ELISA), using the Human IL-17A Platinum ELISA antibody, eBioscience San Diego, CA, USA. The IL-17 tissue expression will be determined immunohistochemically using the Rabbit polyclonal anti-IL17 antibody, ab 9565/Abcam.

**Results:** Blood samples from 120 women diagnosed with early invasive breast cancer were taken before they underwent surgical resection. Serum concentration of IL-17 was measured in the collected samples and compared with the concentration of IL-17 in the serum of 28 healthy women that served as control. We found that the concentration of IL-17 in the serum of women with early invasive breast cancer was significantly higher ($p=0.047$) than in healthy controls.

**Discussion:** The role of IL-17 in the tumor microenvironment is not clearly defined as pro- or anti-tumor activity, but considering the growing interest in the targeting of IL-17, knowing its clinical implications is crucial. As far as we know, this is the first study to measure serum concentration of IL-17 in patients with early breast cancer and compare it with healthy individuals. In further research, we will examine the correlation between serum concentrations and the expression of IL-17 in tumor tissue, analyze the association of IL-17 and other pathohistological indicators, and compare the concentration of IL-17 in the serum of breast cancer patients before and after therapy. Our results may lead to new diagnostic and therapeutic modalities.

**Acknowledgments:**

**MeSH/Keywords:** breast cancer, interleukin 17, IL-17

**Poster code:** R-B-19-117

**Poster Title: MEASUREMENT OF ACETABULAR COMPONENT STABILITY IN TOTAL HIP ARTHROPLASTY IN CORRELATION TO THE SIZE OF ACETABULAR MEDIAL WALL DEFECT IN PIG PELVIS MODEL**

**PhD candidate:** Katarina Barbarić

**Thesis proposal:** Cotyloplasty in dysplastic hip arthroplasty

**Mentor/s:** Professor Domagoj Delimar, MD, PHD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre Zagreb, Department of orthopedic surgery

**Introduction:** Total hip arthroplasty (THA) in patients with dysplastic acetabulum represents a significant challenge for orthopedic surgeons. Because they are mainly younger people, with increased functional requirements, it is necessary to achieve the ideal biomechanical conditions by placing the acetabulum in the ideal center of rotation with maximum medialization, what sometimes require performing even controlled iatrogenic defect of the medial wall of the acetabulum (cotyloplasty).

**Materials and methods:** On the pigs pelvis models iatrogenic medial wall defect in different diameters (1, 2, 2.5 and 3 cm) is made following with acetabular component placement (size 44). Acetabulum is loaded with 70 kg for determining to which diameter of cotyloplasty acetabular component of the THA remains stable, or at which point the remaining medial wall of the acetabulum can´t withstand the load and THA moves through the pelvis for more than 2 mm.

**Results:** We performed our research on 8 pig pelvises till now (2 of each size of defect). Our preliminary results show that instability rises with size of medial wall defect. With load of 70 kg acetabular component didn't move into the pelvis on models with 1 and 1.5 cm, but in all models with defect of 2.5 and 3 cm acetabular component breaks through pelvis for more than 2 mm.

**Discussion:** Preliminary results confirm our hypothesis that acetabular component of THA will have sufficient stability to ensure secondary bone ingrowth around it, if amount of cotyloplasty does not exceed half of the acetabular component diameter. Defining maximal amount of safe cotyloplasty will lead to significantly better biomechanical conditions for achieving longer survival of THA, without reducing the acetabular component stability. We expect significantly better long-term results with this treatment method.

**Acknowledgments:**

**MeSH/Keywords:** cotyloplasty, hip dysplasia, arthroplasty, stability

**Poster code:** R-B-20-51

# Poster Title: CLINICO-PATHOLOGICAL AND MOLECULAR CHARACTERIZATION OF TUBULOCYSTIC SUBTYPES OF RENAL TUMORS

**PhD candidate:** Faruk Skenderi, MD, MSc

**Thesis proposal:** Clinico-pathological and molecular characterization of tubulocystic subtypes of renal tumors

**Mentor/s:** Monika Ulamec, Semir Vranic

**Affiliation:** Department of Pathology, University of Sarajevo Clinical Center, Sarajevo, Bosnia and Herzegovina.

**Introduction:** Renal neoplasms may present with unusual, tubulocystic morphology, overlapping among several subtypes. Precise subtyping is important because of the differences in their clinical behavior and therapeutic approach. Our aim is to characterize the tubulocystic variants of renal neoplasms and determine the most useful properties for their differentiation in diagnostics. Furthermore, we want to elucidate the significance of cystic variants regarding their prognosis, compared to their conventional subtypes.

**Materials and methods:** A total of 152 cases were analyzed. The inclusion criteria were: renal tumor subtypes (renal oncocytoma (RO), chromophobe renal cell carcinoma (CHRCC), papillary RCC (PRCC), tubulocystic RCC (TCRCC)) with at least 50% volume of tubulocystic histologic architecture, and their conventional counterparts, as controls. Clinico-pathological data and tumor morphology, immunohistochemical profile, and molecular-genetic profile using FISH, aCGH and sequencing were analyzed.

**Results:** The average age of the patients at the time of diagnosis for tcRO, tcCHRCC, tcPRCC, and TCRCC was 68.7, 68, 62.7, and 59.8 years, respectively. The mean size of the tumors was 2.5, 5.32, 8.95, and 5 cm, respectively. The stage for tumors was: tcCHRCC - 7 cases at pT1, 2 at pT2, 1 pT not available (NA), tcPRCC - 3 cases at pT1, 6 at pT2, 4 pT NA, TCRCC - 11 cases at pT1, 3 at pT2, 1 at pT3. ISUP grades were for tcRO - 13 cases grade 1, 10 grade 2, 1 grade 3, tcPRCC - 1 case grade 1, 9 grade 2, 3 grade 3, TCRCC - 1 case was grade 1, 5 grade 2, 9 grade 3. The patients were followed up from 0.5 to 19 years and for tcRO - 10 patients were with no evidence of disease (NED), 14 data not available (NA), tcCHRCC - 6 patients NED, 1 died of other cause (DOC), 3 NA, tcPRCC - 6 patients NED, 3 DOC, 4 NA, TCRCC - 10 NED, 1 alive with disease (AWD), 4 died of disease (DOD).

**Discussion:** TCRCC and tcPRCC tend to occur at slightly younger patients than tcRO and tcCHRCC. Further, tcPRCC had the largest average size at the time of diagnosis. The tcRO is not staged as it is a benign tumor, however, majority of tcPRCC were at pT2 stage, in contrast to tcCHRCC and TCRCC where the most of the cases were at pT1 stage at presentation. tcCHRCC is not graded, as the grade does not correspond to prognosis in these tumors. The highest grades were associated with TCRCC, then tcPRCC, and the least grades were seen in tcRO. The most aggressive tumors among the groups were the TCRCC, with 4 cases died of disease.

**Acknowledgments:** The author thanks to Dr Ondrej Hes for the cases and support during the study.

**MeSH/Keywords:** kidney, cancer, renal cell carcinoma, tubulocystic, cystic, chromophobe, papillary, oncocytoma

**Poster code:** R-B-23-31

## Poster Title: IMMUNOHISTOCHEMICAL EXPRESSION OF MATRIX METALLOPROTEINASE-1 (MMP-1) AND CYCLOOXYGENASE-2 (COX-2) IN CUTANEOUS SQUAMOUS AND BASAL CELL CARCINOMA

**PhD candidate:** Sanda Smuđ Orehovec, MD

**Thesis proposal:** Immunohistochemical expression of matrix metalloproteinase-1 (MMP-1) and cyclooxygenase-2 (COX-2) in cutaneous squamous and basal cell carcinoma

**Mentor/s:** Professor Božena Šarčević, MD, PhD

**Affiliation:** Department of Pathology , Clinic for tumors , Clinical Hospital Centre "Sestre Milosrdnice" Zagreb, Croatia

**Introduction:** The most common non-melanoma skin tumors are cell carcinoma, and basal cell carcinoma. Cyclooxygenase-2 (COX-2) is critical for tumor formation, angiogenesis and metastasis. Matrix metalloproteinases (MMPs) are the members of zinc family (Zn) - and calcium-dependent endopeptidases that degrade the extracellular matrix.

**Materials and methods:** A retrospective analysis of 130 specimens that were excisional skin biopsies made in 130 patients for primary skin tumor (squamous cell carcinoma, basal cell carcinoma). The resulting products will be revised with purpose to confirm the histopatological diagnosis and to determine the subtypes of tumors. From each specimen we shall make the two additional cuts for immunohistochemical processing of the COX-2 and MMP-1 using the mouse monoclonal antibodies. For preliminary results we used immunohistochemical methods for the evaluation of COX-2 expression in tissue samples of 30 primary skin basal cell carcinoma (BCC) cases.

**Results:** Immunohistochemical expression of the protein COX-2 was significantly higher in the infiltrating subtype of BCC compared with the nodular (P = 0.005) and superficial (P = 0.041) subtypes in the basal cell carcinoma group. There was not a significant difference between nodular and superficial BCCs for COX-2 expression.

**Discussion:** COX-2 is an enzyme that enhances the synthesis of prostaglandins in inflamed and neoplastic tissues. It was suggested that cellular over-expression of COX-2 has a significant role in the development of cancer through different mechanisms including enhancement of cellular proliferation, promotion of angiogenesis, inhibition of apoptosis, stimulation of invasion and suppression of immune response. Previous reports found that high COX-2 expression may increase the risk of BCC, possibly through the increase in the expression of p53 protein, and suppression of apoptosis. In our study, preliminary results were made for evaluation of COX-2 expression in tissue samples of 30 primary skin basal cell carcinoma cases. COX-2 expression was significantly higher in infiltrating pattern BCC compared with nodular and superficial BCCs. It is necessary to wait for the conclusion of the final results, but our results could suggested that COX-2 expression can be associated with local aggressiveness in BCCs.

**Acknowledgments:** I would like to show my greatest appreciation to Prof. Božena Šarčević. I can't say thank you enough for your tremendous support and help.

**MeSH/Keywords:** MMP1, COX2, basal cell carcinoma, squamous cell carcinoma

**Poster code:** R-B-23-86

## Poster Title: LACUNARITY AND TUMOR BUDDING IN COLORECTAL CARCINOMA

**PhD candidate:** Martina Šarec Ivelj

**Thesis proposal:** The comparison of lacunarity and tumor budding in colorectal carcinoma

**Mentor/s:** Assistant Professor Gorana Aralica, MD, PhD; Paško Konjevoda, MD, PhD

**Affiliation:** University of Zagreb School of Medicine and Clinical Hospital Dubrava Zagreb

**Introduction:** Colorectal cancer is a major health issue. Beside the standard prognostic parameters, the invasive front of colorectal carcinoma should be described and peritumoral budding could be recognised. Tumor budding is considered a parameter of tumor progression and is an indicator of tumor aggressiveness. Pathohistologogical assesment of colonoscopic biopsy sample is the „golden standard" for diagnosis of colorectal cancer. Therefore, an additional histological parameter is used - intratumoral budding. The semiquantitative methods for budding assessment are difficult to reproduce and this is a limiting factor in routine pathology practice. In this study, I will determine lacunarity using computer based image analysis, as a more objective method.

**Materials and methods:** One hundred and ten pathohistological speciments of surgical resection specimens and corresponding preoperative colonoscopic biopsies will be analysed. Tumor budding will be assesed by two pathologists on HE stained specimens using Nakamura method. Lacunarity is defined by computer based image analysis using imunohistochemical slides (cytokeratin AE1/AE3) Data analysis according to AJCC criterias using multivariate tests and algorithms rpart and party.

**Results:** Lacunarity in preoperative colonoscopic biopsies and surgical resection specimens shows statistical significance (Independent Sample T-test, p-value < 0,0001). Arithmetic mean of lacunarity for preoperative colonoscopic biopsies is 1,83 /- 0,02 (arithmetic mean /- SD). For surgical resection specimens arithmetic mean is 1,72 /- 0,03.

**Discussion:** So far, we analysed 25 pairs of pathohistological specimens. The specimens were recorded using different magnifications – 40x, 100x, 250x and 400x. To determine lacunarity only images with 100x magnification were used for computer analysis because we confirmed it is optimal in this research. The result shows that the specimens of preoperative biopsies are more homogenic than surgical resection specimens. To get correlation between tumor budding and lacunarity we have to analyse the rest of our specimens for lacunarity, and to assess tumor budding on all HE stained specimens.

**Acknowledgments:** I express my special thanks of gratitude to my mentors.

**MeSH/Keywords:** carcinoma, biopsy, morphometry, lacunarity, tumor budding

**Poster code:** R-B-23-119

## Poster Title: EARLY BIOMARKERS AND ADVANCED HEMODYNAMIC MONITORING IN ASSESSMENT OF ACUTE KIDNEY INJURY CAUSES IN CHILDREN AFTER CARDIAC SURGERY

**PhD candidate:** Slobodan Galić, MD, MS

**Thesis proposal:** Abstract of preliminary results

**Mentor/s:** Professor Danko Milošević, MD, PhD, Professor Boris Filipović Grčić, MD, PhD

**Affiliation:** University Hospital Centre Zagreb

**Introduction:** Acute kidney injury (AKI) is a serious complication after pediatric surgery. Despite the deleterious impact of pediatric cardiac surgery-associated AKI (pCSA-AKI) on patient outcomes, its pathophysiology remains incompletely understood. So far AKI diagnosis has relied on a rise in serum creatinine (Scr) level. Lines of evidence had shown that NGAL (neutrophil gelatinase-associated lipocalin), KIM-1 (kidney injury molecule 1) and cystatin C (Cys C) were potential markers of AKI. Although the cardiac index (CI) monitoring by transpulmonary thermodilution methodology (TPTDM) has been considered as the gold standard in children, its role in pCSA-AKI evaluation has not yet been validated. The aim of this study is to establish contribution of NGAL, KIM-1 and Cys C, and TPTDM in assesment of pCSA-AKI.

**Materials and methods:** Thirty one children, median age 5.25 years, (min-max 0.5-17) who had undergone cardiac surgery were connected to a PiCCO system (Pulsion Medical System AG, Munich, Germany ) to monitor CI, and pulse contour CI (PCCI), Global End-diastolic Volume Index (GEDVI), Systemic Vascular Resistance Index(SVRI), Global Ejection Fraction (GEF), Oxygen Delivery Index ($DO_2I$) and Oxygen Consumption Index($VO_2I$). Results from each patient were documented before, and immediately after CPB, following 6, 12, and 24 h intervals after CPB. Samples for biomarkers analysis were collected in the same intervals, and their levels were measured according to the manufacturer's recommendations. AKI was defined as a 50% ≥increase in SCr from baseline within 48 h after CPB.

**Results:** According to preliminary data 7 patients (22%) developed AKI. Plasma Cys C levels were significantly higher in AKI patients at 12 h (P=0.016) and 24h (P=0.036) h after CPB. Although statistically not significant, CI/PCCI values were lower in AKI group. GEDVI was significantly lower in AKI group at 6 h (P=0.026) and 12 h (P=0.036) after CPB. SVRI was significantly higher in AKI patients at 6 h after CPB (P=0.022). $VO_2I$ were higher during the first 12 h after CPB, with significant increase 6 h after CPB in AKI group (P=0.021). There were no significant differences in other variables between the two groups.

**Discussion:** Our data suggest that use of investigated biomarkers, primary Cys C, and PiCCO hemodynamic monitoring, could not only provide an earlier diagnosis of pCS-AKI, but also could contribute to a better understanding of its pathogenesis. Additional studies on a larger sample are needed to confirm our results.

**Acknowledgments:**

**MeSH/Keywords:** AKI, Biomarkers, Cardiac Surgery, Hemodynamics, Children

**Poster code:** R-B-24-11

## Poster Title: SURVIVAL PREDICTION OF HIGH-RISK OUTBORN NEONATES WITH CONGENITAL DIAPHRAGMATIC HERNIA FROM CAPILLARY BLOOD GASES

**PhD candidate:** Katarina Bojanić, MD

**Thesis proposal:** Congenital diaphragmatic hernia: the impact of short-term outcome predictors on long-term health and quality of life

**Mentor/s:** Ruža Grizelj, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre Zagreb, Depatment of Pediatrics, University Hospital Merkur, Zagreb, Croatia.

**Introduction:** The presence of respiratory distress in neonates with congenital diaphragmatic hernia (CDH) may indicate severe pulmonary hypoplasia which is a major contributor to morbidity and mortality. In neonates with CDH (i.e., without a concomitant major anomaly or genetic defect), an early presentation of respiratory distress is related to an increased degree of pulmonary hypoplasia. The extent of lung hypoplasia can be assessed from gas exchange. We examined the role of preductal capillary blood gases in prognosticating outcome in patients with CDH.

**Materials and methods:** Medical history was retrospectively reviewed for demographic data, disease characteristics, and preductal capillary blood gases on admission and within 24 hours following admission for 44 high-risk outborn neonates with CDH. All neonates were intubated after delivery due to acute respiratory distress, and were emergently transferred via ground ambulance to the University Hospital Centre Zagreb NICU between 1/2000 and 12/2014. The main outcome measure was survival to hospital discharge and explanatory variables of interest were capillary blood gases obtained on admission and during the first 24 hours following admission.

**Results:** Higher ratio of preductal partial pressure of oxygen to fraction of inspired oxygen ($PcO_2/FIO_2$) on admission predicted survival (AUC=0.69, P=0.04). However, some neonates substantially improve $PcO_2/FIO_2$ following initiation of treatment. Among neonates who survived at least 24 hours, the highest preductal $PcO_2/FIO_2$ achieved in the initial 24 hours was the strongest predictor of survival (AUC=0.87, P=0.002). Nonsurvivors had a mean admission preductal $PcCO_2$ higher than survivors (91±31 vs. 70±25 mm Hg, P=0.02), and their $PcCO_2$ remained high during the first 24-hours of treatment.

**Discussion:** The inability to achieve adequate gas exchange within 24 hours of intensive care treatment initiation is an ominous sign in high-risk outborn neonates with CDH. We suggest that improvement of oxygenation during the first 24 hours, along with other relevant clinical signs, should be used when making decisions regarding treatment options in these critically ill neonates.

**MeSH/Keywords:** congenital diaphragmatic hernia, outcome, survival, clinical prediction, risk assessment, capillary blood gases, neonate, outborn

**Poster code:** R-B-24-34

# Poster Title: GENETIC AND ENVIROMENTAL FACTORS IN CONGENITAL HEART DISEASE DEVELOPMENT

**PhD candidate:** Maša Davidović, MD

**Thesis proposal:** The effect of genetic and environmental factors on congenital heart disease development

**Mentor/s:** Professor Ingeborg Barišić, MD, PhD; Professor Ivan Malčić, MD, PhD

**Affiliation:** Department of Pediatrics, Children's Hospital Zagreb, University of Zagreb School of Medicine/ Department of Pediatrics, University Hospital Centre Zagreb, University of Zagreb School of Medicine

**Introduction:** Congenital heart diseases (CHD) are amongst the most common congenital defects in humans. The etiology of CHD is multifactory, but genetic factors are considered to have a crucial role. Mutations of 55 genes, mostly involved in cardiac development, have been found to cause CHD. Chromosomic abberations are a common cause of CHD, while monogenetic disorders are rare. Gene copy number variants, CNVs, are also considered to have a role in the development of CHD.

**Materials and methods:** Clinical and medical history data as well as blood samples will be collected from 300 patients with CHD. Blood samples will be genetically analyzed, including genome sequencing in selected patients. Sample collection is in progress. Blood samples of 23 patients have been collected and analyzed so far. After collection of all blood samples and clinical information, data will be analyzed statistically.

**Results:** Currently there are 23 patients whose blood samples have been analyzed. Of these 23 patients, 3 patients have DiGeorge syndrome, one has deletion of 8p23.1 (GATA4) and one has mosaic duplication on chromosome locus 8p23. In this small sample 5 out of 23 patients (22%) had a genetic abnormality. However, these results are preliminary and this sample is too small to be of statistical significance. Detailed statistical analysis will be done when all clinical data and blood samples are gathered.

**Discussion:** A large number of genes are involved in cardiac development. Recent studies have proposed that many congenital heart diseases are caused by genetic abnormalities. Unfortunately, the share of genetically caused congenital heart diseases remains unknown to our knowledge. Yet, it is known that around 10% of CHD are caused by chromosomic abberations. In the sample we analyzed until now there were no chromosomic abberations, but this is probably due to the small number of analyzed samples (23). On the other side, 3 out of 23 patients (13%) have DiGeorge syndrome, which is somewhat larger number then expected according to literature data we found. We once again emphasize that our results are incomplete and detailed statistical analysis will be performed when all data is collected.

**Acknowledgments:**

**MeSH/Keywords:** Congenital heart disease CHD/Cardiac development/Chromosomal and single gene disorders/Copy number variants CNVs/exome sequencing

**Poster code:** R-B-24-87

## Poster Title: HEPATIC COMPLICATIONS IN TYPE 1 DIABETES MELLITUS

**PhD candidate:** Mirna Aničić

**Thesis proposal:** Hepatic complications are insufficiently recognized in patients with type 1 diabetes mellitus

**Mentor/s:** Professor Jurica Vuković, MD, PhD

**Affiliation:** Department of Gastroenterology, hepatology and nutrition, University Department of Pediatrics, University Hospital Center Zagreb, Croatia

**Introduction:** Patients with poorly controlled diabetes mellitus type 1(DM1) develop both acute and chronic complications. It is presumed that liver complications are insufficiently diagnosed. Two new entities affecting liver are recognized: glycogen hepatopathy (GH) and nonalcoholic steatohepatitis (NASH). GH is characterized by elevated transaminase, hepatomegaly and accumulation of glycogen in hepatocytes.Wide fluctuations in glucose and insulin concentrations are essential for its pathogenesis.GH can be distinguished from NASH only by liver biopsy. NASH can progress to cirrhosis,while GH seems to be reversible with good glycemic control.

**Materials and methods:** 250 patients (1-25 years), suffering from DM1 more than 1 year will be examined for presence of liver disease.They will be subjected to the following: medical history, physical examination, liver function tests, lipid profile, HbA1c, liver ultrasound(US) and screening for coeliac disease, autoimmune thyroiditis, nephropathy and retinopathy.Patients with abnormal liver function tests will be further investigated to exclude other liver disease (infectious, autoimmune, metabolic-alpha 1 AT deficiency, Wilson disease, hemochromatosis). MRI of the liver will be performed in those with abnormal laboratory and/or US. Percutaneous liver biopsy will be done in patients with verified liver disease.

**Results:** So far 18 patients with DM1 were examined for the presence of liver disease.8 patients had good metabolic control (HbA1c≤8.0), normal transaminase and US. 10 had poor metabolic control (HbA1c>8.0) and among them 2 had elevated transaminase and hepatomegaly on US.They had no chronic complications (nephropathy, retinopathy) or associated autoimmune disease.We excluded other causes of hepatitis. MRI showed abundant steatosis in one patient and that was confirmed on liver biopsy. Liver biopsy of other patient showed signs of glycogen hepatopathy, and MRI was not done due to technical difficulties, but will be as soon as possible. Other 8 patients with poor metabolic control had normal transaminase and US.

**Discussion:** Collected data are yet insufficient for statistical analysis, but preliminary results suggest that liver disease is present in poorly regulated patents with DM1. Our results confirm scarce data in literature, where prevalence of liver disease in DM1 patients is about 10%. We will try to determine the prevalence of liver disease in children and adolescents with DM1 and examine the factors that contribute the most.

**Acknowledgments:**

**MeSH/Keywords:** diabetes mellitus type 1, poor glycemic control, hepatic complications, glycogen hepatopathy, NASH

**Poster code:** R-B-24-116

## Poster Title: IMAGING FEATURES AND CLINICAL PRESENTATION OF BREAST CANCER PATIENTS AT UNIVERSITY CLINICAL CENTER OF KOSOVA – PRISTINA

**PhD candidate:** Ardian Bicaku, MD

**Thesis proposal:** Imaging features and clinical presentation of breast cancer patients at University Clinical Center of Kosova – Pristina

**Mentor/s:** Professor Boris Brkljačić, MD, PhD

**Affiliation:** University of Zagreb, School of Medicine, UH "Dubrava", University Clinical Center of Kosovo, Pristina, Clinic of Radiology

**Introduction:** Breast cancer (BC) is a major source of disease burden among women in developed countries, and in many developing countries the incidence and mortality rates are increasing. Kosovo is a country with no BC screening program and a country with many different features compared to European countries with regard to health care system, population age and attitude of women in public towards BC.

**Materials and methods:** These are preliminary data from 36 patients diagnosed with BC at University Clinical Center of Kosovo, Clinic of Radiology, Department of Breast Imaging (UCCK-CR-DBI). Total sample size will include 250 patients diagnosed with BC through period 2015-2016. Demographic characteristics and clinical data regarding breast care, mammography (MMG), ultrasound (US), histopathologic (HP) data and surgery procedure (if available) data are prospectively analyzed for patients diagnosed with BC. Only subjects with signed informed consent approved by local Ethical Committee (University Clinical Centre of Kosovo) are presented in the study. Descriptive statistical methods are applied in data analysis.

**Results:** At the time of writing this abstract, 36 patients of age group 35-77 diagnosed with BC are included. 19 BC patients are included from pilot screening project of mobile mammography, where screening mammography was the first imaging modality in detecting BC. From 17 patients diagnosed with BC at UCCK-CR-DBI, three patients were referred to our department from spinal-orthopedic clinic with vertebral pathologic fractures from bone metastases and BC was found as primary tumor. In five out 14 patients BC was detected with US as first imaging modality. In nine patients diagnostic mammography due to clinically apparent signs (lump, skin and/or nipple retraction and in two cases skin ulceration) was performed as primary imaging modality in detecting BC. Only one DCIS is found. Lobular invasive carcinoma (LIC) was found in one patient with vertebral pathologic fracture from metastases. Tumor size varied from 1.3 to 5.2 cm.

**Discussion:** Advanced stages of BC with large palpable cancers (often with metastases at the time of detection) predominated before the introduction of organized breast screening, are present in non-attending women for screening and are still present in countries without organized screening.

**Acknowledgments:** I would like to thank my mentor and my colleagues from UCCK.

**MeSH/Keywords:** breast cancer, mammography, morphology, Kosovo

**Poster code:** R-B-25-115

## Poster Title: INFLUENCE OF RADIOTHERAPY ON APPARENT DIFFUSION COEFFICIENT VALUE OF NORMAL BREAST TISSUE AND LESIONS AT MRI

**PhD candidate:** Niko Radović, MD

**Thesis proposal:** Influence of radiotherapy on apparent diffusion coefficient value of normal breast tissue and lesions at MRI

**Mentor/s:** Asst. Prof. Gordana Ivanac, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Dubrava, Clinical Department for Diagnostic and Interventional Radiology

**Introduction:** Magnetic resonance diffusion weighted imaging (MR DWI) accompanied by measurement of apparent diffusion coefficient (ADC) increases specificity for breast cancer detection by 13.5% compared to conventional dynamic contrast enhanced (DCE) MR alone. In the context of residual and recurrent tumor detection at DWI following breast conserving surgery (BCS) with radiotherapy (RT) the influence of radiation-induced changes of breast tissue should be considered, and consequently different ADC values of normal tissue and „non mass" lesions should be expected when compared to values in untreated breast.

**Materials and methods:** The ongoing study will include 100 female patients referred for clinical breast MR imaging with various indications. Exams consisting of conventional non-contrast sequences as well as DWI and DCE MR are performed using a 1.5T machine with dedicated breast coils. ADC measurements are recorded for a given region by drawing regions of interest (ROIs) on the parametric map using b-values of 0, 800 and 1000. All detected lesions are diagnosed according to the ACR-BIRADS lexicon and patients with suspicious lesions subsequently undergo biopsy.

**Results:** Preliminary results obtained from 50 patients are not consistent with our hypothesis that histologic changes induced by RT following BCS result in higher average ADC values of normal breast tissue when compared to values in untreated breast. In contrast, average ADC values of breast parenchyma are shown to be significantly lower ($p < 0.001$) in treated breast. At this moment, preliminary results for ADC values of breast lesions are unavailable.

**Discussion:** Measured ADC values of breast tissue are affected by cellular density as well as its overall water-content. Preliminary results obtained from our study suggest the influence of the former is obscured by the latter in breast tissues of patients who underwent RT. Fibrous tissue, which is very low in water content, proliferates following RT, therefore ROIs drawn on ADC maps of treated breasts will cover areas with significantly lower average water content, resulting in lower values of ADC.

**Acknowledgments:**

**MeSH/Keywords:** breast cancer, MR, DWI, ADC, breast conserving surgery, radiotherapy

**Poster code:** R-B-25-140

**Poster Title: THE RELATIONSHIP BETWEEN NEUROCOGNITIVE STATUS AND PSYCHOPATHOLOGY, TREATMENT RESPONSE AND VARIANTS OF GENES MTHFR AND ZNF804A IN PATIENTS WITH THE FIRST PSYCHOTIC EPISODE**

**PhD candidate:** Ivana Kekin, MD

**Thesis proposal:** The relationship between neurocognitive status and psychopathology, treatment response and variants of genes MTHFR and ZNF804A in patients with the first psychotic episode

**Mentor/s:** Assist. Prof. Martina Rojnić Kuzman, MD, PhD

**Affiliation:** University Hospital Centre Zagreb, University of Zagreb, School of Medicine

**Introduction:** Schizophrenia is one of the most disabling psychiatric illnesses, affecting about 1% of population worldwide. In majority of cases, schizophrenia is a chronic illness with a reccurent course, characterized by alternating periods of acute psychotic illness and its remission Clinical presentation includes cognitive symptoms from the beginning of the disease. Cognitive symptoms in schizophrenia have strong biological basis that is defined from the genetic level.

**Materials and methods:** In this study we are planning to include one hundred of up to that moment untreated patients with FEP, and one hundred of healthy controls. The first test will be conducted in the first two weeks of hospitalization and it will include: a detailed psychiatric interview, taking sociodemo- graphic data, and a variety of clinical questionnaires aiming at assessing the psychiatric and neurological data. During the conduction of the test blood samples will be taken with the aim of genotyping. Also, using the Transcranial Doppler Ultrasonography Method (TCD) we will cerebral blood vessels we will examine the changes in the speed of cerebral blood flow in the medium and anterior cerebral artery while conducting a neurocognitive paradigm consisting of three cognitive tasks, lasting 25 minutes. The second test will be conducted after 12 to 18 months, that is after achieving the full remission and it will again include assessment of psychiatric and neurocognitive status and TCD.

**Results:** Up to this moment we enrolled 45 patients in the study. Also we retested 15 of them. We included patients that were admitted to psychiatric ward with psychotic symptoms highly suggestive of schizophrenia. First assessment and TCD were performed during their inpatient treatment. All of them are treated with antipsychotics and 15 of them have reached a full remission so we retested them as planned. No relevant statistical analyses have been done so far.

**Discussion:** We still don't have preliminary results, but we expect the results of this study to show the changes in the neurocognitive functioning during FEP and a consequential remission in comparison to a healthy control group. Also, we expect to find correlation between the therapeutic response/progression of ilness measured by neurocognitive symptoms and variants of MTHFR and ZNF904A genes.

**Acknowledgments:**

**MeSH/Keywords:** schizophrenia, neurocognitive, MTHFR, ZNF804A

**Poster code:** R-B-29-49

## Poster Title: THE CONCENTRATION OF TRACE ELEMENTS IN THE HAIR OF PEOPLE WITH SCHIZOPHRENIA

**PhD candidate:** Ivana Todorić Laidlaw, MD

**Thesis proposal:** The concentration of trace elements in the hair of people with schizophrenia

**Mentor/s:** Professor Ninoslav Mimica, MD, PhD, Professor Berislav Momčilović, MD, PhD

**Affiliation:** Psychiatric Hospital Sveti Ivan, Zagreb

**Introduction:** Schizophrenia is a severe mental disorder, characterized by profound disruptions in thinking, affecting language, perception, and the sense of self. Differences in the concentration of trace elements can play an important part in the pathogenesis of schizophrenia.

**Materials and methods:** The target population included individuals diagnosed with schizophrenia of both sexes, between 25 and 35 years of age, permanently resident in the area of the City of Zagreb, hospitalized in the Psychiatric Hospital Sveti Ivan and University Hospital Vrapče. The control group was composed by employees, not affected by psychiatric illnesses and homogeneous by age, sex and residence. Samples of hair were taken from the area located between the scalp and the occipital region, cut off and prepared for analysis according to scientific standards. Data about demographic, social, nutritive and clinical parameters are gathered through the questionnaire. The Brief Psychiatric Rating Scale (BPRS) was used to measure psychiatric symptoms.

**Results:** Previous studies have confirmed there are differences between the concentration of bioelements but were conducted using insufficiently sensitive analytical procedures, and with no data on a larger number of bioelements in the same sample of biological matrices. The samples were analyzed using Inductively Coupled Plasma Mass Spectrometry at the Centre of Medical Research in Zagreb but the statistic analysis of the data has not yet been performed.

**Discussion:** Findings about different concentrations and main concentration components of trace elements may contribute to the better understanding of the pathogenesis of schizophrenia and may contribute to understand former contradictory results.

**Acknowledgments:** I would like to thank my mentors Professor N. Mimica and Professor B. Momčilović for their support, teachings and guidance. I also would like to thank doctor Jasna Jurasović for her help and cooperation.

**MeSH/Keywords:** Schizophrenia, Trace elements, Multielement profile, ICP-MS, hair

**Poster code:** R-B-29-50

## Poster Title: GROUP SUPPORTIVE PSYCHOTHERAPY EFFICACY IN TREATMENT OF SCHIZOPHRENIA

**PhD candidate:** Nataša Đuran, MD

**Thesis proposal:** Group supportive psychotherapy (GSP) efficacy in treatment of schizophrenia, a randomized control trial

**Mentor/s:** Professor Vlado Jukić, MD, PhD

**Affiliation:** University Psychiatric Hospital Vrapče

**Introduction:** Schizophrenia is a set of symptoms that affects thinking, mood, perception and behavior. Despite the new anti-psychotics the illness is not well controlled in about 40% of patients. In this randomized controlled trial efficacy of group psychotherapy by Kanas model will be compared to the standard therapy.Below are the preliminary results of clinical trials.

**Materials and methods:** We are conducting a unicentric, prospective, interventional, randomized, controlled study. The research is conducted at a hospital Vrapče in Zagreb. The target population makes the general population of patients diagnosed with schizophrenia (MBK-10, F20), the hospital treated by maintenance therapy with new atypical antipsychotics. We use stratified block randomization, the ratio of the experimental and control groups 1:1. Investigator will do the screening and enrolling patients, and each participant assigned a code number. Randomization is done by an independent IT company. Measurement of the main outcomes will not be blinded because the risk of systematic errors in determining the number of re-hospitalisation is negligible. Measurement of secondary outcome (remission defined PANSS and CGI-) is be blind. Initial measurement and measurement after 12 months will spend a psychiatrist who did not participate in the intervention.

**Results:** Clinical trials began in November 2015. So far in trial we have included thirty-six male schizophrenic patients aged between thirty and sixty. We randomized thirty –five patients. Nineteen patients were treated with pharmacotherapy and usual individual support, this is control group, and 16 patients were included in group psychotherapy. In supportive group were four or five patients. The average age of patients in the control group was forty-five years, and the average age of patients included in group psychotherapy was forty years. Treatment completed seventeen patients in the control group and twelve patients included in group psychotherapy. One patient from control group was re-hospitalized. So far, nobody from the group that is included in the group psychotherapy is re-hospitalized. Differences in the PANSS have not compared yet.

**Discussion:** Effectiveness of the Group supportive psychotherapy can be new knowledge about the psycho-social supportive treatment of schizophrenia and thereby contribute to further understanding and shaping the bio- psycho - social model of treatment.

**Acknowledgments:** Professor Vlado Jukić, MD, PhD, psychiatrist

**MeSH/Keywords:** schizophrenia, group psychotherapy

**Poster code:** R-B-29-60

## Poster Title: SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS OF METHODS OF COMPLEMENTARY AND ALTERNATIVE MEDICINE IN THE TREATMENT OF GENERALIZED ANXIETY DISORDER: IDENTIFICATION AND SELECTION OF STUDIES RESULTS

**PhD candidate:** Hrvoje Barić

**Thesis proposal:** Systematic review and meta-analysis of randomized controlled trials of methods of complementary and alternative medicine in the treatment of generalized anxiety disorder

**Mentor/s:** Professor Vladimir Trkulja, MD, PhD, Professor Veljko Đorđević, MD, PhD

**Affiliation:** University of Zagreb School of Medicine

**Introduction:** There have been no comprehensive systematic reviews on safety and efficacy of Complementary and Alternative Medicine (CAM) therapies in the treatment of Generalized Anxiety Disorder (GAD). A number of randomized controlled trials (RCTs) examining CAM interventions in GAD have been published during the last 15 years. We aimed to examine whether there is empirical evidence of acceptable methodological quality for the clinical efficacy of CAM interventions in GAD treatment. CAM interventions are widely used as therapy, so its efficacy and safety have to be clearly established.

**Materials and methods:** We conducted a comprehensive literature search in PubMed, Web of Science, EBSCO, Scopus, Google Scholar, and the Cochrane library from January 2000 to December 2015 using the following key words: „generalized anxiety" and „randomized trial". We checked the reference sections of previously published meta-analyses and periodically checked for newly published trials until April 2016. Considered eligible were studies which: (a) were randomized controlled trials (RCTs) (b) examined the effects of a CAM intervention, alone or in combination with another treatment, (c) compared the effects of a CAM intervention to a control group, another active treatment or a combination of treatments, (d) included adult subjects, (e) assessed clinically relevant outcomes, (f) assessed the condition (GAD) with established measures and (g) published in peer-reviewed scientific journals in English or German.

**Results:** We examined a total of 7696 records (6609 after duplicates were removed) and excluded 6559 based on inspection of the abstract. We retrieved the full text of the remaining 50 articles. This process resulted in 37 RCTs that met our inclusion criteria and are further to be assessed for quality (Figure 1).

**Discussion:** We conducted a systematic literature search and identified 37 RCTs which investigated CAM safety and/or efficacy in treatment of GAD. RCTs of interventions from four groups of CAM therapies were identified: biologically-based therapies (n=22), manipulative and body-based therapies (n=8), alternative medical systems (n=5), and mind-body therapies (n=2). Before final inclusion in the meta-analysis, all RCTs will be assessed for quality, after which data will be extracted and quantitative analysis will be performed.

**Acknowledgments:** I would like to thank both mentors for guidance and support.

**MeSH/Keywords:** complementary therapies, meta-analyis, generalized anxiety disorder

**Poster code:** R-B-29-83

## Poster Title: PREDICTING RISK OF HIGH HEALTHCARE COSTS IN ALZHEIMER PATIENTS – PROSPECTIVE COHORT STUDY

**PhD candidate:** Jelena Sušac, MD, psychiatrist

**Thesis proposal:** Predicting risk of high healthcare costs in Alzheimer patients - prospective cohort study

**Mentor/s:** Professor Ninoslav Mimica, MD, PhD; Professor Dinko Vitezić, MD, PhD

**Affiliation:** Health Center Zagreb Zapad, University Psychiatric Hospital Vrapče

**Introduction:** Alzheimer's disease (AD) is a neurodegenerative, progressive and incurable disease with a heterogeneous aetiology. Neurodegenerative diseases that lead to dementia in the health, social and economic indicators (costs of support and treatment of patients with AD in the Western world will soon be the same as common costs for cardiovascular disease, cancer and stroke together) have today a huge significance. The objective of this research is to design and internally validated multivariate predictive model on highest expenses for AD.

**Materials and methods:** This research is unicentric, observational and applied (prospective cohort, prognostic study). It is conducted at the Health Center Zagreb Zapad. Target population are patients diagnosed with Alzheimer's disease who live in private households at the time of inclusion in the study. Estimated sample size is 205 patients (by two-stage, stratified random sampling). The main outcome is the upper quartile of the total cost of treatment for formal and informal care. It will be measured by calculating the cost of formal medical and social care and treatment at average prices and with Resource Utilization in Dementia (RUD) questionnaire.

**Results:** The research is in the very early stage and small number of data is collected so far. There aren't any preliminary results available.

**Discussion:** This model can be used in early recognition of patients at higher risk of high costs of future health care and thus more quality and financially accountable organization of health care and more proper allocation of resources.

**Acknowledgments:** Professor Ninoslav Mimica, MD, PhD, Professor Dinko Vitezić, MD, PhD, Miroslav Hanževački, MD, PhD

**MeSH/Keywords:** Alzheimers disease, costs, predictive model

**Poster code:** R-B-29-76

## Poster Title: SUICIDALITY AND AGGRESSION OF ALCOHOL ADDICTS AND OPIATE ADDICTS IN RELATION TO INTERNET DEPENDENCE COMORBIDITY

**PhD candidate:** Irena Rojnić Palavra, MD

**Thesis proposal:** Suicidality and aggression is higher in alcohol addicts and opiate addicts with comorbid internet dependence than in alcohol addicts and opiate addicts without comorbid internet dependence

**Mentor/s:** Prof. Vlado Jukić, MD; Assist. Prof. Ante Bagarić, MD

**Affiliation:** Croatian National Institute of Public Health, Clinic for Psychiatry Vrapče

**Introduction:** Internet dependence is not yet an official diagnosis. Still, it is clear that the number of persons searching professional help due to internet related problems raises. The symptoms usually meet criteria of addiction: loss of control and compulsive use, tolerance, abstinence crisis, continuation of use despite negative consequences, neglect of other life pleasures… Also, in accordance with our thesis, literature data indicate that suicidality and aggression could be higher in alcohol addicts and opiate addicts with comorbid internet dependence than in alcohol addicts and opiate addicts without comorbid internet dependence, but this is to be clarified yet.

**Materials and methods:** Our sample is made of 274 alcohol addicts and 274 opiate addicts, aged 18-50, hospitalized in the Department for addiction treatment of the Clinic for psychiatry Vrapče. The tool for research conduction is a questionnaire made of several parts: socio-demographic characteristics, socioeconomic characteristics, characteristics and circumstances of internet use, Internet addiction test (Young KS), The suicidal behaviors questionnaire-revised - SBQ-R (Osman A et al.), The aggression questionnaire (Buss AH, Perry MP) and The big five inventory (John OP, Benet-Martinez V). Control of confounders will be performed. Statistical analysis will be done with the level of statistical significance $p < 0.05$ and confidence interval CI 95%.

**Results:** From the last year's report, we defended our PhD thesis which was adopted by the faculty. Also, we finished our questionnaire and printed it in 600 copies. We set technical standards for survey conduction and now we are about to start with the pilot phase of the survey on 50 patients. If analysis shows expert and scientific adequacy, we'll proceed with the main survey. So far we don't have preliminary results but tend to have them in the nearest future.

**Discussion:** With this research we hope to identify frequency of internet dependence among alcohol addicts and opiate addicts and to determine differences in suicidality and aggression of persons suffering from alcoholism or opiate addiction with comorbid internet dependence. This data could be of great value, since at the moment there is no similar published information.

**Acknowledgments:** I thank my mentors for guidance and devoted help.

**MeSH/Keywords:** internet

**Poster code:** R-B-29-131

# Poster Title: OBSTRUCTIVE SLEEP APNEA SYNDROME AND AUTONOMIC NERVOUS SYSTEM

**PhD candidate:** Marina Mioč

**Thesis proposal:** Impact of Obstructive Sleep Apnea Syndrome on Macrostructure and Microstructure of Sleep and Function of Cardiovascular Autonomic Nervous System

**Mentor/s:** Assistant professor Mario Habek, MD, PhD, Barbara Barun, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre Zagreb

**Introduction:** In patients with obstructive sleep apnoea syndrome (OSA), upper airways tend to collapse during sleep which leads to intermittent hypoxia and sleep fragmentation. This results in structural damage of the brain which could cause autonomic system damage.

**Materials and methods:** One hundred and six patients will be recruited, 53 patients with OSA and 53 healthy controls. To participate in the study patients have to be older than 18 years. Exclusion criteria are: cognitive and psychiatric disorders, contraindication for tilt-table testing, pregnancy, therapy for sleep disorders and medications that affect autonomic nervous systems. Subjects who meet the criteria will fill out questionnaires for evaluation of sleep quality, do overnight polysomnography and autonomic nervous system testing.

**Results:** The number of patients currently included in the research is forty six. 52.2 percent were men and 47.8 were women, mostly middle-aged (mean 47 years). Based on overnight polysomnography, 16 subjects were diagnosed with OSA (34.8 percent) and 30 were non-OSA subjects. Based on apnoea-hypnoea index six subjects were diagnosed with mild, three with moderate and seven with severe OSA. Four patients were diagnosed with Postural Orthostatic Tachycardia Syndrome (POTS) and ten patients with Orthostatic Hypotension in autonomic system testing. Disorders of adrenergic autonomic system were quantified as mild (score 1), moderate (score 2) and severe (score 3 and 4) based on results from Valsalva manoeuvre and tilt test. Disorders of cardiovagal system were also qualified as mild, moderate and severe, for calculation were used results of deep breathing test and Valsalva ratio. Twenty subjects had normal results of cardiovagal testing, twelve had score 1, seven had score 2 and none had score 3. Seven results could not be interpreted because of patient's inability to perform the test. Adrenergic score couldn't be interpreted in nine patients due the same reason, four patients had score 1, two had score 2, six had score 3, three had score 4 and 22 had normal result of adrenergic testing. In statistical analysis we used Chi-square test and we didn't find a statistically significant difference between OSA and non-OSA subjects and results of their cardiovagal and adrenergic scores.

**Discussion:** Based on previous studies we expected to find higher frequency of impairment of autonomic nervous system in OSA patients. We will take these preliminary results as an incentive for further research.

**Acknowledgments:** I would like to thank my mentors Barbara and Mario.

**MeSH/Keywords:** sleep disorders, sleep microstructure, autonomic nerve function.

**Poster code:** R-B-30-74

## Poster Title: CORRELATION OF THE VEMP SCORE, AMBULATION AND UPPER EXTREMITY FUNCTION IN CLINICALLY ISOLATED SYNDROME

**PhD candidate:** Luka Crnošija, dr.med.

**Thesis proposal:** The modified evoked potentials score in the follow-up of clinically isolated syndrome

**Mentor/s:** doc.dr.sc. Mario Habek

**Affiliation:** School of Medicine, University of Zagreb

**Introduction:** The aim of this study was to investigate the correlation of the brainstem function with upper and lower extremity function, cognitive function and general disability in patients with first symptoms of multiple sclerosis (i.e. patients with clinically isolated syndrome or CIS).

**Materials and methods:** This cross sectional study included 52 consecutive patients diagnosed with CIS from the 1st of August 2014 until 1st of May 2015 at the Department of Neurology, University Hospital Center Zagreb. Brainstem function was estimated by the cervical and ocular vestibular evoked myogenic potentials (cVEMP and oVEMP respectively) expressed in the form of cVEMP, oVEMP and total VEMP scores. oVEMP evaluates the upper part of the brainstem (midbrain and upper pons), while cVEMP evaluates the lower part of the brainstem (lower pons and medulla oblongata). General disability index, the so called Expanded Disability Status Scale (EDSS), was determined and Timed 25-Foot Walk (T25FW), 9-Hole Peg Test (9HPT), and Paced Auditory Serial Addition Test (PASAT) were performed. T25FW was used as a quantitative mobility and leg function performance test, 9HPT as quantitative test of upper extremity function, and PASAT as a measure of cognitive function.

**Results:** oVEMP score correlated with the T25FW (r=0.280, p=0.045), but after controlling for age, gender, PASAT and EDSS the effect of oVEMP score was non-significant (p=0.419). The only predictor of walking impairment in this study was general disability index, i.e. EDSS. After controlling for age, gender, PASAT and EDSS, the effect of the oVEMP score on 9HPT of the dominant hand was statistically significant (p=0.017). Also, after controlling for age, gender and oVEMP score, the effect of the PASAT on 9HPT variable for the non-dominant hand was statistically significant (p=0.001).

**Discussion:** This study indicates a possible effect of brainstem dysfunction on walking impairment, however this was not seen after correction for EDSS and cognitive dysfunction. On the other hand, dominant hand function seems to be influenced by upper brainstem dysfunction measured with oVEMP, while cognitive dysfunction may be related to non-dominant hand function.

**MeSH/Keywords:** clinically isolated syndrome, upper extremity, lower extremity, cognition, brainstem, vestibular evoked myogenic potentials

**Poster code:** R-B-30-160

# Poster Title: THE SIGNIFICANCE OF THE POSTPROCESSING BRAIN MRI (MAGNETIC RESONANCE IMAGING) IN THE PREOPERATIVE DIAGNOSIS OF PATIENTS WITH PHARMACORESISTANT EPILEPSY

**PhD candidate:** Andreja Bujan Kovač, MD

**Thesis proposal:** The significance of the postprocessing brain MRI (magnetic resonance imaging) in the preoperative diagnosis of patients with pharmacoresistant epilepsy

**Mentor/s:** Professor Sanja Hajnšek, MD, PhD and Assistant professor Milan Radoš, MD, PhD

**Affiliation:** University Hospital Centre Zagreb and School of Medicine, University of Zagreb, Department of Neurology, Referral Centre for Epilepsy of the Ministry of Health of the Republic of Croatia

**Introduction:** Epilepsy is chronic disease of the central nervous system that affects 1% of the population. Approximately 25-35% are pharmacoresistant and can be considered for neuro-surgical treatment. The most important neuroradiological procedure in selection candidates for neurosurgery is MRI 3T (magnetic resonance imaging). However, some lesions are CVA (conventional visual analysis) and MRI negative. Post-processing of brain MRI with MAP07 software (Morphometric Analysis Program) is a new sophisticated diagnostic procedure that offers a number of graphical post-processing maps which facilitates detection and localization of subtle structural epileptogenic lesions.

**Materials and methods:** 100 patients with epilepsy will be recruited and processed according to algorithm which includes Phase I and in pharmacoresistant patients Phase II of preoperative assessment. 3T MRI performed according to the protocol for epilepsy will be analysed by neuro-radiologist and classified as MRI positive or MRI negative. Then, postprocessing of brain MRI with MAP07 will be performed and marked as MAP07 positive or negative. After re-examining of all MRI sequences by neuroradiologist findings will be determined as MAP07 positive/MRI positive or MAP07 positive/MRI negative.

**Results:** So far 37 patients with pharmacoresistant epilepsy have been recruited, 23 women and 14 men. The average age of patients is 40 ± 13.67 years. 62% of patients have complex partial seizures with or without secondary generalization. Our analysis indicates that 70.3% findings are MAP07 positive/MRI positive. In 5 patients with normal 3T MRI, MAP07 analysis showed structural epileptogenic lesions (MAP07 positive/MRI negative) which ultimately led to neurosurgical operation in two patients (selective amygdalohippocampectomy) or in one patient minimally invasive neurosurgery and implantation of VNS (Vagus nerve stimulator). Two patients declined operative treatment.

**Discussion:** Preliminary results of this research are promising, especially in the detection of subtle malformations (focal cortical dysplasias, subtle gray matter heterotopias and mesial temporal sclerosis). Implementation of MAP07 in routine preoperative assessment of patients with refractory epilepsy may help in detection of subtle epileptogenic lesions and lead to early decision of resective neurosurgical treatment. However, more patient should be recruited and extensive statistical analysis is needed in order to objectify the results.

**Acknowledgments:** Prof. Sanja Hajnšek, MD, PhD and Assist. Prof. Milan Radoš, MD, PhD

**MeSH/Keywords:** epilepsy, post-processing, malformation of cortical development, hippocampal sclerosis

**Poster code:** R-B-30-162

# 1.3.
## RESEARCH ABSTRACTS
## Public Health and Health Care

## Poster Title: MORTALITY IN FORMER PRISONERS OF WAR – A HEALTHY CONSCRIPT PARADOX

**PhD candidate:** Pero Hrabač, MD

**Thesis proposal:** Specialties of morbidity and mortality in the population of Croatian war veterans from the Homeland war

**Mentor/s:** Prof. Neven Henigsberg, MD, PhD

**Affiliation:** Croatian Institute for Brain Research, School of Medicine, University of Zagreb, šalata 12, 10000 Zagreb, Croatia

**Introduction:** The data on long-term mortality of former prisoners of war (POWs) from Croatian Homeland war are contradictory and scarce. Our aim was to compare all-cause mortality between former Croatian POWs and Croatian general population in the period from 1997 (first year for which data are available) to 2010 (last year for which data are available AND subjects are still identified by the old method ŠJMBGĆ instead of the new OIB number).

**Materials and methods:** The data regarding POW deaths were retrieved from the database of exchange of imprisoned persons and matched with the death registry data for the general population.

**Results:** Among 5.614 former POWs aged 18 to 65 years at the time of release, 743 have died. Among the male ex-POWs, a total number of deceased persons between 1997 and 2010 was 687, resulting in the standardized death rate (SDR) of 10,8/1.000 (95% CIs 8,4 - 13,4) per year, which is significantly different from the average CDR of 15,0/1.000 seen in general population.

**Discussion:** There is a significant number of studies on ex-POWs. A number of studies with results of long-term follow-up in such populations is scarce. Some studies deal with POWs during their captivity or immediately after release (Lee, Korea, N=7,614). Some studies with follow-up element in their design focus on only one disease such as PTSD (Rintamaki), Parkinson's disease (Gale), tuberculosis (Cohen) etc. Historical studies describe consequences of imprisonment in past wars, such as Costa with the American Civil War. Finally, there are studies overcoming mentioned drawbacks, but often suffer from a small sample size - Gill (WWII, N=180), Nice (Vietnam, N=70) and Solomon (Israel, N=154). Our aim was to establish a well-defined and methodologically sound basis for long-term follow-up of the Croatian ex-POWs. First results described here show results up to year 2010, mainly due to bureaucratic reasons. Crude death rates for the ex-POW population were found to be lower compared to general population. This is a paradoxical finding, but it is described elsewhere and based mainly on a "healthy conscript" effect. With the majority of POWs being soldiers, it is expected that this sub-population will have the better long-term results compared to the civilian population because they had to have a more or less clean bill of health before joining the armed forces. However, we expect the differences between POW and the general population to become more pronounced with the passage of time.

**Acknowledgments:**

**MeSH/Keywords:** Prisoners of war, Croatian Homeland war, Mortality

**Poster code:** R-C-1-2

# Poster Title: WEST NILE VIRUS INFECTION IN CROATIA

**PhD candidate:** Iva Pem Novosel, MD

**Thesis proposal:** Risk factors analysis of West Nile Virus infection in Croatia

**Mentor/s:** Assist. Professor Tatjana Vilibić-Čavlek, MD, PhD, Professor Ljubo Barbić, VMD, PhD,

**Affiliation:** Croatian Institute of Public Health (CIPH), Faculty of Veterinary Medicine University of Zagreb

**Introduction:** West Nile (WN) fever/encephalitis is a vector-borne disease caused by globally widespread WN virus that belongs to the genus Flavivirus, family Flaviviridae. The transmission cycle of WNV is maintained in nature in an enzootic cycle between birds and competent mosquitoes. They can act as bridge-vectors that feed both on birds as the principal host as well as on incidental hosts such as humans and horses.

**Materials and methods:** Study design: Series of cross-sectional studies. Human (patients with WNV disease/asymptomatic subjects) and horse serum samples from counties with reported human clinical cases. Stratified multiphase consecutive sample. Human samples were tested for WNV IgM/IgG antibodies by ELISA and confirmed by neutralization test. Horse samples have been tested for WNV IgG antibodies by ELISA. Reactive samples were tested for IgM antibodies.

**Results:** In September 2012, first 7 human cases of WNV neuroinvasive infection were confirmed in three eastern counties. Acute asymptomatic infection was detected in 12 sentinel horses before notification of human cases. After 2012 season, WNV seroprevalence was 10,1-17,4% in horses, 1,7-2,7% in humans from the same area and 1,4-2,2% from northwestern counties. During 2013, WNV infection was confirmed in 20 patients with clinically suspected neuroinvasive disease from Northwest Croatia. WNV IgG seropositivity was 1,6-2,7% in the population of affacted area, 2,7-10,2% in horses, 2,2-3,1% in humans from eastern counties and 7,0-16,3% in horses. In 2014 one human case was detected in Brod-Posavina County with seroprevalence of 2,2%, while in horses was 3,8%.

**Discussion:** Clinical WNV cases were not reported before 2012 in Croatia, only serological evidence of WNV cirrculation in humans and horses was documented. First clinical WNV neuro-invasive disease outbreak with 7 human cases was documented in September 2012 with acute asymptomatic infection in 12 sentinel horses. A seroprevalence rate was analyzed after WNV season and showed an increase in humans from affected area 1,7-2,7% vs.0-0.3% 2011, as well as in sentinel horses 10,1-17,4% vs.1,9-15,2% 2011. Further 20 cases of WNV infection were notified in 2013 in Northwest of Croatia and only one case in 2014. WN seroprevalence in horses increased in most eastern counties during 2013-2014. The occurrence of WN cases is influenced by various factors such as climatological conditions (temperature, rainfall), geomorphological features and vector control measures.

**Acknowledgments:** I would like to thank my mentors and all laboratory personnel.

**MeSH/Keywords:** West Nile virus, epidemiology, Croatia

**Poster code:** R-C-1-149

## Poster Title: EFFECTIVENESS OF COST CONTAINMENT INTERVENTIONS ON PUBLIC PHARMACEUTICAL EXPENDITURE IN CROATIA

**PhD candidate:** Hilarije Baričević

**Thesis proposal:** Effects of European Regulatory Measures for Pharmaceutical Sector on Public Spending of Outpatient Drugs in Croatia

**Mentor/s:** Prof.dr.sc. Stjepan Orešković

**Affiliation:** Krka

**Introduction:** Outpatient pharmaceutical expenditure is one of the largest items in healthcare budgets of EU member states and it is in constant increase. In attempt to restrain this growth health authorities in Europe have introduced numerous regulatory interventions that have affected pharmaceutical sector. This research contributes to the existing literature by providing an accurate in continuo analysis of the impact of repeated pharmaceutical cost containment measures not only on expenditures but also on the accounting factors that explain expenditure growth in Croatia.

**Materials and methods:** In a retrospective, observational study data on public expenditure of outpatient prescription drugs and from 2000-2014 implemented pricing and reimbursement measures were used. For the statistical analysis ARIMA method was used. The method is suitable because it allows determination of statistically significant changes in the outcome variables dependent on the sequencing of the implemented pricing and reimbursement measures (predictor set of variables), taking into account the characteristics of the available data (autocorrelation, trend, seasonality). Dependent variables are average value of total expenditure of outpatient prescription drugs per capita, number of prescriptions per capita and expenditure per prescription. The effectiveness of interventions was defined as any significant change of the dependent variable. The level of significance was $\alpha = 0.05$.

**Results:** Preliminary results show that majority of interventions despite of price reductions were not effective in reducing pharmaceutical expenditure growth in the long term. Expenditure per prescription had CAGR of -2.72% but overall expenditure grew with CAGR of 2.72 % and prescriptions per capita also with CAGR of 4.62 % in period 2000-2014.

**Discussion:** Many measures that were effective in reducing price of outpatient drugs weren't effective in reducing pharmaceutical expenditure in long term. Possible explanation for this behaviour lies in market mechanisms that were developed in anticipation or as reaction on interventions. In many cases prescriptions per capita increased and quickly offset effects of price cutting measures. Further investigation of these phenomena is needed in context of individual ATC groups, especially focusing on ones that contribute most in volume or value on expenditure and focus more on clinical management and rationalizing prescribing patterns in individual indications.

**Acknowledgments:** My mentor, Professor Stjepan Orešković.

**MeSH/Keywords:** Pharmaceutical expenditure, pharmaceutical policy, Europe, Croatia

**Poster code:** R-C-2-145

## Poster Title: PROCESS OPTIMIZATION OF HOSPITAL UNITS USING LIFE-CYCLE ASSESSMENT METHODS

**PhD candidate:** Vitaliy Sarancha, MD

**Thesis proposal:** The optimization of working conditions of the Healthcare System Unit according to sustainability principles leads to higher economic efficiency

**Mentor/s:** prof. Ksenija Vitale PhD, MPH, prof. Stjepan Orešković, MD, PhD

**Affiliation:** School of public health Andreja štampar

**Introduction:** The Healthcare System without resources is doomed to oblivion. In conjunction with the aim to bring economic efficiency and environmental sustainability into alignment for the object of the study - Laboratory of Medical Biochemistry, General Hospital of Zabok - we plan to combine the methods of Financial Analysis, Life Cycle Management, Social Life Cycle Assessment, etc.

**Materials and methods:** The study consists of three phases. In the first phase attention is primarily paid to the collection of data within the Unit system boundaries regarding inputs and outputs together with information about initial economic conditions. In the second phase the possible changes/substitutions of the equipment, staff, working conditions into more ergonomic and environmentally friendly are performed. The third phase should be the examination of the data with the help of statistical methods such as data mining, cluster analysis, correlation, multi-factor analysis, etc.

**Results:** Primary data collection was performed in accordance with the Research Plan as follows: 1: General list of the tests, 2: Reagents used for tests, 3: Number of tests in the period and duration of urgent/general sample processing, 4: Expenses/Purchased (total per reagent, total per period), 5: Equipment used for testing (list of diagnostic equipment and tools), 6: Register of poisonous chemicals (quantity and expenses in the period), 7: Input data: water consumption, natural gas consumption, electricity, consumption of heavy fuel oil, 8: Output data: polluted water, $CO_2$ footprint (calculation), hazardous waste, municipal waste (marked by color labels), 9: Environment quality measurement: noise, temperature, heat loss, 10: Number of employees, 11: Level of education, 12: Working hours/employee in the period, 13: Gross expenses per employee in the period, 14: Level of satisfaction with working conditions: financial satisfaction, people/environment satisfaction, 15: The amount of people tested in the current period, 16: The price list. Data are processed and prepared for mathematical modeling and statistical analysis

**Discussion:** As a result we expect to reveal the effecting parameters in hierarchical order and detect sequences and trends which after modeling and proper application could lead the Unit to optimization. The applicable check list reflecting the degree of unit optimization will be designed.

**Acknowledgments:** prof. Stanislav Sulyma MD, PhD, prof. Vadym Sulyma MD, PhD, Gromada Zlata d.o.o.

**MeSH/Keywords:** Sustainability, Life Cycle Assessment, Innovations in Healthcare, Total Quality Management

**Poster code:** R-C-2-27

# 2. RESEARCH PROPOSALS

# 2.1.
## RESEARCH PROPOSALS
## Basic Medical Sciences

# Poster Title: EFFECT OF PENTADECAPEPTIDE BPC 157 ON COLLATERAL CIRCULATION IN ACUTE OBSTRUCTION OF THE ABDOMINAL AORTA

**PhD candidate:** Katarina Kašnik, MD

**Thesis proposal:** Effect of pentadecapeptide BPC 157 on collateral circulation in acute obstruction of the abdominal aorta

**Mentors:** Professor Zoran Brnić, MD, PhD, Professor Predrag Sikirić, MD, PhD

**Affiliation:** Clinical Hospital Centre Sisters of Charity, Department of Diagnostic and Interventional Radiology, University of Zagreb School of Medicine, Department of Pharmacology

**Introduction:** We hypothesise that positive activity of pentadecapeptide BPC 157 on rapid development of collateral circulation may be the main factor for many protective effects against congestion and ischemia in various tissues. In this experiment, we will explore the effect of BPC 157 on rapid activation of blood vessels/ anastomosis in severe condition of complete obstruction of abdominal aorta.

**Hypothesis:** Pentadecapeptide BPC 157 leads to the rapid development of collateral circulation (opening of present collateral blood vessels/ anastomosis) in conditions of acute and complete obstruction of the abdominal aorta in rats.

**Aims:** The aim of this study is to demonstrate the protective effect of BPC 157 on collateral circulation and opening of anastomosis on the model of complete obstruction of the abdominal aorta in rats. We theorize that BPC 157 will prevent severe tissue damage, congestion and ischemia of distal part of body with opening of present collateral blood vessels/anastomosis.

**Materials and methods:** Female Albino rats weighing 350 g will be used. Deeply anaesthetised rats will be randomly divided in treated and control group. Complete ligature with surgical suture of abdominal aorta will be carried out at the infrarenal or bifurcation level. After the operation, the animals will receive BPC 157 dissolved in saline at a dose of 10 µg/kg and 10 ng/kg as a local bath (2 ml/rat), or in the pre-treatment assessment, 10 µg/kg per-orally in drinking water. Controls will receive an equivalent volume of 0.9% NaCl as a local bath or drinking water only. At intervals of 1min, 1h and 6h, we will analyse the redistribution of collateral circulation using digital subtraction angiography (DSA) and estimate the branching of blood vessels using micro-camera. Also, we will measure arterial blood pressure and take samples for histopathological analysis. 6h ligation/application group will perform walking test and lower extremity muscle strength- motor function index (MFI).

**Expected scientific contribution:** To demonstrate beneficial effect of pentadecapeptide BPC 157 on collateral circulation with existing severe condition of complete obstruction of abdominal aorta.

**Acknowledgments:**

**MeSH/Keywords:** pentadecapeptide BPC 157, ligation, abdominal aorta, collateral circulation, digital subtraction angiography

**Poster code:** T-A-4-112

## Poster Title: LIGATION OF SUPERIOR MESENTERIC ARTERY AND VEIN IN RAT: STABLE GASTRIC PENTADECAPEPTIDE BPC157 BENEFICIAL EFFECT

**PhD candidate:** Mario Knežević, MD

**Thesis proposal:** Ligation of superior mesenteric artery and vein in rat: Stable gastric pentadecapeptide BPC 157 beneficial effect

**Mentors:** Professor Leonardo Patrlj, MD, PhD, Professor Predrag Sikirić,MD, PhD

**Affiliation:** University of Zagreb School of Medicine, Clinical Hospital Dubrava, Zagreb

**Introduction:** Acute mesenteric ischemia is a potentially lethal condition with mortality between 60-80%. Mesenteric ischemia is manifested in damage of the intestinal mucosa, which is characterized by an increase in vascular permeability, oedema and necrobiotic changes. We will investigate the effect of BPC 157 in terms of mesenteric ischemia caused by permanent ligation of the superior mesenteric artery and / or vein in rats. We believe that this effect is mediated by NO system, and should be reflected in the opening of the pre-existing venous and arterial collaterals that normally do not participate actively in the blood supply, but are activated under conditions of ischemia and venous congestion.

**Hypothesis:** The application of BPC 157 reduces ischemic lesions of the small intestine, cecum and ascending colon, leading to unexplored phenomenon of opening pre-existing venous and arterial collaterals in terms of mesenteric ischemia. The effect of BPC 157 is mediated by NO system.

**Aims:** The objective of the research is to show that the application of BPC 157 reduces ischemia and venous congestion of the small intestine, cecum and ascending colon in terms of permanent ligation of the superior mesenteric arteries and / or veins, and that this effect is mediated by NO system.

**Materials and methods:** The experiment will be conducted on female Wistar rats. After the application of anesthetic, medial laparotomy will be preformed. Preparation and ligation of superior mesenteric artery and/or vein will be performed in both group. BPC 157 will be applicated in dose of 10μg/kg ip. Effect of superior mesenteric artery and/or vein ligation will be recorded with micro camera. Recording will be performed for 30 min and following parameters will be observed: bleeding on the surface of the intestine, venous congestion and arterial loading and ramification. Those parameters will be analyzed at 5, 15 and 30 min after the ligation. After 30 minutes the animals will be euthanized according to established standards. The specimen of the small intestine, cecum and ascending colon will be taken after the sacrifice for pathohistological analysis.

**Expected scientific contribution:** Application of BPC 157 reduces ischemic lesions of the small intestine, cecum and ascending colon leading to phenomenon of opening pre-existing venous and arterial collateral in terms of mesenteric ischaemia.

**Acknowledgments:**

**MeSH/Keywords:** Acute mesenteric ischemia, superior mesenteric artery and vein ligation, BPC 157

**Poster code:** T-A-4-97

## Poster Title: THE EFFECT OF PENTADECAPEPTIDE BPC 157 ON EPISCLERAL VEIN CAUTERIZATION MODEL IN RATS

**PhD candidate:** Tamara Kralj, MD

**Thesis proposal:** The effect of pentadecapeptide BPC 157 on episcleral vein cauterization model in rats

**Mentor:** Professor Predrag Sikirić, MD, PhD

**Affiliation:** Department of Pharmacology, School of Medicine, University of Zagreb

**Introduction:** BPC 157, given locally or systemically, counteracts atropine mydriasis in rats, while by itself does not affect normal pupil diameter. This study aimed to evaluate the effect of BPC 157 on glaucoma-like features in rat episcleral vein cauterization model.

**Hypothesis:** Two dorsal episcleral veins and one temporal episcleral vein cauterization in rats leads to permanently raised intraocular pressure, disabled pupillar function, damaged vascularization of the eye fundus and presentation of optic nerve papilla. Using BPC 157 these pitfalls could be both prevented (development counteracted, BPC 157 given immediately after injury induction) and reversed (BPC 157 given after preexisting injury).

**Aims:** To demonstrate the protective effect of BPC 157 on raised intraocular pressure, disabled pupillar function, damaged vascularization of the eye fundus and presentation of optic nerve papilla.

**Materials and methods:** Albino Wistar rats, 200g, randomly assigned will be used. Under deep anaesthesia and Tetrakain 0.5% drops, two dorsal episcleral veins and one temporal episcleral vein will be isolated from the surrounding tissues, cautery will be specifically applied to the selected vein. Intraperitoneal or topical medication (BPC 157 (10µg/kg)(saline 5ml/kg) will be applied either immediately after surgery (early treatment), or at 24h thereafter (delayed treatment). Controls will receive an equivolume of 0.9%NaCl intraperitoneally or topically. Intraocular pressure (IOP,mmHg), pupillar function will be measured at 24h, 2, 4 and 6 weeks after surgery. Non-invasive IOP measurements will be taken after local application of Tetrakain 0.5% drops by aplanation tonometer Tonopen XL in same time of a day. Pupillar function will be photographed by USB Veho Discovery microcamera. Photographs will be taken before and after application of BPC 157 or saline and analyzed with special software bought with camera for measurement of pupillar diameter (r=mm), range (C=mm) and surface (S=mm2). Camera will be calibrated using graph paper. Vascularization of the eye fundus and presentation of optic nerve papilla will be analyzed with microcamera and Digital Widefield lupe 90D at 24 hours, 2, 4 and 6 weeks after procedure and the vessels extending into and out of the optic disc will be analyzed. Retinal changes alterations in vessel caliber and tortuosity, optic disc pallor and leakage of the retinal arterioles and venulas will be scored (1-3).

**Expected scientific contribution:** To demonstrate beneficial effect of BPC 157 on episcleral vein cauterisation in rats.

**Acknowledgments:** Department of Pharmacology

**MeSH/Keywords:** pentadecapeptide BPC 157, beneficial effect, episcleral vein cauterisation

**Poster code:** T-A-4-123

## Poster Title: GUT MICROBIOTA COMPOSITION AND INFLAMMATORY MARKERS IN IBD PATIENTS

**PhD candidate:** Marina Panek, mag.biol.mol.

**Thesis proposal:** Analysis of gut microbiota composition from colon and faeces samples and quantitative determination of inflammatory factors as relevant biomarkers from newly diagnosed IBD patients.

**Mentor/s:** Assistant Professor Donatella Verbanac, PhD; Professor Željko Krznarić, M.D, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre Zagreb

**Introduction:** In healthy humans gastrointestinal (GI) tract is colonized by a broad range of highly diverse microorganisms, which is collectively termed the gut microbiota. Gut microbiota represent a diverse microbial community, estimated to contain over 1000 different bacterial species and play a key role in human health with main influence on nutrition, immunology and pathogenesis. The healthy intestine represents a remarkable interface where host tissues come in contact with microbiota in a balanced state of homeostasis. The imbalance of gut homeostasis is associated with the inflammatory bowel disease (IBD). IBD is a chronic relapsing process in the GI tract with increasing frequency which comprises of two clinically and morphologically different entities: ulcerative colitis (UC) and Crohn's disease (CD).

**Hypothesis:** Changes in the gut microbiota are specific and associated with the inflammatory status of IBD patients. Confirmation of this hypothesis may help in better understanding of the IBD development and hopefully successful therapeutic approach to the disease.

**Aims:** The main goal of this prospective research is to identify the key parameters responsible for the development of IBD and to estimate correlation between altered gut microbiota composition and associated inflammatory factors.

**Materials and methods:** Microbiota composition from colon and faeces samples of 40 newly diagnosed IBD patients and 20 non-IBD individuals, as well as inflammatory status from the blood of each participant will be investigated. The composition of gut microbiota will be determined by amplification and sequencing of bacterial 16S rRNA gene using Ilumina MiSeq next generation sequencing. Inflammatory biomarkers will be detected by proximity extension assay (PEA) method. This method allows simultaneous detection of 92 different inflammatory biomarkers from the blood samples. The obtained results will provide a better insight into the understanding of IBD formation as well as facilitating selection of the most appropriate treatment.

**Expected scientific contribution:** Despite the recent development of next generation sequencing, the current scientific knowledge of specific triggers and diagnostic markers of disease are limited and for better understanding of IBD, new information about microbiota composition and inflammatory factors are needed. This study will help to determine the relationship between gut microbiota composition and inflammatory status in IBD affected patients.

**MeSH/Keywords:** inflammatory bowel disease, gut microbiota, next generation sequencing, proximity extension method

**Poster code:** T-A-5-53

## Poster Title: METHYLATION LEVEL OF ASC/TMS1 AND MyD GENES IN HEALTHY LARYNX AND LARYNGEAL S UAMOUS CARCINOMA

**PhD candidate:** Lana Kovač Bilić, MD

**Thesis proposal:** Methylation level of ASC/TMS1 and MyD88 genes in healthy larynx and laryngeal squamous carcinoma

**Mentor/s:** Professor Srećko Branica, MD, PhD, Research Associate Jelena Knežević, PhD

**Affiliation:** ENT Department University Hospital Center Zagreb, Division of Molecular Medicine Ruđer Bošković Institute

**Introduction:** Genes ASC/TMS1 (apoptosis-associated speck-like protein possessing a caspase-recruting domain /target of methylation-induced silecing-1) and MyD88 (myeloid differentiation primary response gene 88) are key adaptor molecules in innate immunity. ASC is forming protein platform responsible for cleavage of pro-caspase-1 and 8 in active form. In literature ASC is described as tumor suppressor. MyD88 is adaptor molecule essential for activation of NF-κB transcription factor during Toll-like receptors activation. Uncontrolled inflammation is frequently associated with tumor development, so we will correlate methylation status and protein expression level of indicated genes.Since response to chemotherapy and disease course could also be associated with methylation status of suggested genes, in this study we will follow up this parameter, together with overall survival.

**Hypothesis:** The difference in methylation status in the promoter regions of ASC/TMS1 and MyD88 genes between healthy larynx and laryngeal squamous carcinoma is associated with developement and progression of laryngeal squamous carcinoma.

**Aims:** The aim of proposed study is to investigate methylation status of genes MyD88 and ASC/TMS1 in healthy and tumor tissue of the larynx.

**Materials and methods:** During laryngeal surgery tumor tissue and surrounding histologically normal/tumor-free tissue are collected. Tumor tissue is histopathologically analyzed to confirm laryngeal cancer and surrounding histologically normal/tumor-free tissue is also histopathologically analyzed to confirm cancer absence. Genomic DNA is isolated from tissue samples, converted by bisulfite conversion, and methylation patterns are analyzed by pyrosequencing. Protein expression in tumor and healthy tissue is analyzed by Western blotting.

**Expected scientific contribution:** The scientific contribution of this study comprises possible contribution in early diagnosis, therapy and follows up in patients with laryngeal squamous carcinoma as there is still not available clinically established tumor biomarker for laryngeal squamous carcinoma.

**Acknowledgments:**

**MeSH/Keywords:** Epigenetics, Innate Immunity, Laryngeal Cancer

**Poster code:** T-A-6-21

## Poster Title: THE ROLE OF ARYL HYDROCARBON RECEPTOR IN OXIDATIVE STRESS IN THE PATIENTS WITH CHRONIC RHINOSINUSITIS

**PhD candidate:** Aigerim Zhumabayeva, MD

**Thesis proposal:** The linkage between reactive oxygen species and aryl hydrocarbon receptor and their role in the host immunity in chronic rhinosinusitis

**Mentor/s:** Prof.dr.sc. Livije Kalogjera

**Affiliation:** Institute of Ruđer Bošković, Department of Molecular Medicine, University Hospital of Zagreb, Department of Ear, Nose, Throat diseases and Head and Neck Surgery

**Introduction:** Uncontrolled oxidative stress can result in induction of chronic inflammatory response in upper airways epithelium. Aryl hydrocarbon receptor is ligand-activated transcription factor. AhR signalling pathway could regulate oxidative stress through NADPH oxidase mediation in chronic rhinosinusitis.

**Hypothesis:** Reactive oxygen species production in the paranasal sinus mucosa in various CRS subtypes could be regulated by the AhR pathway

**Aims:** 1. Measurement of general oxidative stress in sinus mucosa in subtypes of CRS. 2. Measurement of AhR protein expression in subtypes of CRS. 3. to evaluate oxidative stress response of human primary sinonasal epithelial cell cultures prepared from CRSsNP, CRSwNP tissue samples and healthy controls to AhR ligand stimulation and inhibition identifying NADPH oxidase isoforms expression. 4. To demonstrate correlation between AhR protein expression, NADPH oxidase activity and its isoforms expression in subtypes of CRS smokers and non-smokers and healthy control group. And between atopic and non atopic patients. 5. To assess influence of AhR expression on inflammatory cytokines production and to classify the patients according to cytokine patterns.

**Materials and methods:** Total 57 patients undergoing endoscopic sinus surgery will be included to the study. We suggest measuring general oxidative stress level in subtypes of CRS and AhR protein expression by enzymatic immunosorbent assay. The ex vivo experimental study will be aimed to evaluate the regulatory role of AhR in oxidative stress control through the determination of NADPH oxidase isoforms expression using colorimetric and fluormetric methods in human primary sinonasal epithelial cells line prepared from subtypes of CRS triggered by AhR agonists and inhibitor. Treating peripheral blood monocyte cells of study groups by AhR ligand activators and inhibitor we suggest to measure inflammatory cytokines and superoxide concentrations subsequently NAPDH oxidase activity using the chemiluminiscent method.

**Expected scientific contribution:** Proposed research could contribute to recognition of the mechanisms of antioxidative activity of AhR, that prior was not investigated in the mechanism of the inflammatory process in chronic rhinosinusitis and its phenotypes comparing to controls

**MeSH/Keywords:** chronic rhinosinusitis, aryl hydrocarbon receptor, oxidative stress, reactive oxygen species, local innate imunity, cytokines.

**Poster code:** T-A-7-22

# Poster Title: DISTRIBUTION OF CALRETININ NEURONS IN THE PRIMATE PREFRONTAL CORTEX

**PhD candidate:** Dora Sedmak[1], MD

**Thesis proposal:** DISTRIBUTION OF CALRETININ NEURONS IN THE PRIMATE PREFRONTAL CORTEX

**Mentor/s:** Zdravko Petanjek[1], MD, PhD, Monique Esclapez[2],PhD

**Affiliation:** [1] School of Medicine University of Zagreb, Department of anatomy and clinical anatomy; [2] INSERM, School of Medicine Aix Marseille University

**Introduction:** Current data suggest that during mammalian evolution the proportion of neocortical GABAergic neurons increased approximately 50%. Among three main molecularly defined classes increase in proportion is exclusively related with calretinin expressing neurons. The largest increase is observed in primate associative areas where 12% of all neurons express calretinin (3% in rodents), i.e. half of GABAergic population in primates are calretinin neurons. This increase could be the main correlate of neuronal network rearrangement occurring in monkey and human brain resulting in more efficient complex information processing.

**Hypothesis:** Comparison between higher order associative areas in humans and non-human primates reveals an increase in proportion of calretinin neurons in upper cortical layers concurrent with complexity of primate prefrontal cortex.

**Aims:** The aim of this study is to compare the proportion and laminar distribution of calretinin expressing neurons in several associative frontal regions (mesocortical and neocortical) between macaque monkey and man.

**Materials and methods:** Three postmortem human (Zagreb neuroembryological collection) and three macaque monkey brains (Brain dynamic institute Marseille collection) will be analyzed. Serial sections will include frontal mesocortical Brodmann area 24 and neocortical areas 32 (medial) and 9 (dorso-lateral). NeuN (neuronal marker) and calretinin immunohistolchemical staining will be performed. Estimation of total neuron and calretinin neuron number will be done using stereological (optical fractionator) method (Stereo-investigator software, MicroBrightField, Williston, USA). Statistical analysis will be performed to establish region and species differences. Double labeling method (immunohistochemistry and in-situ hybridization) will be used to affirm GABAergic phenotype of calretinin neurons as well as to determine co-localization with other GABA neuron classes.

**Expected scientific contribution:** This research will propose the pattern of circuitry rearrangement within the cerebral cortex occurring during the primate evolution. This is crucial for the development of the computational model of cortico-cortical circuits to simulate how such increase in proportion of calretinin neurons is enhancing the efficiency of information processing. Quantitative data obtained in the human cortex will allow better insights to changes in proportion of calretinin neurons and laminar neuronal rearrangement in various neurological and psychiatric diseases affecting prefrontal cortex.

**Acknowledgments:**

**MeSH/Keywords:** GABA, interneuron, neocortex, calretinin, human, monkey

**Poster code:** T-A-9-65

## Poster Title: DEPRESSION AND COGNITIVE IMPAIRMENT IN ALZHEIMER'S DISEASE

**PhD candidate:** Eva Berković, mag.psych.

**Thesis proposal:** 1H MRS biological markers of therapeutic response in treatment of depressive symptoms in dementia in Alzheimer's disease

**Mentor/s:** Prof. Neven Henigsberg, MD, PhD

**Affiliation:** Polyclinic Neuron, šalata 12, 10 000 Zagreb

**Introduction:** Neuropathological and neuro-histochemical changes in Alzheimer's disease (AD) indicate reduction of neurotransmitter activity in the cortex and hippocampus. Along with cognitive impairment, depression represents one of the first symptoms. This study will examine the biological correlates of therapeutic response in the treatment of depressive symptoms in relation to cognitive changes. The level of N-acetyl aspartate (NAA) in the hippocampus will be analyzed and the study will be done using 1H MRS at the beginning and after 6 months of treatment.

**Hypothesis:** There is a correlation between the therapeutic response of treating depressive symptoms in patients with AD and the parameters measured with MRS, where changes of NAA levels in the hippocampus correlate with therapeutic response regardless of cognitive functioning.

**Aims:** Investigate the change of NAA levels in the hippocampus and the severity of depressive symptoms in patients suffering from AD dementia before and after initiation of therapy. Investigate the correlation of NAA levels and the severity of depressive and cognitive symptoms. Identify the group that has better therapeutic response by using 1H MRS.

**Materials and methods:** The study will include 24 non-hospitalized participants, male and female, aged 50 years and above, that have depressive symptoms and cognitive impairment caused by mild to moderately severe AD. They will have a diagnosis of dementia caused by AD and confirmed depressive symptoms. The study will not include participants that have comorbid psychiatric disorders, suffer from other serious illness or have significant deviations in laboratory values. The following neuropsychological tests will be applied: Wechsler Bellevue Intelligence Test for Adults, Wechsler Scale for Testing Memory, Auditory Verbal Learning Test, Benton Visual Retention Test, Alzheimer's Disease Assessment Scale Cognitive Subscale, Beck Depression Inventory, Hamilton Scale for Depression, and Mini Mental State Examination Test. Analysis will be performed at the baseline and 6 months after therapy, using 1H MRS apparatus of 3T equipped with "echo speed" gradients. Research will be done in the area of the hippocampus.

**Expected scientific contribution:** Help in clarifying the etiology of depressive symptoms that occur with dementia as part of AD. The research will contribute to the identification of biomarkers in positive therapeutic response measured by 1H MRS. It will also contribute to a better understanding of AD and possibly help in the identification of therapeutic options.

**Acknowledgments:** Croatian Science Foundation

**MeSH/Keywords:** cognitive impairment, Alzheimer's disease, depression, donepezil, 1H MRS, N-acetyl aspartate, hippocampus

**Poster code:** T-A-9-28

## Poster Title: DEVELOPMENT OF THE STRUCTURAL BASIS OF THE SOMATOSENSORY THALAMOCORTICAL SYSTEM IN THE HUMAN FETAL BRAIN: CYTOARCHITECTONIC AND MOLECULAR MARKERS

**PhD candidate:** Višnja Majić, MD

**Thesis proposal:** Development of the structural basis of the somatosensory thalamocortical system in the human fetal brain: cytoarchitectonic and molecular markers

**Mentors:** Željka Krsnik, PhD, Assistant Professor, Ivica Kostović, MD, PhD, Academician Professor

**Affiliation:** Croatian Institute for Brain Research, Nastavni zavod za hitnu medicinu Grada Zagreba

**Introduction:** The neurons of the cerebral cortex begin their migration from the proliferative ventricular zone in the 8 week after conception (PCW) and around 20PCW most neurons arrive at their final destination in the cortical plate. In the mid-fetal period the subplate zone is formed below the cortical plate, where the first synapses and neural circuits in the fetal neocortex appear. During 22PCW thalamocortical fibers "wait" in the subplate zone, and enter the cortical plate between 24-26PCW, thus creating the first synapses in layer 4 of the fetal cortex, followed by elaboration of thalamocortical fibers. Also, thalamus is a key relay station for transmitting sensory information to the cerebral cortex. In recent years great attention was devoted to study the activation of the cortex as a fundamental component of pain perception, mainly because of the increase in the number of intrauterine surgery and the progress in neonatal care. Knowledge of early cortical activity is essential to ensure safe extrauterine environment for premature children and the possibility of treatment of pain.

**Hypothesis:** Neural differentiation of thalamus and transient synaptic subplate is carried out before lamination of the cortical plate, which only happens after the ingrowth of thalamocortical axons.

**Aims:** The main aim of the thesis is to evaluate the development of the somatosensory thalamus (VPL nucleus), thalamocortical projection and the corresponding cortex, using histological sections of telencephalon and their comparison with the corresponding MRI images of fetal telencephalon. Special aims include 1) identifying the prospective SSCX, 2) determine the degree of differentiation of the main territories of the thalamus, 3) define cytoarchitectonical borders between transient fetal zones in SSCX, 4) based on goals 1 and 3, determine the spatial and temporal development indicators of the thalamocortical somatosensory system.

**Materials and methods:** Research will be carried out on sections of postmortem human brains, combining histologic, immunohistologic and MR analysis (in vitro MRI). The study involves brains of premature infants aged from 22nd to 36th week after conception, which are part of the Zagreb Neuroembryological collection.

**Expected scientific contribution:** Our results are significant for the interpretation of the early tactile and pain evoked activity in the late fetal human cortex.

**MeSH/Keywords:** subplate zone, somatosensory cerebral cortex, thalamus, VPL, fetal pain

**Poster code:** T-A-9-47

## Poster Title: CORRELATION OF SYMPTOMATOLOGY OF DEPRESSION, BIOLOGICAL INDICATORS MEASURED BY NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY AT THE ONSET OF FIRST DEPRESSIVE EPISODE WITH REGARD TO PRESENCE OF EXTERNAL FACTORS

**PhD candidate:** Benedict Rak, MD

**Thesis proposal:** 1H-MRS changes in prediction of response to therapy, relapse and resurgence of depression

**Mentor/s:** Prof. Neven Henigsberg, Md, PhD

**Affiliation:** University of Zagreb, School of Medicine, University hospital

**Introduction:** Antidepressive therapy is only effective in 60% of patients, taking 3-4 weeks for clinical effect to be demonstrated. Numerous evidence suggests the potential use of magnetic resonance spectroscopy in the assessment of pharmacological intervention, and that the amino acid neurotransmitter systems measurable by 1 H-MRS are associated with the pathophysiology and treatment of mood disorders.

**Hypothesis:** Differences in the etiology and biological basis of depression episodes cause the differences in the biological indicators measured by 1H-MRS which correlate with therapeutic response, and it is possible to recognize biological correlates associated with favorable therapeutic response at the time of diagnosis.

**Aims:** Identify biological indicators in defined areas of the brain detectable by 1H-MRS in which depressive disorder driven by environmental factors differentiates from one that occurs without the influence of environmental factors, and to explore differences in the correlates of response to therapy which is measured by 1H-MRS separately with depressive disorder caused by environmental factors and one that occurs without the influence of environmental factors.

**Materials and methods:** The research will be conducted on two groups of participants, at the time of the onset of a depressive episode. The first group will consist of patients whose first depressive episode occurred without distinguishing factors from the environment, and in the second the subjects for which it did occur under the influence of external factors that could affect the occurrence of depressive episodes. The study will be monitored through measurable indicators of 1H-MRS in the amygdala and prefrontal dorsolateral cortex, where differences associated with the emergence or during depressive disorder have already been shown, and occipital cortex. The study will include subjects of both genders aged between 18 and 55 years of age, who are not diagnosed with comorbid psychiatric disorder or somatic illnesses directly linked to the onset of etiological depressive episodes. Sample size is determined to be 21 subjects in each group, with the condition $\alpha = 0.05$ and $\beta = 0.8$ for each 1 H-MRS indicator.

**Expected scientific contribution:** Differences in biological parameters measurable by 1H-MRS will contribute to elucidation of the biological basis of the etiology of the emergence of these forms of depressive disorders, prediction of therapeutic response and diferentiation of clinical entities through objectively measurable indicators.

**Acknowledgments:**

**MeSH/Keywords:** depression, endogenous, nuclear magnetic spectroscopy, biological indicators

**Poster code:** T-A-9-91

## Poster Title: INFLUENCE OF CHRONIC STRESS AND AGING ON LIPID RAFTS IN RAT BRAIN AND ADRENAL GLAND CELLS

**PhD candidate:** Marta Balog, mag. biol.

**Thesis proposal:** Influence of chronic stress and aging on lipid rafts in rat brain and adrenal gland cells

**Mentor/s:** Marija Heffer, Svjetlana Kalanj Bognar

**Affiliation:** Faculty of Medicine Osijek, J. J. Strossmayer University of Osijek

**Introduction:** Stress and aging are risk factors for sex specific development of neurodegenerative diseases influencing many different signaling pathways including insulin and leptin. Both pathways are involved in molecular mechanisms of neurodegeneration and they start at the receptors located within the lipid rafts. A large set of transmembrane proteins depend on glycosphingolipids, which are responsible for their correct structure and function. An increase in GM1 ganglioside in Alzheimer´s disease has already been described, however the influence of glycosphingolipids on specific central and peripheral signaling pathways has yet to be determined.

**Hypothesis:** Chronic stress and aging lead to sex specific changes in lipid raft composition and regulate localization and function of insulin (IR) and leptin (Ob-R) receptors. Changes in downstream signalling pathways of IR and Ob-R could be responsible for development of receptor resistance and a trigger for neurodegeneration. Differences in lipid raft content of central (brain) and peripheral (adrenal gland) nervous tissues are expected.

**Aims:** Aim of the study is to test the chronic stress and aging rat model using markers for IR, Ob-R, neuroprotection and neurodegeneration in rat brain (hippocampus, cerebellum) and adrenal gland.

**Materials and methods:** Male and female Sprague Dawley rats will be used in the study. Beside gender division, animals will be divided in young (3,5 months) and old (12 months) experimental groups and their matched control groups. 10 animals will be used per each group. Chronic and sham stress protocol will be performed during 10 days and repeated 3 times with two weeks of pause between each session. Animals will be sacrificed at the ages of 7 and 14.5 months. Following methods will be used for brain and adrenal gland tissue analyses: immunohistochemistry, lipid rafts isolation and Western blotting. Statistical tests will be performed using the statistical software package SPSS.

**Expected scientific contribution:** This research will contribute to elucidating cellular level of aging, stress and neurodegeneration by detecting specific lipid rafts and cell signaling changes as possible triggers of neurodegeneration. The use of chronic stress and aging rat model is useful for research of these complicated pathophysiological conditions and could contribute to developing diagnostic biomarkers and recognition of potential molecular therapeutic targets for neurodegenerative diseases.

**MeSH/Keywords:** chronic stress, aging, lipid rafts, insulin, leptin, neurodegeneration

**Poster code:** T-A-9-98

## Poster Title: COULD ABNORMAL GENERAL MOVEMENTS IN INFANCY INDICATE LATER NONMOTOR DISORDERS?

**PhD candidate:** Ivana Jandroković, Master of Educational Rehabilitation

**Thesis proposal:** Predictive value of general movements assessment for neurodevelopmental outcome in toddlers

**Mentor/s:** Professor Snježana Škrablin Kučić, MD, PhD., Assistant Professor Maja Cepanec, SLP., PhD.

**Affiliation:** Croatian Institute for Brain Research, Clinic for Gynecology and Obstetrics Petrova Hospital, Clinical Hospital Centre Zagreb

**Introduction:** According to the new data one of six children develop neurodevelopmental disorder in early childhood. Advancement in the field of neonatal care led to significantly reduced perinatal morbidity, but the number of high-risk infants is increasing. General movements (GM) in the neonatal period are an indicator of spontaneous neural activity and have high predictive value for the development of cerebral palsy. Predictive value of the GM for other developmental (nonmotor) domains is not yet established.

**Hypothesis:** Quality of GMs is based on the integrity of the subplate zone (SP) and its connections. Abnormal GMs is an indicator of a brain damage or of dysfunction of SP and its efferent connections in the periventricular white matter, which, consequently, can lead to a dysfunctions in a number of abilities that require optimal functioning of complex cortico-subcortical neuronal circuits. Therefore, our hypothesis is that there is a connection between the caracteristcts of the GMs and the developmental outcomes in the following areas: cognition, communication, language, socialization and adaptive behavior.

**Aims:** To determine the predictive value of GMs for the later development of social communication, language, socialization and adaptive behaviour and possible differences in the type of abnormal GMs among children who show delays in nonmotor developmental areas vs. children who show delay solely in the motor development. To identify the contribution of neurorisk factors (including abnormal GMs) for the occurrence of neurodevelopmental delays in various developmental areas at the age of 18 months.

**Materials and methods:** The sample consistes of two groups of children: children with no identified neurorisk factor, children at neurorisk. The research will be carried out in three phases. In the first two phases (newborns and 3-months-old), the assessment of the GM by the Prechtl method will me carried out. At the age of 18 months, an assessment of the child's developmental outcome using Mullen Scales of Early Learning, Vineland Adaptive Behavior Scale, M-CHAT will be made. GMs will be analyzed using Prechtl protocol and compared to reference values. Differences in GM between the groups will be calculated, aw well as the correlation between patological GMs and the neurodevelopmental outcome.

**Expected scientific contribution:** The insights from this study will be used to implement more precise detection of developmental delays and enable early inclusion of children with evident pathology in GMs to early intervention programes.

**Acknowledgments:** I would like to thank to Associate Professor Maja Cepanec, SLP., PhD., and Professor Snježana Škrablin Kučić MD., PhD. for a huge support during creation of this study, for all the time and mentoring. Furthermore I would like to thank to Croatian Institute for Brain Research, Laboratory for Research of Children's Communication and Clinic for Gynecology and Obstetrics Petrova Hospital, Clinical Hospital Centre Zagreb where this study will be performed.

**MeSH/Keywords:** general movements, Prechtl assessment, neurodevelopmental disorders

**Poster code:** T-A-9-72

## Poster Title: HISTOLOGICAL, MRI AND TRANSCRIIPTOME ANALYSIS OF THE REORGANIZATIONAL PROCESSES IN THE DEVELOPING HUMAN HIPPOCAMPUS

**PhD candidate:** Vinka Kovačević

**Thesis proposal:** Histological, MRI and transcriptome analysis of the reorganizational processes in the developing human hippocampus

**Mentor/s:** Prof. Mario Vukšić, MD, PhD

**Affiliation:** Croatian Institute for Brain Research, School of Medicine, University of Zagreb

**Introduction:** Human hippocampal formation develops a different laminar structure in comparison with lateral cortical regions. In contrast to neocortical regions, the subplate zone (SP) in the hippocampal formation is poorly developed and early afferent hippocampal fibers terminate in the prominent marginal zone (MZ), establishing there synapses with apical dendrites of principal hippocampal neurons.

**Hypothesis:** Unlike the isocortex, where the SP is a major site of neurogenetic events, hippocampal MZ seems to be key zone for early molecular neuronal interactions, synaptogenesis and patterning of growing pathways. We suggest that early maturing neurons in the MZ may have a role in the targeting of hippocampal afferents, as similarly do SP cells in the developing neocortex.

**Aims:** The aim of this doctoral thesis is to correlate developmental reorganization of major cellular and extracellular components of the SP and the MZ in fetal human hippocampal formation by combining immunohistochemistry, in situ hybridization, and transcriptome analysis with in vitro MRI.

**Materials and methods:** Histological analysis will be performed on postmortem human brains, ranging from 10 postconceptional weeks to 6.5 years, to analyze the expression patterns of different developmentally regulated proteins in relation to synaptic, laminar, neuronal, glial and extracellular matrix development. These results will be correlated with in vitro MRI findings obtained in age-matched fetuses, infants and children. We will also analyze publicly available gene expression database (Kang et al., Nature 2011) to investigate the relationship between structural changes and spatio-temporal expression of specific candidate genes. For the selected candidate genes we will perform in situ hybridization and immunohistochemistry in order to elucidate in which cells these genes are expressed.

**Expected scientific contribution:** The obtained data will be used for setting the baseline for studying developmental abnormalities characteristic for diverse neurological disorders such as epilepsy, autism and schizophrenia.

**MeSH/Keywords:** archicortex, hippocampus, marginal zone, subplate zone

**Poster code:** T-A-9-96

## Poster Title: EFFECT OF BODY POSITION ON CEREBROSPINAL FLUID VOLUME IN CRANIAL AND SPINAL COMPARTMENTS

**PhD candidate:** Ines Nikić, MD

**Thesis proposal:** Effect of body position on cerebrospinal fluid volume in cranial and spinal compartments

**Mentor/s:** Milan Radoš, MD, PhD, Assistant Professor

**Affiliation:** University of Zagreb Croatian Institute for Brain Research, University hospital "Sveti Duh"

**Introduction:** According to the classical hypothesis, it is believed that the CSF pressure is a result of dynamic balance between secretion, absorption and resistance to the flow of CSF. When changing body position from horizontal to vertical, a decline in intracranial pressure occurs to subatmospheric level, which is according to classical hypothesis considered transient and short-termed because ultimately intracranial pressure must be positive if CSF is continuously secreted, unidirectional flowing and absorbed. According to our research, changes in body position from horizontal to vertical position lead to negative intracranial pressure that is not transient, but represents a physiological condition of the CSF within the cranium in an upright position. Furthermore, we have showed that the changes of intracranial pressure are not necessarily associated with the change of intracranial volume as it is assumed by classical hypothesis of CSF physiology. According to our new hypothesis, changes of body position do not lead to CSF displacement between the cranial and spinal CSF compartment and result with redistribution of CSF exclusively within the spinal compartment.

**Hypothesis:** Changes of body position do not lead to CSF displacement between the cranial and spinal CSF compartment, but result with redistribution of CSF exclusively within the spinal compartment.

**Aims:** To determine how the body position affects the volumes of the cranial and spinal CSF.

**Materials and methods:** We are going to scan complete craniospinal CSF system of healthy volunteers aged 18-30 years in magnetic resonance (3T, Magnetom Prisma, Siemens, Germany) in three different body positions (horizontal, in position with lifted lumbosacral part, in position with elevated head and cervical part). Volumetric analysis of cranial CSF space will be performed using computer programs to analyse the imagery of the brain (MNI toolbox Montreal Neurological Institute, Canada). Manual segmentation will determine the volume of the fluid of the brain and separately cervical, thoracic and lumbosacral part of the spinal system using the program Analyze 8.1 (Mayo Clinic, USA).

**Expected scientific contribution:** The results of our research will show how body position affects the volume of CSF in the cranial and spinal compartment. Proper comprehension of CSF redistribution in different body positions will help us to better understand CSF physiology and pathophysiology of increased intracranial pressure, which is the leading cause of mortality in the younger population of developed countries.

**Acknowledgments:** This study is a part of scientific project entitled The volumetric analysis of craniospinal liquor compartments in humans in different body positions in the magnetic resonance with Marko Radoš, MD, PhD, Full Professor as Head of the project.

**MeSH/Keywords:** cerebrospinal fluid, CSF volume, intracranial pressure, magnetic resonance imaging

**Poster code:** T-A-9-121

## Poster Title: THE IMPACT OF DIFFERENT WHITE MATTER SEGMENTS DAMAGE ON NEURODEVELOPMENTAL AND ELECTROENCEPHALOGRAPHIC FEATURES IN PREMATURE CHILDREN

**PhD candidate:** Petra Grđan, MD

**Thesis proposal:** The impact of different white matter segments damage on neurodevelopmental and electroencephalographic features in premature children

**Mentor/s:** Professor Nina Barišić, MD, PhD

**Affiliation:** The Croatian Institute for Brain Research, University Hospital Centre Zagreb

**Introduction:** Advances in perinatal medical care have a great influence on positive survival rates of preterm born infants. According to the literature, 40 % of prematurely born children have motor development impairment, 10 % cerebral palsy, 26-47 % epilepsy, while 30-60 % cognitive impairment, hyperactivity or visual and hearing disturbances. Periventricular leukomalacia with neuronal-axonal injury and periventricular-intraventricular hemorrhage are two main types of brain injury in premature infants. The imaging studies have shown that pathologies seen after ischemia and hemorrhage show differences, which depend on the location's depth within the different white matter segments. Their impact on the maturation and pathological electroencephalographic features in premature children is unclear.

**Hypothesis:** Damage of the individual white matter segments cause different motor, neurodevelopmental disorders, delayed maturation and pathological electroencephalographic changes in premature infants.

**Aims:** To determine the relationship between lesions of different white matter segments with maturation, specific pathological electroencephalographic (EEG) features and neurological outcome in prematurely born children through the follow-up period of 24 months.

**Materials and methods:** The case-control study will consist of two groups: a group of 25 premature born infants with lesions of different white matter segments on MRI and the control group which will consist of 15 premature infants with normal MR findings. In all subjects will be analyzed: gestational age, birth weight, delivery (caesarean section/vaginal), reanimation (yes/no), Apgar score, perinatal infection (yes/no), mechanical ventilation (yes/no), SNAP II, SNAPPE II. EEG will be recorded in first 14 days of life, then every 4 weeks up to term corrected age, at the age of 3, 6, 9, 12, 18 and 24 months of life. Neurological assessment by Amiel-Tison scale will be performed by the same scheme as EEG recording. US will be performed each week until first month of life and every two weeks during 2 and 3 months of life. Brain MRI will be performed at the corrected term age and at the age of 2 years. For analysis we will use STATISTICA software version 10.0.

**Expected scientific contribution:** Results obtained based on this research will enable better definition and understanding of the relationship between structural and functional disorders in premature infants with different white matter segments damage and their impact on neurodevelopment and epileptogenesis.

**Acknowledgments:**

**MeSH/Keywords:** white matter, leukomalacia, brain magnetic resonance imaging, brain ultrasound, EEG, neurological development, premature infants

**Poster code:** T-A-9-161

# 2.2.
## RESEARCH PROPOSALS
## Clinical Medical Sciences

# Poster Title: COMPARISON OF ROCURONIUM ADMINISTRED IN MULTIPLE SEPARATE DOSES WITH ROCURONIUM GIVEN IN CONTINUOUS INFUSION ON INTRAOPERATIVE CONDITIONS AND THE QUALITY OF RECOVERY AFTER GENERAL ANESTHESIA FOR LUMBAL DISCECTOMY

**PhD candidate:** Martina Miklić Bublić, MD

**Thesis proposal:** Influence of continuous neuromuscular blockade on intraoperative conditions and the quality of recovery after general anesthesia for lumbal discectomy

**Mentor/s:** Assistant Professor Ante Sekulić, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre Zagreb

**Introduction:** Neuromuscular blocking agents are a common part of general anesthesia, and can be administered in mutiple separated doses or in continuous infusion. So far, there has not been sufficient research about comparative influence of these two modes of administration of neuromuscular relaxants on intraoperative conditions and quality of recovery after general anesthesia. The aim of this research is to compare both mentioned ways of dosing and their influence on intraoperative conditions and postoperative recovery after lumbal discectomy.

**Hypothesis:** Administering of neuromuscular blocking agent rocuronium in continuous infusion in comparison with multiple separated doses enables better intraoperative conditions and better quality of recovery after lumbal discectomy.

**Aims:** Comparison of neuromuscular blocking agent rocuronium administered in multiple intravenous separated doses and in continuous intraveous infusion and estimation of different influence on intraoperative conditions (airway pressure, blood pressure, body temperature, heart rate variability), muscle strenght of hand grip and quality of recovery after general anestehesia measured by questionnaire.

**Materials and methods:** Prospective research will be done on 80 patients ASA1-2, aged 18-65, that will undergo elective lumbal discectomy. Excluding criteria are neuromuscular, psychiatric and other systemic illness, and allergies on anesthetic drugs used in research. First group will undergo TIVA (propofol , remifentanil) with rocuronium bolus doses and second group will undergo TIVA (propofol, remifentanil) with contiuous infusion of rocuronium. Intraoperative airway pressures, blood pressure, ECG, heart rate variability and temperature will be recorded. Strenght of handgrip will be estimated before anesthesia, after extubation in theatre and 24 hours after anestehesia. Quality of recovery quaestionnaire (Qor 40) will be given to patients before anesthesia, 24 hours and 30 days after anestehesia. Descriptive statistics, parametric and nonparametric tests wil be performed.

**Expected scientific contribution:** Gathering new data on influence of continuous neuromuscular blockade in neurosurgery of spine on intraoperative conditions and quality of recovery after anesthesia. Less side effects and complications after anesthesia, shorter lenght of stay in hospital, more rapid turnover of patients and reducing hospital costs.

**Acknowledgments:**

**MeSH/Keywords:** rocuronium, continuous neuromusculare blockade, lumbal discectomy, quality of recovery

**Poster code:** T-B-1-32

## Poster Title: COMPARISON OF PHARMACOLOGICAL POSTCONDITIONING USING SEVOFLURANE VERSUS POSTCONDITIONING ISOFLURAN IN ISCHEMIC/REPERFUSION GRAFT LIVER INJURY

**PhD candidate:** Nataša Paklar,MD

**Thesis proposal:** Comparison of pharmacological postconditioning using sevoflurane versus postconditioning isofluran in ischemic/reperfusion graft liver injury

**Mentor/s:** Tatjana Filipec Kanižaj, MD, PhD

**Affiliation:** University Hospital Merkur, Zagreb, Croatia

**Introduction:** Ischemic/reperfusion injury is the leading cause of graft failure after liver transplantation. After ischemic period refreshed blood in flush through graft leads to massive free radical release. Volatile anaesthetics are used worldwide for conducting anaesthesia. Protective effect of volatile anaesthetics if it´s used after ischemia in that case we use term ´postconditioning´. It is considered that protective mechanism of volatile anaesthetics is conducted through ATP mito-chondrial sensitive potassium channel (mitoK_ATP) on heart and brain models. This study is unique because volatile anaesthetics were studded as a possible method in reducing that injury but till now histological changes related with that effects were not studied.

**Hypothesis:** Usage of sevoflurane in postconditioning can reduce incidence and lower degree of morphological change after ischemic/reperfusion injury of liver graft in relationship to usage of isoflurane.

**Aims:** To determine influence using sevoflurane and isoflurane in postconditioning during liver transplantation on liver morphological change after ischemic/reperfusion injury.

**Materials and methods:** In the prospective study we plan to in roll minimal 100 patients who is planned for liver transplantation. In the beginning of study patients will be randomised in 2 groups (anaesthesia with sevoflurane or isoflurane). All other procedures and drugs will be used according to protocol used in our institution. Two biopsy of liver graft would be performed: "0th" biopsy- performed immediately after start of cold ischemia of a graft in donor-determining degree of microvesicular and macrovasicular steatosis, degree of activity of chronical hepatitis and the degree of fibrosis; "1st" biopsy – performed 2 hours after reperfusion of a graft in recipient-degree of ischemic/reperfusion injury would be semiquantitativly determined: mild, moderate and severe on the base of scoring 8 morphological characteristics: balloon degeneration hepatocytes, microvesicular and macrovesicular steatosis, cholangiolar proliferation, cholestasis, apoptotic bodies, granulocytes infiltration and pericentral confluent necrosis. In case that we need vaso-active drugs more than 30 minutes or to decrease MAC (minimum alveolar concentration) less than 0.5 for period longer than 15 minutes we would exclude patient from the study.

**Expected scientific contribution:** Scientific contribution of this study would be to determent benefit of using sevoflurane or isoflurane on better outcome after ischemic/reperfusion injury of liver graft.

**Acknowledgments:**

**MeSH/Keywords:** liver transplantation/adverse effects, ischemic postconditioning/methods, pharmacology, reperfusion injury/prevention

**Poster code:** T-B-1-33

# Poster Title: ALVEOLAR MANOEUVRE PROCEDURE AND USAGE OF END-EXPIRATORY PRESSURE DURING GENERAL ENDOTRACHEAL ANAESTHESIA

**PhD candidate:** Maša Kontić

**Thesis proposal:** Alveolar manoeuvre procedure and usage of end-expiratory pressure during general endotracheal anaesthesia

**Mentor/s:** Professor Dinko Tonković, MD, PhD

**Affiliation:** General Hospital „Dr Ivo Pedišić", Department of Anaesthesiology, Reanimatology and Intensive Medicine, Sisak, Croatia

**Introduction:** Respiratory function as a part of general anaesthesia has been altered because of anaesthetics, position during operation and joined comorbidities. The focus is on the common postoperative respiratory complications and its serious implications. There have been many causes for these complications, such as surgery, drugs, hypoxia and microatelectasis which increase physiological shunt.

**Hypothesis:** The application of protective ventilation strategy compared with standardized treatment diminishes respiratory complications.

**Aims:** To monitor clinical effects regarding inflammation, upper respiratory tract secretion, prolonged mechanical ventilation, intensive care recovery, and the length of hospitalization within and between groups using these treatments.

**Materials and methods:** The study has been planned as a prospective randomized double-blind study The total number of 60 participants with ASA I and ASA II, upper and middle laparotomized, aged 18 to 60, will be divided into two groups. Experimental group of 30 participants will be treated with oxygen inspiratory fraction under 70%, positive end-expiratory pressure under 5kPa, peak pressure under 30kPa, tidal volume 4-6ml/kg, breathing frequency 10-12/min, endotracheal tube kinking, and continuos positive pressure uned 10kPa just in time before extubation. Control group of 30 participants will be treated with inspiratory oxygen fraction to100%, positive end –expiratory pressure under 3kPa, peak pressure under 40kPa,tidal volumen 4-6ml/kg, and breathing frequency 10-12/min. Endotraheal tube kinking will be proceeded after intubation, and every 30 minutes during operation, using peak pressure under 30kPa during 20sec. As far as it concerned, anaesthetics will be administered at previously mentioned doses. Recorded data will be implemented for statistical significance using Statistical Software NCSS version PASS 11.

**Expected scientific contribution:** Determine the optimal treatment regarding perioperative respiratory complications with its role in enhancing respiratory function recovery.

**Acknowledgments:**

**MeSH/Keywords:** atelectasis, chronic obstructive disease, alveolar recruitment manoeuvre

**Poster code:** T-B-1-57

# Poster Title: PERIOPERATIVE MULTIMODAL MANAGEMENT AND OXIDATIVE STRESS IN LAPAROSCOPIC CHOLECYSTECTOMY

**PhD candidate:** Martina Čalušić, MD

**Thesis proposal:** Effects of perioperative multimodal management on oxidative stress and clinical outcome in laparoscopic cholecystectomy

**Mentor/s:** Professor Dinko Tonković, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre - Zagreb

**Introduction:** Although laparoscopic cholecystectomy (LC) is considered to be a less invasive surgical procedure, it may lead to significant levels of oxidative stress. Underlying mechanisms of oxidative stress during laparoscopic surgery primarily include ischemia-reperfusion injury and surgical stress response. Lipid peroxidation is damaging because the formation of toxic aldehydes, which can be used as oxidative stress biomarkers. The most researched aldehydes are malondialdehyde (MDA) and 4-hydroxynonenal (4-HNE). Modern approach to LC includes multimodal anesthesia and surgical procedures. Drugs used within the multimodal approach along with their primary effects also show antioxidant properties.

**Hypothesis:** Multimodal protocol leads to oxidative stress reduction during LC and has a beneficial effect on clinical outcome.

**Aims:** To determine if multimodal management during LC reduces the level of oxidative stress biomarkers (MDA and 4-HNE).

**Materials and methods:** With the approval of the local ethics committee a prospective randomized study will be carried out at the Department of Anesthesiology, Resuscitation and Intensive Care and Department of Surgery, University Hospital Centre Zagreb. Patients undergoing elective LC for symptomatic cholelithiasis classified by ASA (The American Society of Anestesiologists) status ASA I and ASA II, aged between 18 and 65 years will be enrolled in this study and randomized in two groups depending on whether the general anesthesia will be carried out primarily with anesthetic propofol with the implementation of a multimodal approach (M group, 30 patients) or inhaled anesthetic sevoflurane with the classical approach (group C, 30 patients). Multimodal management will include the use of propofol, remifentanil, 2% lidocaine, dexamethasone, ketoprofen, metoclopramide and 0,5 % levobupivacaine. The blood samples of all patients will be collected prior to anesthetic induction, immediately after the procedure and on post-operative day number one. Serum samples will be prepared from each blood sample and stored at -80°C until assay. MDA and 4-HNE levels will be determined by quantitative enzyme-linked immunosorbent assays. Non-parametric tests will be used for the statistical analysis.

**Expected scientific contribution:** This study will determine whether multimodal management reduces levels of oxidative stress, which has still not been established.

**Acknowledgments:**

**MeSH/Keywords:** Oxidative stress, multimodal analgesia, laparoscopic cholecystectomy, malondialdehyde, 4 hydroxynonenal

**Poster code:** T-B-1-93

**Poster Title: THE EFFECT OF INTRAOPERATIVE APPLICATION OF MANNITOL IN HEMODYNAMICALLY UNSTABLE RECIPIENTS ON THE DEGREE OF POSTREPERFUSION HEMODYNAMIC INSTABILITY AND GRAFT´S ISCHEMIA-REPERFUSION INJURY DURING LIVER TRANSPLANTATION**

**PhD candidate:** Matea Bogdanović Dvorščak,MD

**Thesis proposal:** The effect of intraoperative application of mannitol in hemodynamically unstable recipients on the degree of postreperfusion hemodynamic instability and graft´s ischemia-reperfusion injury during liver transplantation

**Mentor/s:** Anita Škrtić, MD, PhD

**Affiliation:** University Hospital Merkur, Zagreb, Croatia

**Introduction:** Liver transplantation is one of the most complex procedures in transplantation medicine which carries excessive possibility for hemodynamic instability. Cutting through numerous collateral blood vessels for liver mobilization during hepatectomy results in extensive surgical trauma. The blood loss correlates with a degree of surgical severity. Second is anhepatic stage which last from hepatal vasculature occlusion to new liver reperfusion. Massive bleeding and hemodynamic instability is mainly a consequence of termination in the synthesis of coagulation factors as well as certain extent off coagulation factors consumption. Despite optimal replacement of volume and blood approximately 50% patients need same extent off vasopressors and/or inotropes to sustain optimal mean arterial pressure (MAP) above 60 mmHg. In neohepatic or postreperfusion stage refreshed blood in flushed through graft which leads to massive free radical release and some degree off postreperfusion hemodynamic instability (PRHN). Most vulnerable are patients already on vasopresors and/or inotropes.

**Hypothesis:** Mannitol will attenuate the PRHN and ischemia-reperfusion injury (IRI) in hemodynamically unstable patients during orthotopic liver transplantations in comparison with placebo.

**Aims:** To investigate the effect of intraoperative application of mannitol in liver transplantation on the incidence and degree of PRHN and IRI in hemodynamically unstable patients.

**Materials and methods:** The study is prospective, double-blind, randomized and controlled, in 116 haemodynamically unstable patients who will underwent liver transplantation. Haemodynamic instability will be defined as necessity to decrease MAC (minimum alveolar concentration) less than 0.5 for period longer than 15 minutes or to include vasopresors and/or inotropes sustain mean arterial pressure above 60 mmHg. Patients will receive 10% mannitol or 0.9% NaCl solution at a dose 5 ml/kg of ideal body weight (0.5 g/kg) for 10 minutes prior to reperfusion. Immediately after reperfusion they will receive a second dose of the same amount of solution in 60 minutes. The degree PRHN will be determined by difference in values of monitoring MAP and heart rate. The degree of IRI will be determined by newly created score based on morphological criteria.

**Expected scientific contribution:** Confirming the hypothesis that mannitol attenuate PRHN and IRI in hemodynamically unstable patients could contribute to the introduction of mannitol as standard therapy during liver transplantation.

**Acknowledgments:** I would like to thank my mentor Anita škrtić, MD, PhD

**MeSH/Keywords:** liver transplantation, hemodynamic, post reperfusion syndrome, ischemia-reperfusion injury, mannitol

**Poster code:** T-B-1-165

# Poster Title: ASSOCIATION OF THE CLINICAL PRESENTATION AND VIRAL GENOTYPES IN GENITAL INFECTIONS WITH HUMAN PAPILLOMAVIRUS IN MEN

**PhD candidate:** Ivana Čulav Košćak, MD

**Thesis proposal:** Association of the clinical presentation and viral genotypes in genital infections with Human papillomavirus in men

**Mentor/s:** Professor Mihael Skerlev, MD, PhD

**Affiliation:** Department of Dermatovenereology and Department of Clinical and Molecular Microbiology, University Hospital Centre Zagreb and School of Medicine Zagreb

**Introduction:** Genital infection due to Human papillomavirus is the most common viral sexually transmitted disease. Specific HPV genotypes can induce the premalignant lesions as well as invasive cancers in genitoanal region. According to recent investigation oncogenic HPV genotypes can also induce the benign genital lesion. In our study we will correlate clinical appearance and localization of genital lesions with certain HPV genotypes.

**Hypothesis:** Oncogenic HPV genotypes can induce clinically benign lesions in genitoanal region in men. Variations in the clinical presentation of HPV genital infection in men can be caused by specific HPV genotypes.

**Aims:** The main objective of the study is to determine the representation of 18 HPV genotypes in clinically altered skin and/or mucosa of the genitoanal region in men and to correlate the specific HPV genotypes with localization and clinical manifestations of lesions. Specific aims are: 1) to determine the prevalence the oncogenic HPV genotypes in benign lesions and of the low-risk HPV genotypes in premalignant lesions, 2) to make a multivariate analysis of the monitored variables with the occurrence of the oncogenic HPV genotypes in benign lesions and of the low-risk HPV genotypes in premalignant lesions, 3) to correlate the sensitivity and specificity of the two methods for detection of HPV genotypes in men, 4) to determine the optimal method for identification of HPV genotypes in genitoanal lesions in men.

**Materials and methods:** The observational cross-sectional study will be conducted for a period of six months in the Department of Dermatovenereology and the Department of Clinical and Molecular Microbiology, University Hospital Centre Zagreb. 80 male patients aged 18-65 years with clinical manifestations of HPV genital infection will be included in the study. The material obtained by curretage from the affected skin and/or mucosa will be analysed by the standard Hybrid Capture II method. Each HC II probe positive for the oncogenic HPV genotypes, as well as negative or inconclusive test sample will be additionally assessed with INNO-LiPA method which allows to selectively determine the specific HPV genotype.

**Expected scientific contribution:** The results of the study will contribute to: 1) early detection of oncogenic viral types based on the highly specific HPV DNA typing tests, 2) persistence in treatment of genitoanal lesions in which oncogenic viral genotypes had been detected regardless their clinically benign appearance, 3) prevention of invasive cancer of genitoanal region in male population.

**Acknowledgments:** I would like to thank my mentor Professor Mihael Skerlev, MD, PhD and Assistant Professor Lidija Žele Starčević, MD, PhD for scientific guidance and support.

**MeSH/Keywords:** HPV, male, sexually transmitted infections, Hybrid Capture, HPV DNA typing

**Poster code:** T-B-2-106

## Poster Title: SONOGRAPHY-BASED AUTOMATED VOLUME COUNT FOLLICLE (SONOAVC) METHOD FOR PREDICTION OF OOCYTE YIELD IN A STIMULATED OVARIAN CYCLE

**PhD candidate:** Ivan Bolanča

**Thesis proposal:** Sonography-based Automated Volume Count follicle (SonoAVC) method for prediction of oocyte yield in a stimulated ovarian cycle.

**Mentor/s:** Prof. Davor Ježek, MD, PhD, Assist Prof. Krunoslav Kuna, MD, PhD

**Affiliation:** University Hospital "Sestre milosrdnice", Department of Human Reproduction, Vinogradska 29, Zagreb

**Introduction:** A prediction of ovarian response is a crucial step in evaluation of patients for IVF/ICSI program. It may help to estimate a proper initial gonadotropin dose, or in cases of severely diminished ovarian reserve to direct a patient towards alternative methods of infertility treatment. Golden standard in ovarian reserve assessment for the long period of time was AFC (Antral follicle count) measured by two-dimensional ultrasound. During the last decade, AMH (Anti-Müllerian hormone) is becoming a promising marker. The newest method is an automated three-dimensional antral follicle count (Sonography-based Automated Volume Count follicle - SonoAVC) with some clear potential advantages compared to AMH and AFC.

**Hypothesis:** Based on number and/or size of antral follicles on day 2 of stimulated antagonistic IVF/ICSI cycle measured by SonoAVC, one can reliably predict a number of collected oocytes.

**Aims:** The general aim of this study is to determine a predictive value of number and/or size of antral follicles on day 2 of stimulated antagonistic IVF/ICSI cycle measured by SonoAVC on oocite yield. We have 2 co-primary aims, considering two different variations of SonoAVC (completely automated and automated with subsequent manual correction). Secondary aim is to compare predictive values of serum AMH and SonoAVC on oocite yield.

**Materials and methods:** Patients planned for stimulated IVF/ICSI cycle in our Institution, age 18-42, BMI<30kg/mČ2, FSH < 15 IU/L. In the cycle preceding the stimulated cycle AFC will be determined in standard fashion. On the cycle day 2 a blood sample (6mL) for the AMH testing will be collected and both ovaries will be scanned with vaginal probe and analysed with SonoAVC. Based on the AFC value, from the day 2 the starting dose of the recombinant gonadotrophins will be administered (AFC <6 375IU/day, AFC 6–15 225 IU/day and AFC>15 150 IU/day) and further corrected acoording to the ovarian reponse. From day 6 GnRH antagonist will be administered. With leading foliicule reaching 18mm, a recombinant hCG will be administered and oocite pickup performed 36 hours later. Transfer up to 2 embryos is planned on day 3 or day 5, based on the quality of the embryos.

**Expected scientific contribution:** SonoAVC is a promising noninvasive method of ovarian reserve assessment, with some clear advantages compared to AMH and AFC.

**Acknowledgments:** None

**MeSH/Keywords:** Ovarian reserve, Anti-Mullerian Hormone, Ultrasonography, Antral Follicle Count (AFC)

**Poster code:** T-B-5-10

# Poster Title: WNT PATHWAY IN OVARIAN CANCER

**PhD candidate:** Vedran Kardum MD

**Thesis proposal:** The role of Wnt signaling pathway in ovarian cancer development

**Mentor/s:** Associate Professor Ljiljana Šerman MD PhD

**Affiliation:** University of Zagreb School of Medicine, University hospital Merkur

**Introduction:** Ovarian cancer is the most lethal gynecological malignancy. Absence of early symptoms and lack of effective screening contributes to high mortality. Wnt signaling pathway is a highly conserved signal transduction pathway critical for embryonic development. It is activated by binding of an extracellular Wnt-protein ligand to a Frizzled family of membrane receptors, which then activates a family of cytoplasmic Dishevelled proteins (DVL). DVL acts as the central mediator which regulates and directs all events downstream of frizzled receptor, finally resulting in activation of genes necessary for achievement of the invasive phenotype. The pathway is regulated by Wnt antagonists, family of 5 secreted frizzled receptor proteins (SFRP1-5). SFRPs contain frizzled-like cysteine rich domain (CRD) which allows binding to Wnt ligands or Frizzled receptors directly and thus acts as competitive inhibitors of Wnt signaling. Increased expression of SFRP genes in cancer cells indicates better prognosis, whereas the reduction of their expression contributes to tumor progression and invasiveness.

**Hypothesis:** SFRPs act as competitive inhibitors of Wnt signaling pathway, thus we expect a decreased expression of SFRP1 and SFRP3 in ovarian cancer as well as an increased expression of DVL1, DVL2 and DVL3, the positive regulators of Wnt signaling pathway.

**Aims:** The aim of this study is to determine the expression of less studied positive and negative regulators of Wnt signaling pathway in ovarian cancer, and link them with patients' clinical data which will allow us to gain insight into the etiopathogenesis of ovarian cancer.

**Materials and methods:** The research will include approximately 100 archive samples of various ovarian cancers. SFRP1, SFRP3, DVL1, DVL2 and DVL3 antigen distribution will be analysed by immunohistochemistry. Antigen expression will be scored using quantitative stereological analysis of volume density. The results will be correlated with patients' clinical data and a comparison of protein expression with respect to survival rate, chemosensitivity and time of relapse will be examined.

**Expected scientific contribution:** Little is known about the molecular basis of ovarian cancer development. The proposed thesis would contribute to a better understanding of ovarian cancer etiology as well as the possibility of early detection, novel therapy and prognosis of survival.

**Acknowledgments:**

**MeSH/Keywords:** Wnt, carcinoma, ovary, SFRP, DVL.

**Poster code:** T-B-5-44

## Poster Title: THE INFLUENCE OF PREOVULATORY AND POSTOVULATORY PROGESTERONE SERUM CONCENTRATION ON THE OUTCOME OF THE IN VITRO FERTILIZATION

**PhD candidate:** Emina Ejubović[2], MD

**Thesis proposal:** The influence of preovulatory and postovulatory progesterone serum concentration on the outcome of the in vitro fertilization

**Mentor/s:** Professor Miro Kasum[1], MD, PhD

**Affiliation:** [1] University of Zagreb School of Medicine, University Hospital Center-Zagreb, Department of Obstetrics and Gynaecology, [2] Cantonal Hospital Zenica, Bosnia and Herzegovina

**Introduction:** Previous discoveries about the impact of elevated preovulatory and postovulatory progesterone (P4) on the outcome of in vitro fertilization (IVF) are the subject of many discussions in contemporary reproductive endocrinology. Numerous studies discuss about the adverse effect of elevated preovulatory P4 on the outcome of IVF. Other studies, contrary, prove that there is no adverse effect of elevated preovulatory P4 on the outcome of IVF. Hence, the occurrence of the preovulatory P4 rise is a riddle with no clearly established strategies in the treatment of such patients.

**Hypothesis:** The unfavorable impact of an increased preovulatory P4 on the pregnancy outcome during the ovulation induction in IVF treatment is absent despite the high P4 on day 5 among high responders and with normalized P4 on day 5 among normal responders.

**Aims:** The aim is to determine the impact of the preovulatory and postovulatory P4 after the ovarian stimulation during the IVF treatment on the pregnancy outcome through the implantation and clinical pregnancy rate in normal and high responders with the fresh (BET) or frozen/thawed blastocysts transfer (FET).

**Materials and methods:** Total of 400 patients will be included in the study (300 patients with normal preovulatory P4 in the control group and 100 patients with the high preovulatory P4 in the study group). Inclusion criteria: patients undergoing IVF treatment, patients with normal P4 on the 2nd, 3rd and 4th day of the cycle, patients aged 18-37, normal responders (E2<3000 pg/ml, number of oocytes <20) and high responders (E2>3000 pg/ml, number of oocytes>20). Patients will be paired according to their age, BMI, stimulation protocol, gonadotropin dosage, the number of retrieved oocytes and transferred embryos. Implantation and clinical pregnancy rate in the study group will be analyzed, in terms of high preovulatory P4 with the FET or BET, for the statistical significance using SPSS 21 and MedCalc Statistical Software version 13.1.2.

**Expected scientific contribution:** The determination of P4 on the 5th day will be used in the selection of a more appropriate method of embryo transfer at the blastocyst stage resulting in improved implantation and clinical pregnancy rate. This research will contribute to the implementation of new policies and strategies in the treatment of patients during IVF procedures with no additional effort, time and cost of cryopreservation/thawing and subsequent blastocyst transfer in the natural cycle.

**Acknowledgments:**

**MeSH/Keywords:** in vitro fertilization, progesterone, embryo transfer

**Poster code:** T-B-5-26

## Poster Title: EFFECTS OF LATERAL EPISIOTOMY ON THE PELVIC FLOOR AND SEXUAL FUNCTION

**PhD candidate**: Krešimir Živković, MD

**Thesis proposal:** Effects of lateral episiotomy on the function of pelvic floor and sexual function after vaginal delivery in primiparas

**Mentor/s:** Full Professor Slavko Orešković, MD, PhD

**Affiliation:** Sveti Duh University Hospital, Zagreb, School of Medicine, University of Zagreb.

**Introduction:** Episiotomy is an incision which extends the vestibule of the vagina during fetal expulsion. Most texts describe two types, the mediolateral and the median episiotomy, although there are more types. Lateral episiotomy cut starts 1-2 cm from the posterior fourchette towards the tuberosity of the ischium and is often used but rarely cited in the literature. There are no published studies dealing with effects of lateral episiotomy on urinary and fecal continence and sexual function in primiparas. Moreover the results of studies dealing with mediolateral and median episiotomy are mostly in favor of the negative effect of episiotomy on the pelvic floor.

**Hypothesis:** Lateral episiotomy has a protective effect on the occurrence of urinary and fecal incontinence and on sexual dysfunction in primiparas during the first year after delivery.

**Aims:** To explore the effect of lateral episiotomy on the pelvic floor and the occurrence of urinary and fecal incontinence and sexual dysfunction in primiparas as compared to women without episiotomy.

**Materials and methods:** This is a prospective cohort study. 200 examinees will be divided in 2 groups. The first group will consists of women who delivered by lateral episiotomy and another group of women who delivered with perineal rupture of lesser degree. The study will include primiparas with singleton pregnancies and spontaneous onset of labor with fetuses in cephalic presentation. Clinical examination of pelvic floor will be performed at time interval of 5 and 8 months after delivery accompanied by specific questionnaires. International Consultation on Incontinence Questionnaire-Urinary Incontinence-Short Form will assess urinary incontinence, Wexner Scale will assess fecal incontinence while Female Sexual Function Index will assess sexual function. Exam of pelvic floor will be done by Pelvic Organ Prolapse Quantification system, Bonney test, ultrasound of the anal sphincter and the muscle levator ani plus valuation of the pelvic muscles by perineometry. Proper parametric and/or non-parametric analysis will be applied. P values < 0.05 will be significant and Statistica 12.0 will be used.

**Expected scientific contribution:** Evaluation of the effects of lateral episiotomy on the observed indicators of the of women life quality through medium-term outcomes after first delivery, in particular about quality of sexual life, urinary and fecal continence will contribute to a better understanding of recent issues in obstetrics and urogynecology.

**Acknowledgments:** To my mentor Professor Slavko Orešković for guidance.

**MeSH/Keywords:** episiotomy, urinary incontinence, fecal incontinence, primipara.

**Poster code:** T-B-5-30

# Poster Title: EARLY PREGNANCY PREDICTION OF PREECLAMPSIA

**PhD candidate:** Petrana Beljan, MD

**Thesis proposal:** Early predictive model for the development of preeclampsia: combination of biomarkers PP13 and copeptin and maternal risk factors

**Mentor/s:** Vesna Elveđi Gašparović, Assistant professor, MD, PhD, Dept. of Ob/Gyn, School of Medicine, University of Zagreb, Zagreb, Croatia

**Affiliation:** Dept of Ob/Gyn, School of Medicine, University of Zagreb, Zagreb, Croatia

**Introduction:** Preeclampsia is a multisystem pregnancy related disorder of unknown etiology, with the progressive course and with no established therapy. It complicates 3-7% of all pregnancies and it is the most common cause of fetal and maternal death. The cardinal clinical features of the condition are hypertension and proteinuria, or hypertension and some liver dysfunction occurring after 20 weeks of gestation in previously normotensive women. Preterm delivery is often the only curative treatment for preeclampsia

**Hypothesis:** Increased levels of copeptin and decreased levels of PP13 biochemical markers in the first trimester of pregnancy can predict preeclampsia before clinical diagnosis.

**Aims:** The aim of this study is to find an early predictive model for preeclampsia during the first trimester of pregnancy using the combination of biochemical markers PP13 and copeptin with some known maternal risk factors and uterine artery Doppler.

**Materials and methods:** This is a prospective study which will include 400 pregnant women who will undergo routine first trimester (11-14 weeks) laboratory test in the Department of Obstetrics and Gynecology, University Hospital Center Zagreb. There are some factors associated with increased risk of developing preeclampsia, so we will use some of them as the inclusion criteria for our study: nulliparity, age >35, BMI >25, smoking and some other chronic diseases in personal history. Participants will be asked to provide some short questionnaire with personal and medical informations. Blood samples will be collected and maternal serum PP13 and copeptin will be measured using routine automated analyzers. All patients will also do uterine artery Doppler. Data on pregnancy outcome will be collected after the delivery from maternal and pediatric records.

**Expected scientific contribution:** If this model proves to be a reliable early predictor of preeclampsia it could be a great opportunity to integrate these into routine testing already performed as part of prenatal care in the first trimester. This is the way to detect preeclampsia before the appearance of clinical symptoms and to prevent some of the most serious consequences which are still a significant burden for perinatal outcome and for the health care system in the worldwide.

**Acknowledgments:**

**MeSH/Keywords:** preeclampsia, PP13, copeptin, perinatal outcome

**Poster code:** T-B-5-110

## Poster Title: CERVICAL ELASTOGRAPHY IN TERM PREGNANCIES

**PhD candidate:** Ivka Djaković, MD

**Thesis proposal:** Elastography can register physiological changes in cervical ripening in term pregnancies

**Mentor/s:** Assist. Prof. Berivoj Mišković, MD, PhD; Assist. Prof. Gordana Ivanac, MD, PhD

**Affiliation:** Clinical Department of Gynecology and Obstetrics, Sestre milosrdnice University Hospital Center, Zagreb, Croatia

**Introduction:** In order to achieve the most optimal perinatal outcome modern obstetrics often induce labour for medical indications. Sometimes induced labour is method of programmed delivery. Based on physical findings in cervix and foetal head engagement clinician chooses a method of induced labour. Cervical length ultrasound measurement never became routine in clinical practice. Besides subjective evaluation clinicians currently do not use any objective method for assessment of cervical maturity. New ultrasound non-invasive method, elastography, for determination of the hardness of tissue, could objectify cervical finding and facilitate the decision on labour induction and method selection for labour induction.

**Hypothesis:** Elastography can register physiological changes in cervical ripening in term pregnancies

**Aims:** The aim of this study is to explore the possibilities of elastography to assess the physiological changes in the cervix consistency in order to estimate pregnancy duration and outcome of the spontaneous and induced labour. The correlation of elastography with anthropological caracteristics, mode of delivery, perinatal outcome, use of oxytocin, episiotomy and epidural analgesia, as well as feasibility of clinical use of elastograpy will be studied too.

**Materials and methods:** Longitudinal cohort study of 100 in term pregnancies of healthy primiparas in University Hospital Center Sestre milosrdnice will be performed. Other conditions like hypertension, gestational diabetes, thrombophilia, preeclampsia, kidney diseases and infections will be excluded by detailed history. Data will include cervical elastography, age, height and weight, body mass index, gestational age, mode of delivery (vaginal, vacuum extraction, Caesarean section), duration of the delivery, oxytocin use, rate of episiotomy and epidural analgesia. Perinatal outcome will be measured by birthweight, Apgar score and intensive care unit days. Elastography will be performed in three intervals. First one in weeks 36-37, second one in weeks 38-39 and last one in weeks 40-41. The results will be presented in tables and graphically. Statistical significance is 0.05. The data will be statistically analysed by SPSS 15.0 for Windows.

**Expected scientific contribution:** This study should give new understanding of elasticity features of the cervix in healthy women in term pregnancies. Feasibility of this new ultrasound method in clinical practice will also be evaluated.

**Acknowledgments:**

**MeSH/Keywords:** elastography, term pregnancy, spontaneous and induced labour, primiparae

**Poster code:** T-B-5-150

## Poster Title: RELATIONSHIP BETWEEN RIGHT VENTRICULAR FUNCTION AND RED CELL DISTRIBUTION WIDTH IN PATIENTS WITH SYSTEMIC SCLEROSIS

**PhD candidate:** Sandra Jakšić Jurinjak M.D.

**Thesis proposal:** Relationship between right ventricular function and red cell distribution width in patients with systemic sclerosis

**Mentor/s:** Assoc. Prof. Diana Delić-Brkljačić, MD, PhD

**Affiliation:** University Hospital Dubrava, Institute of Cardiovascular Diseases, Zagreb

**Introduction:** Systemic sclerosis (SSc) is a chronic disease with autoimmune pathogenesis that affects connective tissue, microvessels and small arteries, characterised by fibrosis and vascular obliteration in the skin and internal organs. Primary myocardial involvement is common in systemic sclerosis. The prognosis of systemic sclerosis worsens with cardiopulmonary involvement, heart failure and pulmonary hypertension. Red cell distribution width (RDW) is a measure of red blood cell size heretogeneity (anisocytosis), with evidence that suggests that RDW is now proved to be a powerful predictor of outcomes in patients with left heart failure and it can be used to identify patients with right heart failure.

**Hypothesis:** Echocardiographic parameters of right ventricular function are correlated with levels of red cell distribution width in patients with systemic sclerosis without pulmonary hypertension.

**Aims:** The aim of this investigation is attempt to connect right ventricular funtion parameters using transthoracic echocardiography tissue doppler imaging with levels of RDW, which may be used to indentify SSc patiens with increased risk of right ventricular involvement, primary cardiac involvement and possible cardiac complication in SSc.

**Materials and methods:** The present study is designed to investigate the association between RDW values and parameters for the detection of right ventricular (RV) systolic and/or dyastolic dysfunction in patients with systemic sclerosis (SSc) without pulmonary hypertension. Seventeen consecutive SSc patients without pulmonary hypertension are investigated at baseline and after 4,8,12 month of follow-up. Subjects will underwent standard echocardiography with tissue doppler imaging (TDI) to assess RV function at each visit. Hematological parameters, RDW is analyzed by standard methods on scheduled visits. RDW will be analyzed showing a positive or negative correlation with tissue doppler imaging right ventricular peak myocardial systolic velocity, right ventricular Tai index, and tricuspid E/E' as standard tissue doppler imaging right ventricular function parameters.

**Expected scientific contribution:** If correlation is found, RDW in patients with SSc may represent an integrative measure of multiple pathological processes that may indicate an early right ventricular impairment in patients with SSc without pulmonary hypertension. This could be useful tool with predictive power to detect early right ventricular impairment with implication in early treatment of patients with SSc.

**Acknowledgments:**

**MeSH/Keywords:** systemic sclerosis, red cell distribution width, right ventricular function, echocardiography

**Poster code:** T-B-9-35

## Poster Title: ASSOCIATION OF PLATELET SEROTONIN WITH ASTHMA SEVERITY, CONTROL AND PHENOTYPE

**PhD candidate:** Katherina Bernadette Sreter, MD (1)

**Thesis proposal:** Platelet serotonin and asthma

**Mentor/s:** Professor Sanja Popović-Grle, MD, PhD (2)

**Affiliation:** (1) University Hospital Centre „Sestre Milosrdnice", Zagreb, Croatia, (2) University Hospital Centre Zagreb, Clinic for Respiratory Diseases „Jordanovac", Zagreb, Croatia.

**Introduction:** Asthma is a common, but complex and heterogeneous, chronic inflammatory disease of the respiratory airways characterized by inappropriate immune response. Serotonin (5-hydroxytryptamine, 5-HT), a neuro-immunomodulator-transmitter well known for its role in depression, has been shown to be important in pulmonary function and immune responses. There is mounting evidence that the serotonergic system may be involved in the pathophysiology of asthma, but the precise role of platelet 5-HT (p-5-HT) in asthma is unknown.

**Hypothesis:** This study will investigate the hypothesis that p-5-HT may be a potential blood-based biomarker in asthma.

**Aims:** The general objective of this study is to investigate the involvement of the serotoninergic system in the pathogenesis of asthma. Specifically, 1) to investigate the role of circulating p-5-HT in discriminating between those with and without asthma, 2) to compare p-5-HT levels in asthmatics, and to assess the associations of these concentrations with asthma phenotypes, severity and control of disease, and known biomarkers of allergic asthma, such as FeNO and serum total IgE antibodies, and 3) to integrate bench and bedside parameters for classification of novel asthma phenotypes.

**Materials and methods:** This observational study will include 142 asthmatics treated at the Clinic for Respiratory Diseases „Jordanovac", Zagreb, Croatia, as well as a control group of 150 healthy blood donors from the Croatian Institute for Transfusion Medicine (CITM), Zagreb, Croatia. Clinical and laboratory data related to this study, collected prospectively during the recruitment period (2014–2015), will be analyzed. For determination of p-5-HT and protein levels, blood specimens were processed at the Division of Molecular Medicine of the Ruđer Bošković Institute (RBI), Zagreb, Croatia. Appropriate non-parametric and/or parametric statistical tests will be applied to the data.

**Expected scientific contribution:** A personalized medicine approach to asthma research, using p-5-HT as a potential biomarker that may be able to distinguish various asthma phenotypes and severity, has the potential to become a valuable diagnostic tool. Investigating the involvement of the serotoninergic system should improve understanding of the pathogenesis of asthma, thus impacting future diagnostic and treatment options.

**MeSH/Keywords:** asthma, serotonin, 5-hydroxytryptamine (5-HT), biomarkers, phenotype

**Poster code:** T-B-9-69

# Poster Title: ENDOSCOPIC CHARACTERISATION OF COLORECTAL POLYPS USING NARROW BAND IMAGING (NBI)

**PhD candidate:** Ivana Tirić

**Thesis proposal:** Endoscopic characterisation of colorectal polyps using narrow band imaging

**Mentor/s:** Professor Nadan Rustemović, MD, PhD

**Affiliation:** Department of Gastroenterology and Hepatology, University Hospital Centre Zagreb. Department of Internal medicine, General Hospital „ dr. T. Bardek" Koprivnica

**Introduction:** Narrow Band Imaging (NBI) is advanced endoscopic technology allowing for real time characterisation of polyp histology by means of mucosal and capillary patterns at a single push of a button (virtual biopsy). Although the NBI system is available in all new generation colonoscopes its capabilities are not used in clinical practice, part of the reason behind that being the existence of few unharmonised, nonvalidated NBI classifications. Compared to existing classifications recently developed NBI International Colorectal Endoscopic (NICE) classification is validated and is characterized by simplicity and standardization. The implementation of this classification in routine clinical practice could potentially lead to changes in present practice towards "resect and discard" strategy for diminutive polyps (≤mm) and "do not resect" strategy for diminutive hyperplastic polyps in the distal colon. If implemented, these strategies allow us to avoid exposing patients to risks stemming from žunnecessary' polypectomies and to significantly cut health care costs without adverse effects on patients' health.

**Hypothesis:** Pathohistological assessment of diminutive (≤5mm) and small (6-10mm) colorectal polyps characterised by in vivo NICE classification is not mandatory after removal.

**Aims:** The aim of this study is to assess the reliability of virtual biopsy of diminutive (≤5mm) and small (6-10mm) colorectal polyps in routine clinical practice.

**Materials and methods:** Our study will include 100 consecutive patients referred for a colonoscopy to our clinic. Determination of lesion histology using NICE classification will be done in patients with lesions detected during colonoscopy. Endoscopist will then predict the optimal treatment strategy and surveillance interval. All analysed lesions will be resected and submitted for pathologic assessment. Finally, differences in the endoscopic and pathologic determination of lesion histology will be analysed as well as differences in proposed optimal treatment strategy and surveillance interval.

**Expected scientific contribution:** Results obtained in this study would enable the use of virtual biopsy in routine clinical practice, thus improving the efficiency of the colonoscopy and lead to substantial savings in time and cost.

**Acknowledgments:**

**MeSH/Keywords:** virtual biopsy, NBI, characterisation of colorectal polyps, NICE classification

**Poster code:** T-B-9-67

## Poster Title: THE SEVERITY OF CORONARY ARTERY DISEASE IN THE ROMA MINORITY IN RESPECT TO THE SOCIO-DEMOGRAPHIC AND CARDIOVASCULAR RISK FACTORS: IS THERE A SPECIFIC CORRELATION?

**PhD candidate:** Vanja Hulak Karlak

**Thesis proposal:** The severity of coronary artery disease in the Roma minority in respect to the socio-demographic and cardiovascular risk factors

**Mentor/s:** Assist. Prof. Boris Starčević, MD, PhD

**Affiliation:** University Hospital Dubrava, Institute of Cardiovascular Diseases, Zagreb, Croatia

**Introduction:** Cardiovascular diseases (CVD) represent a significant public health problem, in as much that these diseases may be even labeled as global epidemics. Coronary artery disease (CAD) is the most common of the aforementioned group. In developed countries, a plethora of efforts are taken in order to establish preventive measures and programs to reduce the prevalence of associated risk factors, and thus place CVD under scientific and medical control. The situation is somewhat different in developing countries, albeit there is a positive trend in tackling CVD in a similar fashion. The difficulties in both of these groups of countries may be found in small, indigenous and largely homogeneous minorities containing their own set of particularities. An eminent example of such minorities is the relatively secluded Roma population. The contemporary literature on the issue of CVD in the Roma minority provides scant information, even though the Roma's modus vivendi, socio-economic factors and the relative reproductive restraint of the community provide certain data.

**Hypothesis:** Roma patients, at the first presentation of CAD, in the form of acute coronary syndrome (ACS), have a more severe form of a CAD than non-Roma.

**Aims:** To assess severity of CAD, to identify the frequency and the differences of specific cardiovascular risk factors in Roma compared with non-Roma CAD patients. We will try to establish, in subgroup of Roma, is there a specific correlation between socio-demographic and cardiovascular risk factors and severity of CAD

**Materials and methods:** The patients hospitalized under the leading diagnosis of the treated in the 5-year period between 2011 and 2015 in the University hospital Dubrava, Zagreb. The patients will be divided based on their ethnicity into two groups, Roma and non-Roma. Medical records will be reviewed and data on angiographic severity of CAD, socio-demographic and cardiovascular risk factors will be obtained. After matching Roma and non-Roma according to gender and age, quantitative analytic paradigm will be used and optionally regression analyses.

**Expected scientific contribution:** The results of the ongoing research hold as their objective obtaining more accurate insight into the characteristics and peculiarities of CAD in the Roma minority. This would, in consequence, benefit the intervention plan, or, in simpler terms, the targeted measures of primary and secondary prevention.

**Acknowledgments:**

**MeSH/Keywords:** Roma, coronary artery disease, cardiovascular, risk factors

**Poster code:** T-B-9-52

## Poster Title: THE CROATIAN VALIDATION OF QUESTIONNAIRE FOR QUALITY OF LIFE EVALUATION AND OUTCOME IN PULMONARY HYPERTENSION „CAMPHOR"

**PhD candidate:** Ana Hećimović

**Thesis proposal:** The Croatian validation of questionnaire for quality of life evaluation and outcome in pulmonary hypertension „CAMPHOR" („Cambridge Pulmonary Hypertension Outcome Review" )

**Mentor/s:** Professor Sanja Popović Grle, MD, PhD, Professor Nataša Jokić Begić, Professor of Psychology, PhD

**Affiliation:** University Hospital Centre Zagreb, Clinic for Pulmonary Disease Jordanovac, Faculty of Humanities and Social Science, University of Zagreb

**Introduction:** Pulmonary arterial hypertension (PAH) is a rare disease defined as an increase mean pulmonary arterial pressure which leads to right-sided cardiac failure and death. Most common symptoms are dyspnea, fatigue, chest pain, syncopa and edema. Debilitating symptoms of the disease impair patient's quality of life so today we have disease-specific questionnaires of quality of life (QoL). One of them is CAMPHOR (Cambridge Pulmonary Hypertension Outcome Review) which is originally written in English. QoL questionnaires can help to improve treatment and evaluation of the patients. Till today there is no disease- specific questionnaire for PAH validated in Croatian language.

**Hypothesis:** Croatian version of CAMPHOR questionnaire is valid and reliable instrument in following up the quality of life of Croatian patients with pulmonary arterial hypertension and it can be used in everyday practice. Quality of life is in correlation with patients walking distance and NYHA functional status.

**Aims:** To validate first questionnaire for PAH in Croatian language which could help us in disease evaluation and improving patient's quality of life.

**Materials and methods:** The adaptation of CAMPHOR questionnaire involved three steps: translation process (employing bilingual and lay panels), cognitive debriefing interviews of patients and validation.
We will recruit 60 patients with PAH and chronic thromboembolic pulmonary hypertension to validate Croatian version of CAMPHOR. During the visit to the Clinic questions about demography (sex, age, marital status, occupation) and current condition (time since diagnosis, duration of symptoms, oxygen use and perceived general health) will be asked. All participants will perform 6 minute walking test and NYHA function status will be determined. Participants will complete CAMPHOR questionnaire for two times two weeks apart. They will also complete SF-36 questionnaire as the comparator instrument for construct validity. For the date analysis non-parametrical statistical tests will be used (SPSS, version 21.0). Internal consistency will be assessed using Cronbach's alpha coefficients. Test-retest reliability will be assessed using Spearman's Rank correlation.

**Expected scientific contribution:** To validate first questionnaire for PAH in Croatian language which could help us in disease evaluation and improving patient's quality of life.

**Acknowledgments:**

**MeSH/Keywords:** pulmonary arterial hypertension, quality of life, questionnaire, validation

**Poster code:** T-B-9-61

## Poster Title: CLINICAL SIGNIFICANCE OF YKL-40 AND CHITOTRIOSIDASE IN PATIENTS WITH PHILADELPHIA-NEGATIVE CHRONIC MYELOPROLIFERATIVE NEOPLASMS

**PhD candidate:** Ivan Krečak, MD

**Thesis proposal:** Clinical significance of YKL-40 and chitotriosidase in patients with Philadelphia-negative chronic myeloproliferative neoplasms

**Mentor/s:** Assistant professor Nadira Duraković, MD, PhD

**Affiliation:** Department of Internal Medicine, General Hospital of Šibenik – Knin County and University of Zagreb, School of Medicine, Department of Internal Medicine, Division of Hematology, Croatia

**Introduction:** The Philadelphia – negative chronic myeloproliferative neoplasms (MPNs), polycythemia vera (PV), essential thrombocythemia (ET) and primary myelofibrosis (MF), are clonal hematopoietic stem cell disorders, in which the JAK2 and CALR mutations are detected in more than 80% pts. Clonal myeloproliferation is accompanied with inflammatory changes responsible for a clinical phenotype. As biomarkers of inflammation, serum YKL-40 and chitotriosidase (CHIT1) levels in MPN pts are expected to be higher than those from healthy volunteers and their expression should correlate with disease activity, tumor burden and be independent of JAK2 or CALR status.

**Hypothesis:** Serum YKL-40 and CHIT1 levels are higher in MPN pts then those from general population and independent of JAK2 or CALR status.

**Aims:** GENERAL AIM: To correlate serum YKL-40 and CHIT1 levels in MPN pts with their clinical features. SPECIFIC AIMS: 1) To analyze serum YKL-40 and CHIT1 levels in relation to a) healthy volunteers, b) JAK2 and CALR status, 2) To analyze serum YKL-40 and CHIT1 levels in primary and secondary MF, 3) To analyze serum YKL-40 and CHIT1 levels in relation to: a) total leukocyte, granulocyte, platelet and blast count, b) LDH levels, c) splenomegaly grade, d) constitutive symptoms, 4) To analyze serum YKL-40 and CHIT1 levels in MF pts in relation to: a) anaemia grade, b) ECOG grade, c) marrow fibrosis grade, d) DIPPS score.

**Materials and methods:** This cross - sectional study will be performed on 100 adult MPN pts recruited from General Hospital of Sibenik–Knin County and University Hospital Centre Zagreb, Croatia. Input parameters will include pts' data: medical history, clinical status, laboratory and diagnostic procedures. 20 mL of full blood samples will be collected. Using a ELISA test, serum YKL–40 levels will be measured and fluorometry will be used to measure serum CHIT1 levels. RT – PCR will be used to assess JAK2 and CALR status.

**Expected scientific contribution:** Serum YKL-40 and CHIT1 levels should correlate with disease activity and tumor burden independently of JAK2 or CALR status and might separate pts with an advanced disease who could benefit from aggressive diagnostic and therapeutic approach.

**MeSH/Keywords:** JAK2V617F, calreticulin, YKL-40, chitothriosidase, biomarker, chronic inflammation, cytokines, myeloproliferative neoplasia (MPN)

**Poster code:** T-B-9-77

## Poster Title: METABOLIC SYNDROME IN PATIENTS WITH PITUITARY MACROADENOMA

**PhD candidate:** Božidar Perić, MD

**Thesis proposal:** Metabolic syndrome in patients with pituitary macroadenoma

**Mentor/s:** Professor Milan Vrkljan, MD, PhD

**Affiliation:** University Hospital Centre

**Introduction:** Metabolic syndrome (MS) is a group of metabolic disordes, including at least 3 of 5 clinical entities (visceral obesity, high blood pressure, impaired glucose metabolism, increased triglycerides and decreased high-density cholesterol). The most important risk factors for MS development are visceral obesity and insuline resistence. MS is linked to HP axis activity.Increased levels of insuline are found in patients with type 2 diabetes and visceral obesity, indicating increased HP axis activity. Changes in HP axis is directly linked with insuline resistance.Hypopituitarism, as a independent risk factor, is linked to high blood-pressure and visceral obesity. No individual marker was identified to show link between HP axis changes and MS. Latest reseach indicate prolactin as a potential risk factor in MS development.

**Hypothesis:** Hyperprolactinemia is an independent risk factor on key components of MS in patients with macroprolactinoma, somatotropinoma and non-functioning (NF) pituitary macroadenoma.

**Aims:** The aim of this study is to investigate metabolic effects of hypeprolactinemia in patients with macroproactinoma, macrosomatotropinoma in relation to NF pituitary macroadenoma on MS prevalence.

**Materials and methods:** Data base search with 150 hospitalized patients in Department of Endocrinology "Mladen Sekso", University Hospital Centre "Sestre milosrdnice" in the period from January 1, 2012 to October 1, 2015 will be carried out. As there has not been done any similar study before, pilot study will be done in order to determine number of participants. The sample size is determined by comparing two mean values and their standard deviations (2-sided equility). Power analysis will be performed for bivariant and and multivariant logistic regression, in order to detect risk factors for MS development in patient with macroprolactinoma, macrosomatotropinoma and NF pituitary macroadenoma.

**Expected scientific contribution:** Study should find link between altered metabolic profile of patients with macroprolactinoma, macrosomatotropinoma and NF pituitary macroadenoma and MS. It will be determined whether hyperprolactinemia is related to individual components of MS as individual risk factor, as well as impact of hyperprolactinemia on other hormones and it's impact on MS.

**Acknowledgments:** My mentor Prof Milan Vrkljan, MD, PhD for guiding and support, Ivan Kruljac, MD for helping me with statistics.

**MeSH/Keywords:** metabolic syndrome, hypothalamic-pituitary axis, macroprolactinoma, macrosomatotropinoma, non-functioning pituitary macroadenoma, prolactin, insuline resistance, visceral obesity

**Poster code:** T-B-9-124

# Poster Title: SIGNIFICANCE OF EXTRACAPILLARY PROLIFERATION IN IGA NEPHROPATHY

**PhD candidate:** Luka Torić

**Thesis proposal:** Extracapillary proliferation in IgA nephropathy outcome

**Mentor/s:** Professor Krešimir Galešić, MD, PhD

**Affiliation:** Clinical Hospital Dubrava, Zagreb

**Introduction:** IgA nephropathy is the most common primary glomerulonephritis worldwide, diagnosed by the presence of IgA-dominant mesangial immune deposits and the absence of C1q deposits. The Oxford classification is a histopathologic grading system that predict risk for progression of IgA nephropathy and consists of: mesangial hypercellularity (M), endocapillary proliferation (E), segmental glomerulosclerosis (S) and tubular atrophy and interstitial fibrosis. In about 20% of patients, extracapillary proliferation (EP) is present.

**Hypothesis:** Patients with IgA nephropathy and biopsy-proven presence of extracapillary proliferation (EP) have poor renal outcome.

**Aims:** To show correlation between pathologic lesions and management (RAS blockade, immunosuppressive therapy) with renal outcome. To determine a correlation between EP and clinical features and MEST score. To show importance of the serum IgA, intensity of IgA deposits on immunofluorescent microscopy and deposits on electronic microscopy with clinical features and EP.

**Materials and methods:** 150 patients with biopsy-proven IgA nephropathy are included in retrospective study, from the beginning of 2005 to the end of 2014. Patients with inadequate biopsy sample (with <7 glomeruli), those with secondary IgA mesangial deposition (systemic lupus erythematosus, chronic liver disease) and patients with Henoch-Schonlein purpura are excluded. Clinical features (serum creatinine, blood urine nitrogen, proteinuria in daily urine, serum IgA, blood pressure (high >140/90 mmHg), glomerular filtration rate (by MDRD formula) and histologic features (Oxford classification, EP, IgA, C3, IgM, IgG deposits on immunofluorescent and electronic microscopy deposits) will observe. We will form two patients groups: patients with and without presence of EP and correlate presence of EP with clinical and histological features, management (antihypertensive drugs, immunosuppressive) and renal outcome. The outcome is 50% decline in glomerular filtration (GFR) and the onset of end-stage renal disease (GFR <15 ml/min/1.73 m2 and initiation of renal replacement therapy. Univariate and multivariate linear regression analyses will determine an independent association between histopathological features and the renal outcome and Harrell's C index will determine the value of EP in renal outcome.

**Expected scientific contribution:** The results can be useful in reevaluation of Oxford classification and in predicting renal outcome in patients with IgA nephropathy.

**Acknowledgments:** I would like to thank mentor and my family for their support.

**MeSH/Keywords:** IgA nephropathy, extracapillary proliferation, Oxford classification

**Poster code:** T-B-9-155

## Poster Title: EXPRESSION OF WNT4, FGF23 AND KLOTHO PROTEIN IN THE WALL OF INFERIOR EPIGASTRIC ARTERY OF PATIENTS WITH END-STAGE RENAL DISEASE

**PhD candidate:** Lea Katalinić, MD

**Thesis proposal:** Expression of Wnt4, FGF23 and Klotho protein in the wall of inferior epigastric artery of patients with end-stage renal disease

**Mentor/s:** Professor Nikolina Bašić Jukić, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre Zagreb, Croatia

**Introduction:** Fibroblast Growth Factor 23 (FGF23) is a newly discovered hormone produced by osteoblasts/osteocytes. Its effects are achieved by binding to a cofactor, protein αKlotho, and FGF receptor (FGFR). FGF23 has other effects through the indirect pathways, leading to many complications, especially to left ventricular hypertrophy and arterial calcifications. On the other hand, there is an important role of the Wnt signaling pathway in promoting smooth muscle cell proliferation and their migration to the intima of the arterial wall, leading to the formation of atherosclerotic plaque. The expression of Wnt in the artery walls of chronic kidney disease (CKD) patients has still not been clearly defined.

**Hypothesis:** The expression of FGF23 and Wnt4 increases, while expression of αKlotho declines in the artery walls of CKD patients, which is associated with allograft function and patient survival after renal transplantation (TX).

**Aims:** The primary aim of our research is to determine the expression of FGF23, αKlotho and Wnt4 in the wall of inferior epigastric artery of CKD patients. The secondary objectives are to examine whether there is a specific spot of the strongest expression in the artery wall, as well as possible correlation between their expression and the outcomes after TX.

**Materials and methods:** Prospective research will be conducted including 75 CKD patients, transplanted in our center. As a control group, samples of epigastric artery of 16 patients obtained during nephrectomy due to renal tumors will be used. Immunohistochemical analysis will be performed on the specimens of the inferior epigastric arteries obtained during renal TX. Anti-human recombinant FGF23, αKlotho and Wnt4 antibodies will be used for the analysis. Immunoreactivity in cells will be accessed by grading (0-3) and the results will be expressed as percentage of positive cells. Pelvic X-rays obtained at the day of transplantation will be evaluated for the presence of vascular calcifications and classified as present or absent. Clinical data will be obtained from the medical records and charts.

**Expected scientific contribution:** The results of our research will show whether, to what extent and in which layers of the arterial wall protein products of these pathways are expressed. It will also explain whether the degree of expression is associated with pretransplant characteristics of the study population, or the short- and long-term outcomes after renal TX.

**MeSH/Keywords:** chronic kidney disease, vascular calcifications, FGF23, Klotho, Wnt signaling pathway

**Poster code:** T-B-9-88

# Poster Title: CONTINUOUS SYSTEMIC INFLAMMATION AND ARTERIAL DYSFUNCTION IN RHEUMATOID ARTHRITIS

**PhD candidate:** Ivan Marković, MD

**Thesis proposal:** Continuous systemic inflammation intensity and arterial dysfunction in patients with rheumatoid arthritis

**Mentor/s:** Prof. Jadranka Morović-Vergles, MD, PhD

**Affiliation:** Division of Clinical Immunology and Rheumatology, Department of Internal Medicine, Dubrava University Hospital, School of Medicine, University of Zagreb

**Introduction:** The patients with rheumatoid arthritis (RA) are at increased cardiovaskular risk compared to general population. Chronic systemic inflammation is postulated to be a major contributor to accelerated atherosclerosis. So far, the impairment of vascular function and morphology has been demonstrated in RA, but the correlation between systemic inflammation and vascular dysfunction remains less clear. In most studies a single-point measurement of acute phase reactants was used, which is not adequate for evaluating the intensity of a chronic process, as is the systemic inflammation in RA.

**Hypothesis:** There is a positive correlation between the intensity of chronic systemic inflammation and endothelial dysfunction, arterial stiffness and carotid intima-media thickness in patients with RA.

**Aims:** To investigate the effect of continuous systemic inflammation intensity on vascular dysfunction in RA patients.

**Materials and methods:** A minimum of 40 patients with RA are going to be included, who fulfill the 2010 ACR/EULAR classification criteria and have moderate or high disease activity (DAS28-CRP > 3.2), within 2 years since the diagnosis. Exclusion criteria will be the presence of a cardiovascular disease, traditional cardiovascular risk factors, another systemic inflammatory disease, active infectious or malignant disease. All subjects are going to be treated according to the treat-to-target principle and followed-up for 9 months. The serum concentrations of CRP, IL-6 and TNF-alpha are going to be measured in 6-weeks interval. Continuous systemic inflammation intensity is going to be calculated by the integration of each of these parameters in time (area under curve). Endothelial dysfunction is going to be evaluated initially and 9 months later by fingertip digital thermal monitoring, using an automated, operator-independent protocol (VENDYS®, Endothelix Inc). Reactive hyperemia after the occlusion of arm with a cuff is going to be estimated by the calculation of temperature rebound and vascular reactivity index. Arterial dysfunction is going to be estimated initially and 9 months later by calculating ambulatory arterial stiffness index from the 24-hour blood pressure reading. The ultrasonographic measurement of carotid intima-media thickness is going to be performed at the same time.

**Expected scientific contribution:** The results would show more clearly whether the impact of chronic inflammation on arterial dysfunction exists in patients with RA. This study might form the basis for further studies of longer duration and larger sample size.

**Acknowledgments:**

**MeSH/Keywords:** Rheumatoid arthritis, Atherosclerosis, Arterial stiffness, Carotid intima-media thickness

**Poster code:** T-B-9-92

## Poster Title: ASSESSMENT OF SEXUAL HEALTH AND SLEEP QUALITY IN EVALUATING QUALITY OF LIFE OF PATIENTS WITH RHEUMATOID ARTHRITIS

**PhD candidate:** Anamarija Sutić, MD

**Thesis proposal:** Assessment of sexual health and sleep quality in evaluating quality of life of patients with rheumatoid arthritis

**Mentor/s:** Professor Jadranka Morović Vergles, MD, PhD

**Affiliation:** Division of Clinical Immunology, Allergology and Rheumatology, Department of Internal Medicine, School of Medicine, University of Zagreb, Dubrava University Hospital, Avenija Gojka Suska 6, 10 040 Zag

**Introduction:** Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease that progresses rapidly and can lead to disability of patients if not treated. Disease activity is evaluated by disease activity score (DAS28) and the quality of life by Health Assessment Questionnaire (HAQ). Sexual functioning and sleep quality are neglected areas in evaluating the quality of life in patients with RA.

**Hypothesis:** There is a negative correlation between sexual functioning and sleep quality of patients with rheumatoid arthritis and disease activity.

**Aims:** Assessment of sexual health and sleep quality of patients with rheumatoid arthritis and determination of the correlation between sexual health, sleep quality and disease activity.

**Materials and methods:** At least 110 patients with RA will be included in the study. Sociodemographic, clinical and laboratory characteristics will be assessed. The disease activity will be judged by DAS28 CRP. Participants will complete self-administered questionnaires, namely Health Assessment Questionnaire (HAQ), Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), men Sexual Health Inventory for Men (SHIM) and women Female Sexual Function Index (FSFI).

**Expected scientific contribution:** It is important to include other questions about sexual health and sleep quality in evaluating the quality of life of patients with rheumatoid arthritis.

**Acknowledgments:**

**MeSH/Keywords:** rheumatoid arthritis, quality of life, sleep quality, Female Sexual Function Index, Sexual Health Inventory for Men

**Poster code:** T-B-9-94

# Poster Title: A NEW METHOD FOR PARAMETER IDENTIFICATION IN A LUMPED MODEL OF PULMONARY CIRCULATION

**PhD candidate:** Fabijan Lulić, MD

**Thesis proposal:** Non-invasive method for parameter identification in a mathematical model of pulmonary circulation

**Mentor/s:** Assistant Professor Marko Jakopović*, MD PhD, Full Professor Zdravko Virag**, PhD

**Affiliation:** University of Zagreb, *Clinic for Pulmonary Diseases, **Faculty of Mechanical Engineering and Naval Arhitecture

**Introduction:** The input impedance ($Z\_in$) of the pulmonary circulation is the ratio of pulmonary artery (PA) pressure ($p\_PA$) and flow ($Q\_PA$) in the frequency domain, and it comprehensively characterizes the pulmonary vascular bed (afterload to the right ventricle (RV)). Unfortunately, for the determination of $Z\_in$ invasive measurements of $p\_PA$ and $Q\_PA$ during whole cardiac cycle are needed, and it is a great challenge to find a way of its non-invasive determination.

**Hypothesis:** We hypothesize: (1) that the pulmonary input impedance can be calculated from the data taken from the ejection time only, (2) the right ventricle pressure ($p\_RV$) during the ejection time, can be properly estimated from the regurgitant tricuspid flow, (3) the pulmonary artery pressure $p\_PA$ at the PA root may be well approximated by the pressure $p\_PAB$ obtained from the $p\_RV$ using the Bernoulli equation. These three hypotheses make a conceptual framework of a non-invasive method for determination of $Z\_in$.

**Aims:** To define a method for the non-invasive determination of input impedance of the pulmonary circulation and its crucial physiological parameters.

**Materials and methods:** Within the proposed research the mathematical model of pulmonary circulation will be used to describe the main features of pulmonary vascular bed (input impedance and the effects of reflection waves of pressure and flow). The model parameters will be identified by using: (1) non-invasive method based on echo-Doppler recordings of pulmonary and triscuspid regurgitant flow, (2) invasive Swan-Ganz catheter recordings of the right ventricle (RV) pressure ($p\_RV$), wedge pressure $p\_w$, and non-invasive echo-Doppler recordings of the velocity $v\_pv$ through the pulmonary valve obtained. The results of the non-invasive method for the determination of $Z\_in$ will be compared with the results of the invasive one.

**Expected scientific contribution:** The proposed method will allow a generation of a database of pulmonary circulation parameters, and drawing of certain correlations that might be useful in diagnosis, treatment and follow-up of patients with pulmonary hypertension.

**Acknowledgments:**

**MeSH/Keywords:** Pulmonary circulation, input impedance, parameter identification, non-invasive method

**Poster code:** T-B-9-107

## Poster Title: ASSESSMENT OF BODE INDEX AS INDICATOR OF CARDIORESPIRATORY FUNCTION IN LUNG RESECTION FOR BRONCHIAL CARCINOMA

**PhD candidate:** Vjekoslav Karadža M.D.

**Thesis proposal:** BODE index changes after lung resection

**Mentor/s:** Prof. Dinko Stančić-Rokotov M.D. Ph.D., Jasna Špiček Macan M.D. Ph.D.

**Affiliation:** University of Zagreb School of Medicine University Hospital Centre Zagreb

**Introduction:** Lung resection leads to change in lung function. FEV1 (forced expiratory volume in 1 second), DLCO (carbon monoxide diffusing capacity) and cardiorespiratory exercise tests are used for risk assessment before lung resection for bronchial carcinoma. BODE index is multidimensional index used for staging of patients with COPD (chronic obstructive pulmonary disease). BODE index is composed of the body mass index (B), degree of airflow obstruction (O), level of functional dyspnea (D) and exercise capacity (E). As BODE index scoring includes measurement of FEV1 and performance of 6-minutes walk test (exercise testing), it could be included in selection of patients undergone lung resection for bronchial carcinoma.

**Hypothesis:** Lung resection (no less than lobectomy) will significantly change BODE index in patients with bronchial carcinoma.

**Aims:** Analysis of perioperative changes of cardiorespiratory function in patients undergone lung resection. Specific aim: Analysis of perioperative changes of BODE index in patients undergone lung resection.

**Materials and methods:** One hundred patients will undergone spirometry and 6-minutes walk test with scoring of BODE index during patient preparation before surgery and on control survey one month after surgery. Collected data will be analyzed.

**Expected scientific contribution:** This study will help in better understanding of cardiorespiratory function after lung parenchyma reduction. BODE index could be simple method of risk assessment for patients before lung resection for bronchial carcinoma.

**Acknowledgments:**

**MeSH/Keywords:** BODE index, Carcinoma, Bronchogenic, Pulmonary Surgical Procedure, Spirometry, Exercise Test, 6-minutes walk test, FEV1

**Poster code:** T-B-10-14

## Poster Title: MASSETER AND TEMPORALIS MUSCLES ACTIVITY IN MANDIBULAR CONDYLE AND ANGLE FRACTURES

**PhD candidate:** Kaltrina Kryeziu

**Thesis proposal:** Masseter and temporalis muscles activity in mandibular condyle and angle fractures.

**Mentor/s:** Emil Dediol, MD, PhD, Prof. Assoc. Dr.Sami Salihu

**Affiliation:** Univesity Clinical Center of Kosovo, Department of Maxillofacial Surgery

**Introduction:** In the practice of emergency medicine commonly are encountered maxillofacial injuries that are associated with high morbidity from physical, functional, and cosmetic consequences. Road traffic accident was the most frequent cause. Condylar fractures account for 25-35% of all mandibular fractures, whereas fractures of the angle account for 23-43%. The main aim in fracture treatment is therefore the restauration of normal occlusion. Closed reduction is a blind technique that relies on the correct positioning of the teeth. Normal loading of the fracture side might be expected with open treatment with miniplate osteosynthesis. Patients treated open did tend to have a lower working/balancing ratio than patients treated closed, suggesting less neuromuscular adaptation to protect the fracture site. Changes in skeletofacial complex such as posterior height might be related to lowered bite forces because some of jaw muscles might be shortened. EMG evaluates muscle function at patients suffered from trauma.Maximal biting and increased contraction time, might be reduced in subjects with pain and tenderness of masticatory muscles.

**Hypothesis:** Masseter and temporalis muscle function (activity, bite force) is altered by operative treatment of mandibular angle or condyle fractures and is never identical to the non-affected side.

**Aims:** To compare operative versus non operative treatment of the mandibular angle and the condyle fractures regarding the masseter and temporalis muscle activity.

**Materials and methods:** This is a prospective study in 50 patients with a mandibular angle or condyle fracture. First group of 25 patients will undergo closed treatment. Second group of 25 patients will undergo open treatment will titanium mini and microplates. Both groups of patients will undergo measurements preoperatively, postoperatively after 6 weeks and after 6 months: EMG tests for masseter and temporal muscles activity, T-scan III for bite force of masseter and temporal muscle, and dolorimeter for measuring the pain.

**Expected scientific contribution:** This study will thoroughly asses function of major chewing muscles such as chewing force, EMG activity and pain in mandibular trauma and reveal whether additionally operative procedure prolongs recovery time of these muscles. Also we will assess long term outcomes of chewing muscle activity and whether this affects normal patient functioning.

**Acknowledgments:** I would like to thank my both mentors.

**MeSH/Keywords:** Angle, condyle, bite force.

**Poster code:** T-B-10-129

## Poster Title: THE ROLE OF MAGNETIC RESONANCE IMAGING AND THE EXPRESSION OF MMP-9 AND COX-2 PROTEINS IN THE ANALYSIS OF CAROTID ATHEROSCLEROTIC PLAQUES IN PATIENTS WITH INDICATED CAROTID ENDARTERECTOMY

**PhD candidate:** Davorin Šef, MD

**Thesis proposal:** Analysis of Carotid Atherosclerotic Plaques in Patients with Indicated Carotid Endarterectomy

**Mentor/s:** Assistant Professor Anita Škrtić, MD, PhD, Professor Vinko Vidjak, MD, PhD.

**Affiliation:** Magdalena – Clinic for Cardiovascular Diseases

**Introduction:** Atherosclerosis is a major cause of stroke. Majority of strokes are ischemic with carotid artery atherosclerotic disease representing an important risk factor. Patients with hemispheric transient ischemic attack or stroke are considered symptomatic. Magnetic resonance imaging (MRI) can analyse the components of carotid atherosclerotic plaque. Current studies suggest that MRI can reliably distinguish between stable and unstable carotid plaque, and furthermore improve patient selection for surgery or stenting. Matrix metalloproteinase 9 (MMP-9) and COX-2 protein have a role in remodelling of atherosclerotic plaques and correlate with the presence of unstable plaques.

**Hypothesis:** Morphological features and characteristics of atherosclerotic unstable plaques analysed by MRI and immunohistochemical staining of MMP-9 and COX-2 protein would be highly expressed in symptomatic patients with indication for carotid endarterectomy. Atherosclerotic plaque features analysed by MRI would be able to distinguish patients with unstable atherosclerotic carotid plaque.

**Aims:** The aim of the research is to analyse the characteristics of atherosclerotic plaque by magnetic resonance imaging, morphological features of plaque and expression of MMP-9 and COX-2 proteins, to determine their correlation and identification of unstable atherosclerotic plaques in patients with an indication for carotid endarterectomy.

**Materials and methods:** Minimum of 60 patients for carotid endarterectomy will be included in the study, 30 asimptomatic and 30 simptomatic patients. Preoperatively carotid MRI, laboratory analysis of biomarkers of inflammation, coagulation factors and lipid status will be performed. MRI will be performed on Toshiba Excelart Vantage 1.5T MRI machine, and AHA classification of atherosclerotic plaque will be applied. Excised carotid plaque will be analysed morphologically using H?E and special histochemical trichrome staining. Semi quantitative analysis of collagen fibres will be performed. Immunohistochemical staining of MMP-9 of COX-2, semi quantitative analysis of CD68 PG-M1 marked macrophages, SMA marked smooth muscle cell as well as micro vessel density using CD34 will be obtained. Expression and intensity of MMP-9 and COX-2 immunohistochemical staining in macrophages and smooth muscle cells will be semi quantitatively analysed.

**Expected scientific contribution:** Research results may indicate a better definition of patients with an indication for carotid endarterectomy as well as a possibility to predict the outcome of surgery.

**MeSH/Keywords:** Carotid endarterectomy, unstable carotid atherosclerotic plaque, magnetic resonance imaging, matrix metalloproteinase 9, COX-2.

**Poster code:** T-B-10-66

# Poster Title: TUMOR BUDDING AND MICROSATELLITE INSTABILITY IN PATIENTS WITH SPORADIC COLON AND RECTAL CANCER STAGE II

**PhD candidate:** Josip Baković, MD

**Thesis proposal:** Tumor budding and microsatellite instability in patients with sporadic colon and rectal cancer stage II

**Mentor/s:** Groan Aralica, MD, assistant professor

**Affiliation:** Department of Clinical Pathology and Cytology, Clinical Hospital Dubrava and Medical school Zagreb

**Introduction:** Pathological findings of colon and rectal cancer based on TNM classification represents basis on which patients are informed about the survival and continuation of treatment. However it is noted that the outcome of treatment in many patients suffering from colorectal cancer with the same stage of the disease is different, particularly in stage II, and that some patients suffering from colorectal cancer stage II have a poorer survival regarded on stage III. Due to observed shortcomings of TNM classification other tests are developed that have prognostic significance and are not part of the TNM system. Tumor budding as histology and microsatellite instability (MSI) from the molecular sets could have a predictive and prognostic value.

**Hypothesis:** The hypothesis of proposed work is that tumor budding and MSI provide new information that could help stratify patients with colon and rectal cancer stage II and as such should be included in the standard pathology report.

**Aims:** In this paper, we set up several primary objectives: to establish the association of tumor budding and MSI on the survival of patients with adenocarcinoma of the colon and rectum, stage II and they interrelationship, to determine the possible criteria for stratification of patients within stage II on the basis of the standard pathological findings complemented with the findings of MSI and tumor budding, establish mutual coincidence of tumor budding and MSI in the sample of endoscopic biopsy and tumor resection during surgery.

**Materials and methods:** We will analyze 120 consecutive colorectal carcinoma stage II from the archives of Department of pathology, with their associated endoscopic biopsies in the period from January 2009. to December 2012. Selected tumors will be stained by routine immunohistochemistry method. Thereafter, two pathologists with expertise in the pathology of the gastrointestinal tract will determine the degree of peritumoral and intratumoral budding according to Nakamura method. Also, the matched samples will be tested by immunohistochemistry on MSI (MLH1, MSH2, MSH6 and PMS2).

**Expected scientific contribution:** Tumor budding and MSI have not been part of the standard pathological findings in patients with carcinoma of the colon and rectum. The scientific contribution of this work is based on the fact that tumor budding and microsatellite instability and their possible interdependence can further stratify patients suffering from colon and rectal cancer, especially patients in stage II to achieve better survival and quality of treatment.

**Acknowledgments:**

**MeSH/Keywords:** colon cancer, rectal cancer, TNM classification, microsatellite instability (MSI), tumor budding

**Poster code:** T-B-10-75

## Poster Title: THE USE OF MEDICAL THERMOGRAPHY IN EVALUATION OF CLAVICLE FRACTURE HEALING IN CHILDREN

**PhD candidate:** Ivan Romić

**Thesis proposal:** Medical thermography may be able to detect skin temperature changes over the fractured clavicle in pediatric patients during the healing process.

**Mentor/s:** Professor Anko Antabak

**Affiliation:** University Hospital Centre Zagreb

**Introduction:** Clavicle fractures are one of the most common pediatric fractures, which are detected by radiography and usually treated by immobilization. Because of the harmful ionizing radiation during the X-rays testing, additional diagnostic methods are trying to be found and one of the possible methods is thermography which has not been routinely used. In limited number of studies on thermographic analysis of long bone fractures, evidence suggests that there is a difference in the skin temperature overlying fracture site during the different phases of healing process. This biological characteristic of bone healing may be of scientific interest especially in evaluation of bones that are lying directly under the skin such as clavicle.

**Hypothesis:** Local temperature changes at the site of fracture are directly caused by biological healing process, and measured temperature changes and its dynamic follow morphological, radiological and biological particularities of the clavicle healing in children.

**Aims:** Our aim is to detect skin temperature changes at the site of fractured clavicle and compare it with the healthy side during the healing period.

**Materials and methods:** This is prospective study with estimated duration of 3 years that will include all pediatric patients aged 0-18 years with radiologically evident clavicle fracture. Patients will be divided into 4 age groups and into 3 groups depending on degree of fracture dislocation. On regular follow-ups after 1,2, 4 and 6th weeks we will perform thermographic analysis of healthy and non-healthy side using high resolution infrared camera, check functional status of the affected shoulder and evaluate pain degree after which standard statistical tests will be created.

**Expected scientific contribution:** Results on larger number of patients will explain us thermo-biological characteristics of bone healing and asnwer if thermography, as an easy available, noninvasive, cheap and simple method can be of use in detection of bone healing disorders and be implemented in everyday clinical practice.

**Acknowledgments:** I would like to thank my mentor and Institute for medical research and occupational health-Zagreb.

**MeSH/Keywords:** Thermography, Clavicle fracture, Children, Temperature changes

**Poster code:** T-B-10-118

## Poster Title: PROLONGED VERSUS STANDARD INFUSION OF PIPERACILLIN/TAZOBACTAM – A PROSPECTIVE, RANDOMIZED, CONTROLLED STUDY IN CLINICAL HOSPITAL CENTRE ZAGREB

**PhD candidate:** Iva Kraljičković

**Thesis proposal:** Prolonged versus Standard Infusion of Piperacillin/Tazobactam- a Prospective, Randomized, Controlled Study in Clinical Hospital Centre Zagreb

**Mentor/s:** Assist. Prof. Robert Likić, MD, PhD

**Affiliation:** Division of Clinical Pharmcology, Department of Medicine, Clinical Hospital Centre Zagreb

**Introduction:** The treatment of complicated infections and sepsis represents a significant challenge for physicians due to high mortality rates and high costs. The early and appropriate antimicrobial therapy is the most effective intervention when treating sepsis. Optimization of empirical therapy application is a priority. The standard antibiotic dosage and administration intervals were determined based on data obtained mainly from trials with healthy volunteers, while patients with severe infections may have significantly altered drug volume of distribution and clearance. Therefore, pharmacokinetic variability may affect the antibiotic concentration at the site of infection. This can be particularly evident for beta-lactam antibiotic witch have time-dependent bacterial killing effect. Their standard dosage and mode of application in severe infections may be of questionable efficacy. Convincing pharmacokinetic and pharmacodynamic data are showing that extending the duration of antibiotic infusion reduces the possibility of free drug concentration falling below the minimum inhibitory concentration of the pathogen, but data on the clinical effect of this approach remain unclear.

**Hypothesis:** The use of piperacillin/tazobactam, when indicated, in prolonged infusion over 4 hours per dose leads to a better clinical outcome at day 14 compared to the treatment with standard duration of infusion of 30 minutes with the same total daily dose of the drug in both groups.

**Aims:** The overall objective of this research is to show if this intervention leads to better clinical and microbiological outcome at 14th day of therapy estimated based on rates of clinical and microbiological cure. Specific objectives are to determine if there is a difference in early clinical and microbiological response (at 3rd day) between the two groups and assess the impact of intervention on time to cessation of fever, time to cure, length of hospital stay, mortality at day 28 after enrollment, and the occurrence of adverse reactions.

**Materials and methods:** It is a prospective, randomized, open, clinical trial of two parallel groups of patients who meet the inclusion criteria.

**Expected scientific contribution:** In the time of increasing pathogen resistance and rising MIC, as well as the limited number of new antibiotic, it is necessary to explore ways to maximize the effectiveness of existing antibiotics. Due to the high health care costs and expensive medicines, it is necessary to explore interventions that do not generate any additional cost while yielding potential clinical benefits.

**Acknowledgments:**

**MeSH/Keywords:** antibiotics, piperacillin tazobactam, prolonged infusion, sepsis

**Poster code:** T-B-13-13

## Poster Title: THE IMPACT OF F-18 CHOLINE PET/CT IN PROSTATE CANCER PATIENTS

**PhD candidate:** Anja Tea Golubić, MD

**Thesis proposal:** The value of positron emission tomography/computed tomography (PET/CT) with fluor-18 choline in prostate cancer patients follow up

**Mentor/s:** Professor Dražen Huić, MD, PhD

**Affiliation:** Department of Nuclear Medicine and Radiation Protection, University Hospital Centre Zagreb

**Introduction:** Variable biological behavior of prostate cancer and often equivocal findings of conventional diagnostic imaging in patients with completed primary radiotherapy or radical prostatectomy have increased the demand for functional imaging, positron emission tomography/computed tomography (PET/CT). In vivo molecular imaging with F-18/C-11-choline and Ga-68 PSMA PET/CT has an increasing role in the evaluation of disease extent. F-18-choline is a new radiopharmaceutical with currently undefined role in restaging and follow-up of patients with prostate cancer.

**Hypothesis:** F-18-choline PET/CT is valuable in disease activity assessment in prostate cancer patients with suspected biochemical relapse.

**Aims:** The aim of this study is to explore and better define the role and value of diagnostic functional imaging with F-18 choline PET/CT in prostate cancer patients with suspected biochemical relapse. It will examine the impact of the procedure on patient follow up and further therapy modification.

**Materials and methods:** A minimum of 150 patients with suspected disease recurrence after initial prostate cancer therapy will be scanned at the Department of Nuclear Medicine and Radiation Protection, University Hospital Centre Zagreb. After presenting the procedure and obtaining patient history, demographic data and consent, 2-3 MBq/kg of F-18-choline will be administered, 20 minutes after which whole body acquisition will begin, 2-3 min/per bed position. Pathological findings of focal activity higher than that of the surrounding tissue and foci of activity in the lymph nodes or bone structures in the regions where prostatic cancer metastases can be often found (pelvis, central skeleton) will be expressed qualitatively and in semiquantitative SUV analysis (standardized uptake value). PET/CT report will be correlated with FNAC or biopsy, when applicable. Reports of other imaging methods (x-rays, CT, MRI scans, bone scintigraphy), PSA values, as well as any therapy modification will be monitored for a minimum 6 month period of follow up to determine the value of F-18-choline PET/CT in prostate cancer patients. The data received will be analyzed statistically (StataSE 12, StataCorp) and presented graphically.

**Expected scientific contribution:** The proposed study will demonstrate the value of F-18-choline PET/CT in the follow-up of prostate cancer patients with suspected biochemical relapse. The results obtained from this research will be used to present clinical guidelines for easier and better patient management.

**Acknowledgments:**

**MeSH/Keywords:** F-18-choline, PET/CT, prostate cancer, biochemical relapse

**Poster code:** T-B-17-42

## Poster Title: VALUATION OF FACTORS INFLUENCING THE LEVOTHYROXINE REPLACEMENT/SUPRESSIVE TREATMENT OF THYROID CANCER

**PhD candidate:** Josip Staničić, MD

**Thesis proposal:** Valuation of factors influencing the levothyroxine replacement/supressive treatment of thyroid cancer

**Mentor/s:** Prof. Zvonko Kusić, MD, PhD, Academician

**Affiliation:** Department of oncology and nuclear medicine, University hospital center Sestre Milosrdnice, Zagreb

**Introduction:** Thyroid cancer (TC) is a most common cancer of endocrine system. Its rising incidence has risen fivefold during the last 3 decades to 13.4/100000 inhabitants in Croatia, while its mortality has remained low during the same period (0.5/100000). The increase in TC incidence can be mostly attributed to differentiated thyroid carcinomas, which include papillary and follicular TC. Treatment of differentiated TC includes total thyroidectomy, in most cases followed by radioiodine therapy. All of these patients require hormone substitution, provided by daily dose of oral levothyroxine, which has to be specifically tailored using serum thyroid stimulating hormone (TSH) level. However, because there is proof that TSH stimulates eventually present metastatic cells, patients with higher risk require lower serum TSH level – TSH suppression.

**Hypothesis:** Heavier and younger patients require higher daily dose of levothyroxine, as well as men compared to women. Patients on TSH suppressive therapy require higher daily dose of levothyroxine than patients on hormone substitution.

**Aims:** To determine the initial empirical, specifically per patient tailored dose of levothyroxine in relation to age, sex and weight, which is required for more rapid reaching of adequate level of hormone substitution or TSH suppression in patients treated for thyroid cancer.

**Materials and methods:** The study will include around 400 patients who underwent total thyroidectomy for differentiated thyroid cancer during their regular follow-up in the Department of oncology and nuclear medicine, University hospital center Sestre Milosrdnice, Zagreb. During the visit, patient's height and weight will be measured, with noting of the serum TSH and dose of levothyroxine. Patients will be divided into groups depending on their serum TSH level: low risk group on hormone substitution with TSH level from 0.5 to 2.0 IU/ml, moderate risk group with TSH level from 0.1 to 0.5 IU/ml, and high risk group with TSH level less than 0.1 IU/ml. After achieving optimal hormone substitution or TSH suppression, the influence of age, sex, body weight on required dose of levothyroxine will be determined. Participation in the study will be voluntary and anonymous.

**Expected scientific contribution:** This study will help clinicians in achieving the optimal dose of levothyroxine more rapidly, which is extremely important in treatment and follow-up of thyroid cancer patients, primarily because the optimal level of TSH prolongs their survival, but also to avoid hypo or hyper dosing.

**Acknowledgments:**

**MeSH/Keywords:** Thyroid cancer, levothyroxine, hormone substitution, levothyroxine suppressive therapy

**Poster code:** T-B-17-39

**Poster Title: EFFECTS OF BEVACIZUMAB AND TRIMACINOLONE ACETONIDE ON MACULAR EDEMA AFTER THE EXTRACTION OF SILICON OIL IN PATIENTS WITH DIABETES TYPE 2**

**PhD candidate:** Lucija Vojvodić, MD

**Thesis proposal:** Effects of bevacizumab and trimacinolone acetonide on macular edema after the extraction of silicon oil in patients with diabetes type 2

**Mentor/s:** Assoc. Prof. Tomislav Jukić, MD, PhD

**Affiliation:** Department of Ophthalmology, Zagreb University Hospital Centre, Zagreb. General Hospital Dubrovnik, Dubrovnik.

**Introduction:** Diabetic retinopathy is the leading cause of visual impairment in the population age between 20 and 60 and its frequent manifestation is macular edema which is the main cause of blindness. The gold standard in treatment of macular edema is laser photocoagulation. Its low efficiency requires discovery of new methods such as bevacizumab and triamcinolone acetonide application. They are used as "off-label" drugs for the treatment of diabetic retinopathy. In resistant cases pars plana vitrectomy with silicone oil takes place. Silicone oil is removed from eye after 3 months because of the tendency to emulsify and to induce glaucoma. Diabetes is a public health problem. Therefore, this research will try to clarify the role of intravitreal application of bevacizumab and triamcinolone acetonide after removal of silicone oil.

**Hypothesis:** Bevacizumab and triamcinolone acetonide intravitreal application reduces central retinal thickness after silicone oil extraction, improving central visual acuity and quality of life for patients with type 2 diabetes.

**Aims:** Determining the effects of bevacizumab and triamcinolone acetonide on central retinal thickness, visual acuity and quality of life as compared to placebo after removing the silicone oil.

**Materials and methods:** Patients diagnosed with diabetes type 2 with indicated operation PPV with silicone oil installation will be informed about the research, giving them a written consent to participate. Patients who had cataract/glaucoma surgery and IVT/IVB application will not be included. Triamcinolone acetonide 8 mg/0.1 mL and bevacizumab 1.25 mg/0.05 mL will be used intravitreally. The best corrected visual acuity will be determined. Detailed ophthalmological examination will be performed preoperative and postoperative: on reception, every 7 days, after 1 month, 3rd and 6th month, post operational extraction of silicone oil. Standardized instrument „EQ-5D-5L" will be used to measure health outcomes, 3 and 6 months after IV application. Silicone oil is removed via standardized pars plana approach. Statistical significance: $p < 0.05$. Confidence Intervals: 95% level. Two-tailed tests of significance will be used.

**Expected scientific contribution:** The study scientific contribution will be the explanation what is known about bevacizumab and triamcinolone acetonide effects and the macular edema pathogenesis understanding.

**Acknowledgments:**

**MeSH/Keywords:** Diabetic macular edema, bevacizumab, triamcinolone acetonide, silicone oil

**Poster code:** T-B-18-82

## Poster Title: LOCAL CORTICOSTEROID THERAPY IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS ASSOCIATED UVEITIS ON SYSTEMIC IMMUNOMODULATORY THERAPY

**PhD candidate:** Marija Barišić Kutija, MD

**Thesis proposal:** Local corticosteroid therapy in patients with juvenile idiopathic arthritis associated uveitis on systemic immunomodulatory therapy

**Mentor/s:** Prof. Nenad Vukojević, MD, PhD

**Affiliation:** Zagreb University Hospital Centre, Department of Ophthalmology, Zagreb, Croatia

**Introduction:** Juvenile idiopathic arthritis (JIA) is one of the most common chronic diseases of children. The most common extra-articular manifestation of the disease is anterior uveitis (JIA uveitis), which develops in 12-20% JIA patients. JIA uveitis has insidious, chronic, refractive course, corticosteroid dependent and with severe complications. Therefore, the treatment of JIA uveitis in pediatric ophthalmology is a great challenge. The first line of treatments are local and systemic corticosteroids. Topical corticosteroids (TCS) increase the risk of cataract and glaucoma, and the risk of complications is dose-dependent. JIA uveitis in about 80% cases requires therapy for several years, therefore, the aim in the long-term treatment for chronic, recurrent or refractive cases is to minimize the number of TCS drops and introduce immunomodulatory therapy (IMT). IMT includes methotrexate (MTX) and biological therapy. Despite all the listed therapeutical options, more than 65% patients on IMT need TCS to control the inflammation in the anterior chamber, but so far dynamic of IMT effectiveness on local disease activity and consequently the need for TCS during the whole course of the disease is not known.

**Hypothesis:** Systemic biologic IMT in JIA uveitis patients reduces the need for TCS more effective than systemic IMT whithout biologic therapy.

**Aims:** GENERAL AIM: To evaluate effectiveness of IMT on intraocular inflammation control in JIA uveitis patients. SPECIFIC AIMS: 1. To determine whether the need for TCS in JIA uveitis patients is lower in patients on systemic biologic therapy, than on systemic MTX therapy, whithout biologic therapy. 2. To determine the best corrected visual acuity in JIA uveitis patients on the beginning and the end of the disease course

**Materials and methods:** Inclusion criteria: 1. JIA uveitis on systemic IMT, 2. Age: 1-18 years. Non-inclusion criteria: 1. Uveitis of some other etiology, 2. Corneal opacities. Exclusion criteria: 1. Suspension of IMT before 9 months follow-up, 2. Cornea opacities development. PhD student (Marija Barišić Kutija, MD) will collect all the data from the clinical medical records from all follow-up examinations in patients, who satisfy criteria from 2011 untill 40 patients (about 80 eyes) are included. Study design: longitudinal observation study. Statistical analysis: repeated measures ANOVA analysis

**Expected scientific contribution:** Our study leads to new insights into the dynamics of disease activity changes, depending on the applied combination of systemic and local therapy.

**Acknowledgments:** I would like to thank my mentor, prof. Nenad Vukojević, on the infinitely patience and support.

**MeSH/Keywords:** Juvenile Idiopathic Arthritis, Anterior Uveitis, Immunomodulatory Therapy, Biologic Therapy, Methotrexate

**Poster code:** T-B-18-108

## Poster Title: MRI IN PROSTATE HIGH-DOSE-RATE BRACHYTHERAPY

**PhD candidate:** Jure Murgić, MD

**Thesis proposal:** MRI as image guidance in HDR brachytherapy for prostate cancer

**Mentor/s:** Professor Zvonko Kusić, MD, PhD and Professor Cynthia Ménard, MD, FRCPC

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre Sisters of Mercy, Princess Margaret Cancer Centre/University Health Network University of Toronto Department of Radiation Oncology

**Introduction:** High-dose-rate brachytherapy (HDR-BT) is well established method of radiotherapy dose escalation necessary to cure prostate cancer (PCa). Combination of HDR-BT and external beam radiotherapy (EBRT) is appealing definitive treatment option that offers high disease control coupled with favorable toxicity profile. Magnetic resonance imaging (MRI) allows superb soft tissue resolution, is the method of choice in local staging of PCa and is potentially the best image guidance modality for HDR-BT for PCa. Encouraged by our previous experience in MRI-guided and tumor directed HDR brachytherapy as salvage treatment for locally recurrent prostate cancer we decided to prospectively include patients planned to receive standard-care HDR-BT whole gland boost to EBRT in primary setting and to perform HDR-BT component of the treatment solely using MRI image guidance.

**Hypothesis:** MRI is safe and efficient method of image guidance for HDR-BT for PCa.

**Aims:** To assess feasibility, safety and value of a technique using interventional MRI for online guidance of catheter insertion and treatment planning in patients receiving HDR-BT boost for intermediate- and high-risk localized prostate cancer. Specific aims include determination of frequency, nature and impact of gross tumor visualization through the course of the HDR brachytherapy, procedure-related workflow efficiencies, dose metrics of implant quality, acute and late toxicity and patients' health related quality of life.

**Materials and methods:** Forty patients with localized PCa planned to receive whole gland prostate HDR-BT combined with external beam radiotherapy will be enrolled in single institution prospective phase II study with interventional MRI used for online guidance of brachytherapy catheter insertion and treatment planning of HDR-BT. This is an exploratory study which will provide estimates of variance in the data related to feasibility (measuring procedure time and achieved implant dose metrics) and safety (measuring side-effects and health related quality of life) of the study procedure. Data related to the incidence and impact of gross tumor visualization revealed using MRI image guidance will also be acquired and analysed.

**Expected scientific contribution:** Proposed project is innovative as it incorporates exclusive use of MRI for both image guidance and treatment planning of HDR-BT, potentially leading to highly patient-customized treatment with improved cure rates and less long-term side-effects.

**Acknowledgments:** I would like to thank University of Toronto Department of Radiation Oncology GU Tumor Site Group, Prostate Brachytherapy Group, and especially to Dr. Cynthia Menard and Dr. Rob Bristow for providing me exceptional mentoring support and guidance in my research project.

**MeSH/Keywords:** Prostate cancer, MRI, HDR brachytherapy

**Poster code:** T-B-19-3

## Poster Title: IMMUNOHISTOCHEMICAL ANALYSIS OF CANCER/TESTIS ANTIGENS IN NONINVASIVE DUCTAL BREAST CANCER

**PhD candidate:** Ana Roguljić, MD

**Thesis proposal:** Immunohistochemical analysis of cancer/testis antigens in noninvasive ductal breast cancer

**Mentor/s:** Associate Professor Božena Šarčević, MD, PhD and Associate Professor Antonio Juretić, MD, PhD

**Affiliation:** University Hospital for Tumors, University Hospital Centre Sisters of Mercy

**Introduction:** Breast cancer is the most common cancer in women. The WHO Working Group made histological classification of breast tumors: epithelial tumors, mesenchymal tumors, fibro-epithelial tumors, benign tumors of the nipple, malignant tumors of the nipple, precursor lesions, malignant lymphoma, metastatic tumors, myoepithelial lesions, benign epithelial lesions and male breast tumors. Epithelial tumors can be divided in invasive and noninvasive tumors. Cancer testis (C/T) antigens are encoded by group of genes expressed physiologically in human germ line cells and aberrantly in various malignancies. The most important among antigens are „melanoma-associated antigens" (MAGE) and antigen NY-ESO-1 which discovery gave necessary momentum to the attempts of applying immunotherapy

**Hypothesis:** Cancer/testis antigens expression correlates with tumor aggressiveness. Their expression in noninvasive breast cancers (DCIS-Ductal carcinoma in situ) could be associated with aggressiveness of tumors, and could show which type of DCIS has more chance to become invasive.

**Aims:** The aim od these study is to determine expression of cancer/testis antigen (MAGE-A and NY-ESO-1) in noninvasive breast cancer.The results will be correlated with standard pathohistological parameters for noninvasive breast cancer (tumor size, tumor grade, expression of estrogen and progesterone receptors, necrosis and margin). Evaluation of tumor-infiltrating lymphocytes (TILs) will be also performed and (defined as exist or not).

**Materials and methods:** This study will include pathohistological material from patients with noninvasive cancer operated at the University Hospital for Tumors, University Hospital Centre Sisters of Mercy from 2007.-2014. Immunohistochemistry will be performed on tumor samples and expression of cancer/testis antigen (MAGE-A and NY-ESO-1) will be determined. The results will be correlated with standard pathohistological parameters for noninvasive breast cancer. Results will be determined semiquantitatively.

**Expected scientific contribution:** If there is correlation between expression of cancer/testis antigen and standard pathohistological prognostic values or if expression is independent prognostic value for DCIS, expression could be used for definition of biological behaviour of the tumor and evaluation of tumor-infiltrating lymphocytes (TILs).

**Acknowledgments:**

**MeSH/Keywords:** non-invasive breast cancer, cancer/testis antigene, MAGE, NY-ESO-1, tumor infiltrating lymphocytes

**Poster code:** T-B-19-43

## Poster Title: PROTEOMIC ANALYSIS OF ACHILLES TENDON IN CHILDREN WITH CLUBFOOT

**PhD candidate:** Marijana Šimić Jovičić

**Thesis proposal:** The protein composition and regenerative potential of Achilles tendon in children with congenital idiopathic clubfoot

**Mentor/s:** Professor Vladimir Trkulja, MD, PhD, Associate Professor Robert Kolundžić, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, Children's Hospital Zagreb

**Introduction:** The regenerative potential of the Achilles tendon decreases with development and ageing so that during fibrotic repair in response to injury a qualitatively poorer tendon is produced. The regenerative potential of the Achilles tendon in early childhood is well-known and the use of this fact is made in the well-established Ponseti's method of treatment of congenital clubfoot deformity. However, little attempt has been made to characterize the proteomic structure of the immature tendon. The purpose of this study is to clarify whether the protein composition of the Achilles tendon differs in newborns and school children with idiopathic congenital clubfoot and to identify proteins that could be involved in the process of tendon generation and development.

**Hypothesis:** There is a difference in qualitative and quantitative protein composition of a clubfoot Achilles tendon between children aged 4 to 10 weeks and children aged 7 to 10 years.

**Aims:** The general aim of the study is to identify proteins which could be associated with regenerative potential of the human Achilles tendon. Specific aims are to: a) identify and describe cellular and protein composition of the Achilles tendon samples obtained from babies with clubfoot aged 4 to 10 weeks whose Achilles tendon regenerative potential is maintained; and to b) identify and describe cellular and protein composition of the Achilles tendon samples obtained from school children with clubfoot aged 7 to 10 years whose Achilles tendon regenerative potential is decreased so the healing tissue forms a fibrotic scar.

**Materials and methods:** One 4x1x1 mm Achilles tendon sample will be obtained from each child with clubfoot in age group 4 to 10 weeks, as well as from each child with clubfoot in age group 7 to 10 years during operative procedure for unilateral equinus correction at the Children's Hospital Zagreb. Samples will be processed immunohistochemically and mass spectrometry proteomic analysis will be performed at the Department of Proteomics, Center for Translational Medicine, University of Zagreb School of Medicine. Presumed number of children included in the study will be close to the number of examinees in similar studies of protein expression analysis in various conditions.

**Expected scientific contribution:** Knowledge of the protein composition changes during development of Achilles tendon could lead to new therapeutic treatments that favor regenerative over fibrotic repair and improve functional outcomes in adult tendon healing.

**Acknowledgments:**

**MeSH/Keywords:** Achilles tendon, regeneration, proteomics, child, congenital idiopathic clubfoot

**Poster code:** T-B-20-114

## Poster Title: VIDEOREHABILITATION IN RECOVERY AFTER TOTAL KNEE ARTHROPLASTY

**PhD candidate:** Jakov Prenc, MD

**Thesis proposal:** Videorehabilitation in recovery after total knee arthroplasty

**Mentor/s:** Professor Esmat Elabjer, MD, PhD, Assistant Professor Damir Hudetz, MD, PhD

**Affiliation:** Clinic of Traumatology Zagreb, University Hospital Center Sestre Milosrdnice

**Introduction:** Knee joint replacement, ie. knee arthroplasty is divided into partial, total and revision. Total knee endoprosthesis replaces all three damaged compartment knee joint and can be cemented or cementless. Indication for total knee arthroplasty (TKA) is knee arthritis. The three most common types of knee arthritis are: osteoarthritis or gonarthrosis, rheumatoid arthritis and posttraumatic arthritis. The first line of treatment is conservative therapy such as physical therapy and medications. If the knee stops responding positively to conservative therapy, it is followed by TKA. The main goal of rehabilitation after TKA is establishing a painless functional range of motion of the knee. Over 90% of patients have a successful outcome after TKA.

**Hypothesis:** Patients who use videorehabilitation everyday as an additional method of recovery in the early stage of recovery after TKA, show significantly better results after 1 and 3 months in a clinical rating scale than patients who do not use videorehabilitation, but only stationary classical rehabilitation in the hospital.

**Aims:** The main objective is to analyze the effect of videorehabilitation in recovery after TKA in the way to determine the difference between the tested and control groups in clinical and functional tests of the knee joint.

**Materials and methods:** The subjects were selected according to inclusion and exclusion criteria. In study we included 60 patients into 2 groups of 30 patients each (experimental and control). All were treated according to the same protocol (preoperative preparation, surgery and post-operative rehabilitation). The information about to which group patient is located will be familiar only to the operator and the patient. The study will thus be a randomized, prospective and blind. Methods: - Diagnostics - Gonarthrosis. - Procedures - Surgery is being done in the pale track. - Rehabilitation - On-line help through the recorded video. - Evaluation: KOOS, Lysholm, IKDC, Tegner, SF-36 questionnaires, the range of motion of the joint, the extent of the thigh muscles.

**Expected scientific contribution:** With the help of this method, the patient could be given important messages on a daily basis in the early stages of recovery and the ability to perform kinesiotherapy through the video instructions which could shorten the postoperative period of rehabilitation and improve clinical outcomes.

**Acknowledgments:** I would like to thank both my menthors for all the support you've shown me throughout my career.

**MeSH/Keywords:** knee, videorehabilitation, total knee arthroplasty, gonarthrosis, randomization

**Poster code:** T-B-20-141

## Poster Title: HEDGEHOG SIGNALING PATHWAY IN ORAL SQUAMOUS CELL CARCINOMA

**PhD candidate:** Sandra Baranović, MD

**Thesis proposal:** Expression of Hedgehog signaling pathway molecules as a prognostic factor in squamous cell carcinoma of the oral cavity

**Mentor/s:** Assist. Prof. Ivica Lukšić, MD, MSc, PhD; Prof. Spomenka Manojlović, MD, MSc, PhD

**Affiliation:** University of Zagreb School of Medicine,University Hospital Dubrava/University Hospital Center Sisters of Mercy, University Hospital for Tumors

**Introduction:** Hedgehog (HH) signaling pathway is related with progression of tumor growth, recurrence of malignant tumors and resistance to different treatment modalities. Although multimodal treatment is often applied, patients with squamous cell carcinoma (SCC) of the oral cavity have poor outcome because of early presence of neck lymph node metastases. HH pathway plays an important role in epithelial-to-mesenchymal transition, via HH ligands. Sonic Hedgehog (SHH) activates signalization. Transmembranic proteins Patched (Ptch) and Smoothened (Smo) are the next cascade, with signal then travelling to the cell nucleus and activating transcription factors Gli. Transcription of genes, involved in cell cycle and migration, angiogenesis and apoptosis, then begins.

**Hypothesis:** Higher expression of HH signaling pathway molecules in patients with SCC of the oral cavity is a negative prognostic factor, associated with higher recurrence rate, regional metastases and worse overall survival.

**Aims:** The aim of this study is to determine expression of SHH, Ptch, Smo, Gli1 in SCC tissue of oral cavity and to correlate it with standard clinical and pathological characteristics. We aim to determine the prognostic value of these proteins for local/regional recurrence and overall survival.

**Materials and methods:** In this retrospective study tissue specimens were obtained from 100 patients with histologically confirmed oral SCC (T1-T3N0M0), treated primary surgically at the Department of maxillofacial surgery, University Clinical Hospital Dubrava, between 1st of January 2006 and 31st of December 2010. Expression of SHH, Ptch, Smo and Gli1 will be semiquantified in 4 stages depending on percentage of stained cells, using immunohistochemistry. Disease free survival will be calculated using the Kaplan-Meier method, while the log-rank test will be used to test differences between the actuarial curves. Only $p < 0.05$ will be considered statistically significant. Follow-up intervals were calculated in months from the date of first treatment at our Department to the date of last follow-up or death. All patients have a minimum of 5-year follow-up.

**Expected scientific contribution:** We will determine the expression of SHH, Ptch, Smo and Gli1 in oral squamous cell carcinoma, and its correlation with loco-regional recurrence. Results of the study will define whether Hedgehog signaling pathway molecules can be used as a prognostic factor and therefore influence choice of treatment.

**Acknowledgments:**

**MeSH/Keywords:** oral squmous cell carcinoma, Hedgehog signaling pathway, loco-regional recurrence, immunohistochemistry, prognostic factor.

**Poster code:** T-B-21-58

## Poster Title: WIDEBAND TYMPANOMETRY IN OTOSCLEROTIC EARS

**PhD candidate:** Iva Kelava, MD

**Thesis proposal:** Diagnostic value of wideband tympanometry in patients with otosclerosis

**Mentor/s:** Professor Vladimir Bedeković, MD, PhD

**Affiliation:** Department of Otorhinolaryngology, Sisters of Charity University Hospital Center

**Introduction:** The diagnosis of otosclerosis is confirmed definitively during the surgery but clinical and audiological evaluation is crucial for preoperative diagnosis and indication for surgery. Diagnosis is traditionally made based on combination of characteristic clinical findings and standard audiological evaluation which include pure-tone audiometry, standard single frequency tympanogram and cohleostapedial reflex. Among these tests only pure-tone audiometry provides quantification of hearing loss, upon which the indication for surgery is based. Pure-tone audiometry has its limitation since it depends on patient subjective responses. Wideband tympanometry is a new technique for assessing middle ear transfer function in which probe tone of 226 Hz is replaced by a probe "click" that covers the 226 to 8000 Hz range. Some studies have already shown that wideband tympanometry may be useful in diagnosis of otosclerosis. However, all these studies were done with insufficient number of patients and patterns of wideband tympanogram typical for otosclerosis have not been defined yet. Also it is not clear whether wideband tympanometry can be used to objectively assess the level of hearing impairment.

**Hypothesis:** Wideband tympanometry has sensitivity comparable to combination of standard tympanometry and cohleostapedial reflex in diagnosis of otosclerosis.

**Aims:** To assess the difference in wideband tympanogram in otosclerotic ears comparing to the normal wideband tympanogram and to explore the correlation between the degree of wideband tympanogram change and the level of hearing disorder.

**Materials and methods:** Longitudinal prospective study will be conducted. We will include 100 patients with otosclerosis diagnosed according to standard diagnostic procedure. We expect about 50 of these patients to be surgically treated.Control group will contain 50 individuals with normal hearing and normal standard tympanogram. Wideband tympanometry will be performed for all subjects. Wideband tympanogram in otosclerotic ears will be compared to the normal wideband tympanogram. We will also explore the correlation between the degree of wideband tympanogram change and the level of hearing disorder. In group of operated patients connection of the degree of wideband tympanogram change in relation to postoperative hearing improvement will be explored.

**Expected scientific contribution:** We expect our results to identify patterns in wideband tympanogram specific to otosclerotic ears that might be useful for more objective diagnosis and prediction of the success of surgery

**Acknowledgments:**

**MeSH/Keywords:** wideband tympanometry, otosclerosis, cohleostapedial reflex

**Poster code:** T-B-21-78

## Poster Title: THE ROLE OF NATIONAL REGISTRY FOR CHILDREN WITH INFLAMMATORY BOWEL DISEASE

**PhD candidate:** Lana Ivković, MD

**Thesis proposal:** The role of national registry for children with inflammatory bowel disease

**Mentor/s:** Sanja Kolaček, MD, PhD

**Affiliation:** Children's Hospital Zagreb, Klaićeva 16, 10000 Zagreb

**Introduction:** Inflammatory bowel disease, Crohn's disease, ulcerative colitis and inflammatory bowel disease-unclassified are chronic diseases characterized by relapsing course. Disease in children, when compared to adults, is more aggressive and extensive, but also changes phenotype over time from mild to severe form. Due to many disease specifics regarding pediatric population, the only way for long-term systematic monitoring of children is through the patients' registry. According to previous studies, national registries were established to determine national incidence and prevalence of disease, and their most important value is possibility of long-term patient follow-up as well as outcome of disease - development of malignancy and mortality level. Incidence of inflammatory bowel disease in Croatian children is unknown. Moreover, there are no epidemiological studies to determine the incidence and phenotype of the disease at diagnosis.

**Hypothesis:** The incidence of inflammatory bowel disease in children in Republic of Croatia is more similar to Mediterranean than other European countries, and shows north - south gradient. Disease phenotype is distinctive for pediatric population.

**Aims:** To determine incidence and disease phenotype at diagnosis of inflammatory bowel disease in Croatian children. To compare obtained data with other Mediterranean countries, and to study disease differences in children from different parts of Croatia.

**Materials and methods:** National registry will be established in cooperation with all pediatric gastroenterologists in Croatia. The study will include all pediatric patients (under 18 years) with newly diagnosed inflammatory bowel disease during one year in Croatia. Database with all required details (age, sex, anthropometric measures, symptoms, extraintestinal manifestations, disease phenotype, results of laboratory, radiology, endoscopic and histological assessment, and disease activity index) will be formed. After one year expiration, obtained data will be processed.

**Expected scientific contribution:** Creating a national registry will determine incidence of inflammatory bowel disease of children in Croatia, and disease phenotype at diagnosis which will contribute to better care for patients as well as better health care organization.

**Acknowledgments:**

**MeSH/Keywords:** inflammatory bowel disease, registries, child, Croatia

**Poster code:** T-B-24-111

# Poster Title: ERYTHROCYTE GLUTATHIONE S-TRANSFERASE ACTIVITY IN CHILDREN WITH HENOCH-SCHÖNLEIN PURPURA

**PhD candidate:** Marijan Frković, MD

**Thesis proposal:** Erythrocyte glutathione s-transferase activity in children with Henoch – Schönlein purpura

**Mentor/s:** Assist. Professor Marija Jelušić, MD, PhD

**Affiliation:** Division of immunology and rheumatology, Department of pediatrics, University Hospital Centre Zagreb

**Introduction:** Henoch - Schönlein purpura (HSP) is the most common vasculitis of childhood. Although the first descriptions of the disease are dated over 200 years ago, there are still doubts about etiopathogenesis, disease activity following criteria and prediction factors for permanent disruption of kidney function as the almost only cause of morbidity and mortality in HSP. Recent papers describe the value of erythrocyte glutathione s-trasferase (e-GST) activity determination in disease activity following in patients with systemic sclerosis (sSC), in early detection of kidney function impairment in patients with diabetes mellitus type II (DM II) and degree of kidney function impairment in patients with chronic renal disease.

**Hypothesis:** Continuously increased activity of e-GST in children with HSP indicates prolonged duration of autoimmune process and represents an early predictor of chronic kidney function impairment.

**Aims:** The main aim is to determine the value of e-GST activity monitoring in assessment of early risk for chronic kidney function impairment in children with HSP. Specific aims are: 1) to determine the e-GST activity in children with HSP at the time of diagnosis and the comparison with the e-GST activity in healthy children, 2) to determine the e-GST activity in children with HSP after 3 and 6 months from diagnosis, 3) to determine the correlation of e-GST activity with the age of affected children, expression of clinical features and commonly monitored laboratory parameters in children with HSP.

**Materials and methods:** The research will take place in University Hospital Centre Zagreb. It will be conducted with at least 90 subjects: at least 45 children with the diagnosis of HSP and at least 45 healthy children with same age and sex distribution. All patients will undergo blood sampling for e-GST activity determination using commercial „Glutatione S-Transferase (GST) Assay Kit". Clinical data will be obtained from medical history and present clinical evaluation.

**Expected scientific contribution:** Determination of the e-GST activity in children with HSP will enable an early risk assessment for chronic kidney function impairment, as almost the only cause of morbidity and mortality in HSP.

**Acknowledgments:**

**MeSH/Keywords:** Henoch - Schönlein purpura, erythrocyte glutathion s-tranferase, kidney function failure

**Poster code:** T-B-24-122

## Poster Title: THE ROLE OF GLUTATHIONE S-TRANSFERASE GENE POLYMORPHISMS ON TREATMENT OUTCOMES IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

**PhD candidate:** Sanda Huljev Frković, MD

**Thesis proposal:** The role of glutathione S-transferase genes polymorphisms on treatment outcomes in children with juvenile idiopathic arthritis

**Mentor/s:** Assist. Professor Marija Jelušić, MD, PhD

**Affiliation:** Division of genetics, Department of pediatrics, University Hospital Centre Zagreb

**Introduction:** Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease of childhood. According to clinical characteristics and possible outcomes it is divided into seven types (ILAR criteria 1994.). Treatment protocols developed by ACR (2011., 2013.) for all seven types of disease, include methotrexate (MTX) as the main drug of second therapeutic line. According to literature, the overall probability of achieving JIA remission during MTX therapy is 45-75%. The glutathione S-transferases (GSTs) are a family of phase II xenobiotic metabolizing enzymes that protects cells against endogenous and exogenous metabolites through conjugation of glutathione. So far, several studies have examined the potential contributions of GSTM1 and GSTT1 gene polymorphisms on efficacy and toxicity of different drugs in treatment of different diseases. Homozygous deletion in the GSTM1 and GSTT1 genes or null genotype leads to absence of enzymatic activity. The aim of this study is to determine the effects of GSTM1 and GSTT1 gene polymorphisms on efficacy of MTX therapy in JIA patients.

**Hypothesis:** GSTM1 and GSTT1 null polymorphisms in JIA patients are associated with a greater likelihood of achieving remission during MTX treatment.

**Aims:** The aim of this study is to determine the proportion of GSTM1 and GSTT1 genes null polymorphisms in JIA patients and their correlation to overall probability of achieving JIA remission during MTX therapy.

**Materials and methods:** The research will take place in University Hospital Centre Zagreb, Department of Pediatrics and Department of Laboratory Diagnostics. It will be conducted with at least 90 subjects fulfilling the ILAR criteria for JIA: at least 45 patients on MTX therapy with complete remission and at least 45 patients on biologics, due to previous MTX therapy failure. All patients will undergo blood sampling for gene analysis performed in laboratory in our institution. Isolation of DNA from the blood will be implemented Flexigen DNA kit for DNA isolation, genotyping GSTM1 and GSTT1 polymorphisms will be performed using the polymerase chain reaction. Clinical data will be obtained from medical history and present clinical evaluation.

**Expected scientific contribution:** Determination of GSTM1 and GSTT1 genes null polymorphisms in JIA patients can be used in everyday practice for calculating the complete remission probability during MTX therapy.

**Acknowledgments:**

**MeSH/Keywords:** juvenile idiopathic arthritis, glutathione S-transferases, polymorphisms, methotrexate

**Poster code:** T-B-24-146

## Poster Title: THE ROLE OF TRANSITIONAL CARE IN ADOLESCENT PATIENTS WITH INFLAMMATORY BOWEL DISEASE

**PhD candidate:** Tena Trbojević, MD

**Thesis proposal:** The role of transitional care in adolescent patients with inflammatory bowel disease

**Mentor/s:** Professor Sanja Kolaček, MD, PhD; Iva Hojsak, MD, PhD

**Affiliation:** Children's Hospital Zagreb

**Introduction:** Inflammatory bowel disease (IBD) is a chronic disease of the digestive system with relapsing and remitting course that occurs in one third of cases in childhood and adolescence. Pediatric patients, at some point, are transferred to the adult health care where autonomy and responsibility are required. However, adolescents with IBD are mostly insufficiently competent in respect to disease management skills what can lead to poor disease outcome. Therefore, to enable adolescent patients bridging the gap between pediatric and adult services by gaining independence in disease management (without parental assistance), organized and structured transition (transitional care) is required, whereby for a defined period of time health care is provided by both, pediatricians and adult specialists. Transition is defined as purposeful, planned movement of adolescents and young adults with chronic physical and medical conditions from child-centered to adult-orientated health care systems. During transition, adolescents learn to be proactive in medical care, make decisions and communicate effectively with the medical team.

**Hypothesis:** Organized transitional care program significantly improves quality of life and disease control in IBD patients.

**Aims:** To found the organized transitional care program for adolescent IBD patients in Croatia and evaluate its impact on patient's quality of life and disease course.

**Materials and methods:** Adolescent IBD patients (17 years of age and older) who are finishing high school education therefore ending the pediatric care are dived in two groups. Patients in group 1 are transferred to adult health care system without organized transitional care program. Patients in group 2 are transferred to adult care through organized transitional care program. Quality of life, activity of disease using disease-specific index, also number of relapses and number of hospitalizations over one year will be evaluated in both groups at the time of transfer (group 1) or beginning of transitional program (group 2) and one year after. Organized transitional care program is provided during first six months after inclusion (group 2) and it's compound of three visits: first two visits are provided by both pediatric and adult gastroenterologist, where one visit involves patient and their parents. The third visit is provided by pediatric gastroenterologist.

**Expected scientific contribution:** Evaluation of the efficacy of organized transitional care program on quality of life and disease course in adolescent IBD patients.

**Acknowledgments:** This research is financially supported by five pharmaceutical companies: AbbVie, Dr. Falk Pharma/Würth, MSD, PharmaS and Alvogen/Hospira.

**MeSH/Keywords:** Inflammatory bowel disease, transition, adolescent

**Poster code:** T-B-24-163

# Poster Title: MULTIPARAMETRIC MAGNETIC RESONANCE ANALYSIS OF FEMALE BREAST CARCINOMA

**PhD candidate:** Marko Petrovečki, MD

**Thesis proposal:** Multiparametric magnetic resonance analysis of female breast carcinoma could predict response outcome to neoadjuvant therapy

**Mentor/s:** Prof. Maja Prutki, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre – Zagreb

**Introduction:** Breast cancer is the most common malignancy in Croatian women and a leading cause of death due to malignant disease. In patients with locally advanced breast cancers or metastatic disease neoadjuvant therapy is given according to guidelines of Croatian Society of Oncology from 2010. Considering the toxicity of medication an early detection of tumor response to therapy is needed. Mammography and ultrasound together are very good tool for screening purposes but magnetic resonance imaging (MRI) still remains the most sensitive method of breast imaging.

**Hypothesis:** Breast MRI made early after second cycle can predict which patient will be a good responder to neoadjuvant therapy.

**Aims:** Determine if water diffusion, Göttingen score, kinetic analysis and MR spectroscopy measured before neoadjuvant therapy and after second cycle can separate responders from non-responders at the end of neoadjuvant therapy. Are water diffusion, Göttingen score, kinetic analysis and MR spectroscopy independent predictors of final response to neoadjuvant therapy and could a cut-off score be determined for each one.

**Materials and methods:** Prospective study will include 45 female patients with newly discovered inoperable breast cancer that are eligible for neoadjuvant therapy. Each patient will have breast MRI exam made before, after second cycle and at the end of neoadjuvant therapy. Besides standard MRI protocol additional imaging sequences will be done: diffusion weighted imaging (DWI) and MR spectroscopy (MRS). Morphological and kinetic characteristic of tumor before and after second cycle of neoadjuvant therapy will be correlated to histopathology of tumor and final response to therapy. All data will be saved in table form and parametric or non-parametric statistics will be done according to data distribution.

**Expected scientific contribution:** Toxicity of neoadjuvant chemotherapy is common and can in seldom cases cause fatal cardiotoxic effects. Therefore it is important to determine as early as possible whether a cancer will respond to given therapy and if not start other forms of treatment. Multiparametric MRI could give precise prediction of breast cancer final response after second or even after first cycle of neoadjuvant therapy. Multiparametric MRI could also be used in patient management before final decision for operative and adjuvant therapy treatment or neoadjuvant therapy prior to surgical treatment.

**Acknowledgments:** I would like to thank my mentor, Maja Prutki, for passing her knowledge, help in patient management and study planing. Also I would like to thank my father, Mladen Petrovečki, for help with statistics, doctoral thesis formation and structure.

**MeSH/Keywords:** MRI, breast cancer, neoadjuvant therapy

**Poster code:** T-B-25-5

## Poster Title: CORRELATION OF FMD AND WALKING DISTANCE IN PERIPHERAL ARTERIAL DISEASE

**PhD candidate:** Stipe Radoš, MD

**Thesis proposal:** Association of sonographically estimated endothelial function with claudications and ankle brachial indices in PAD

**Mentor/s:** Professor Boris Brkljačić, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Dubrava

**Introduction:** Peripheral artery disease (PAD) has a prevalence of 25% in general population over 70 y,and with accelerated aging of population number of patient with PAD is increasing rapidly. As for the CAD (coronary artery disease), diabetes is one of main risk factors for development of PAD. It is important to have noninvasive diagnostic tool for early detection of the disease, like ABI test. Based on previous research we can conclude that ABI test have limited value in some patients with the PAD and especially in those with diabetes. Endothelial function is an important factor in the development of the PAD. The assessment of endothelial function can be performed indirectly by measuring FMD using an ultrasound machine. The lower value of FMD indicates endothelial dysfunction.

**Hypothesis:** Flow mediated dilatation (FMD) measured in brachial artery is in correlation with walking distance and caludications in patients with PAD

**Aims:** General goal: to show that FMD is an independent predictor of vascular status in peripheral arterial disease (PAD). Specific goals: 1. Investigate correlation of FMD and ankle brachial indices (ABI)in PAD; 2. Investigate influence of diabetes on correlation between FMD and ABI; 3.Investigate is there significant difference in correlation of FMD with vascular status between two groups of patients (with diabetes and without diabetes).

**Materials and methods:** The research will be conducted prospectively at two test groups with 60 patients within each group. The key difference to form group will be presence of diabetes. Including criteria for both groups will be symptomatic PAD, and in diabetic group that the duration of the disease is more than five years. Exclusion criteria for both groups will be renal insufficiency with a GFR less than 45 ml/min calculated by MDRD formula, acute infectious disease, great surgery within 30 days. The control group will include 20 patients without symptoms of PAD and without diabetes. In all patients will be performed measuring of flow mediated dilatation (FMD) in the upper arm artery using standard protocol, and ABI. For FMD measuring will be used ultrasound device Aloka Alpha 10. The FMD measuring will be carried out according to the guidelines of the American College of Cardiology. The ABI will be measured by a conventional device that uses continuous Doppler.

**Expected scientific contribution:** If the hypothesis is correct, FMD mesauring could be used for assessment of atherosclerosis severity in patients with diabetes type II who have symptomatic PAD and normal ABI.

**Acknowledgments:**

**MeSH/Keywords:** PAD, CAD, diabetes, FMD, ABI

**Poster code:** T-B-25-56

# Poster Title: HYPERTROPHY AND HYPERPLASIA OF LEYDIG CELLS IN MEN WITH NON-OBSTRUCTIVE AZOOSPERMIA

**PhD candidate:** Dinko Hauptman

**Thesis proposal:** Hypertrophy and hyperplasia of Leydig cells in men with non-obstructive azoospermia

**Mentor/s:** Professor Željko Kaštelan, MD, PhD, Professor Davor Ježek, MD, PHD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre – Zagreb

**Introduction:** Non-obstructive azoospermia is a type of male infertility caused by failure of spermatogenesis at the testicular level. Biopsies of men with non-obstructive azoospermia often reveal histological changes described as enlarged islets of Leydig cells. Combination of cell growth (hypertrophy) and cell proliferation (hyperplasia) of Leydig cells could be caused by a disruption of the hypothalamo-hypophyseal-gonadal axis's negative feedback mechanism, causing "bombardment" of Leydig cells with gonadotropins. This condition is characterized histologically by an increased total volume of Leydig cells and presence of atypical nuclei with more numerous nucleoli. Generally, hyperplastic Leydig cells tend to more closely resemble their derivative mesenchymal cells than mature Leydig cells. Interestingly, one study found that the changes previously described as Leydig cell hyperplasia may in fact be hypertrophic in nature, contrasting previous literature and raising questions about the true nature of the interstitial histological anomalies in azoospermic men.

**Hypothesis:** We hypothesize that the expansion in total Leydig cell volume observed in men with non-obstructive azoospermia is the result of a combination of cell growth (hypertrophy) and cell proliferation (hyperplasia). We expect that our analysis shall reveal a more heterogeneous population of Leydig cells in men with NOA, with some hypertrophic cells and some cells resembling mesenchymal Leydig cell precursors.

**Aims:** To investigate both proliferation and growth of Leydig cells.

**Materials and methods:** We shall perform stereological analysis from samples of testicular biopsis in men with non-obstructive azoospermia. As control group we shall include patients with obstructive azoospermia who have normal spermatogenesis. Samples shall be fixed and stained using hemotoxylin and eosin staining and shall be graded on an infertility scale based on spermatogenic success. One-hundred to two-hundred microscopic fields shall be analysed for each testis. A microscope with a 42-point grid shall be used to determine the volumes of seminiferous tubules, interstitial space, and Leydig cells. Semithin sections shall be obtained using a microtome and shall be stained using toluidine blue.

**Expected scientific contribution:** We believe that this scientific work could reveal and understand patohystological changes in patients with idiopatic men infertility.

**MeSH/Keywords:** hypertrophy, hyperplasia, Leydig cell, azoospermia

**Poster code:** T-B-28-54

## Poster Title: THE ROLE OF PSYCHOSOCIAL FACTORS IN OUTCOMES OF IN VITRO FERTILIZATION METHODS

**PhD candidate:** Dunja Jurić

**Thesis proposal:** The impact of religiosity on the outcome of treatment of depression: clinical and biological indicators

**Mentor/s:** Assist. Prof. Zorana Kušević, MD, PhD

**Affiliation:** Zavod za javno zdravstvo Sisačko-moslavačke županije, Klinički bolnički centar Zagreb

**Introduction:** Psychological problems that sometimes occur with infertility often remain unrecognized. Studies have shown that some of the psychological disorders such as depression and anxiety can have a negative effect on the outcome of IVF and can also be the reason of drop out from further treatment of infertility. In recent literature there is little work linking psychosocial factors with infertility and assisted reproductive techniques, and the results are often contradictory.

**Hypothesis:** The levels of alexithymia, anxiety and depression are higher among women in the process of IVF than in the general population, and high levels of alexithymia, anxiety and depression are significant predictor of negative outcomes of IVF methods.

**Aims:** Because of the potential benefits of interdisciplinary treatment of infertility, this study aims to determine the prevalence of alexithymia, depression and anxiety and their impact on the outcome of IVF.

**Materials and methods:** Research will be conducted individually, using: sociodemographic questionnaire, including questions about age, level of education, psychiatric and other chronic diseases in personal and family medical history, relationship with the partner, number of children, duration of infertility, number of IVF, question about attending psychotherapy and question was there any stressful event during IVF process, more stressful than procedure alone. Revised NEO Personality Inventory (NEO PI-R), 60 items personality inventory which assesses the Big Five personality traits: Extraversion, Agreeableness, Conscientiousness, Neuroticism, and Openness to Experience. Toronto Alexithymia Scale questionnaire–20 (TAS-20) is a 60 items inventory of deficiency in understanding, processing, or describing emotions. - Clinical Outcomes in Routine Evaluation – Outcome Measure (CORE-OM), a scale designed as a measure of general psychological distress. It has 34 items covering problems (depression, anxiety, physical problems and trauma), well-being, functioning (general and social) and risk behaviour. - Religiosity questionnaire consists of 24 items relating to three dimensions of religiosity: spirituality, ritual dimension and impact of religion on behavior dimension.

**Expected scientific contribution:** Insight into the level of alexithymia, depression and anxiety among women in the IVF process could contribute to the implementation of an interdisciplinary approach to the treatment of infertility with the purpose of reducing the psychological problems.

**Acknowledgments:** doc. dr. sc. Marina Šagud, prof. dr. sc. Nataša Jokić Begić, prof. dr. sc. Rudolf Gregurek, doc. dr. sc. Marijana Braš, prof. dr. sc. Snježana Škrablin Kučić

**MeSH/Keywords:** In vitro fertilization, alexithyimia, depression, anxiety

**Poster code:** T-B-29-153

# Poster Title: IDENTITY IMPAIRMENTS IN ADOLESCENTS WITH NON-SUICIDAL SELF-INJURY BEHAVIOR AND SUICIDAL ATTEMPTS

**PhD candidate:** Nela Ercegović, MD

**Thesis proposal:** Identity impairments in adolescents with non-suicidal self-injury behavior and suicidal attempts

**Mentor/s:** Associate Professor Darko Marčinko, MD, PhD; Vlatka Boričević Maršanić, MD, PhD

**Affiliation:** Psychiatic Hospital for Children and Adolescents, Zagreb

**Introduction:** Identity is a fundamental organizing principal which allows one to function autonomously from others. Establishing a stable identity is important developmental task in adolescence. Identity diffusion is a pathological concept which represent pathological identity development, leading to a broad spectrum of maladaptive and dysfunctional behaviors, like non-suicidal self injury behavior and suicidal behavior. They represent a major public health problem in adolescents, with high rates of self harm in teenage years, and suicide being the third most common cause of death in young people worldwide.

**Hypothesis:** Impairments of identity differ between adolescents with non-suicidal self-injury behavior (NSSI) and adolescents with suicidal attempt (SA).

**Aims:** The main aim is to investigate the difference in the identity development and the relationship of impairments in identity between adolescents with NSSI behavior and adolescents with SA. Secondary goal is to examine age and gender differences in auto-aggressive behaviors (NNSI and SA) in adolescents inpatient and the role of socio-demographic, family factors and traumatic experiences in self harm behaviors (NNSI and SA).

**Materials and methods:** Participants will be adolescents aged 12 to 18 years, hospitalized in the Inpatient unit 2of the Psychiatric Hospital for Children and Adolescents. Estimated sample size is 150 patients. Inclusion criteria will be the presence of NSSI behavior or SA in the past six months. According to these criteria participants will be assigned to two groups: adolescents with NSSI behavior and adolescents with SA. Differences between two groups will be analysed by the test set including: Assessment of Identity development in Adolescence (AIDA), Youth Self-Report for ages 11-18 (YSR 11-18),Childhood Trauma Questionnaire (CTQ), Deliberate Self Harm Inventory (DSHI), Family Adaptability and Cohesion evaluation Scale (FACES III), and sociodemographic questionnaire.

**Expected scientific contribution:** We expect the study will clarify the impact of identity impairments to self harming and suicidal behavior in adolescents. The study will examine the factors that hinder development of identity and their influence in predicting and distinguishing NSSI and SA in adolescents. We hope this may help to improve assessment and treatment of adolescents with these severe psychiatric problems.

**Acknowledgments:**

**MeSH/Keywords:** Identity, Adolescence, Non suicidal self injury behavior, suicidal attempt

**Poster code:** T-B-29-144

## Poster Title: ROLE OF GENETIC POLYMORPHISM OF ENDOTHELIAL NITRIC OXIDE SYNTHASE IN THE ASSESMENT OF RISK OF INTRACRANIAL ANEURYSM GROWTH AND RUTPURE

**PhD candidate:** Josip Ljevak, MD

**Thesis proposal:** Role of genetic polymorphism of endothelial nitric oxide synthase in the assesment of risk of intracranial aneurysm growth and rutpure

**Mentor/s:** Professor Zdravka Poljaković, MD, PHD

**Affiliation:** University Hospital Center Zagreb, Department of neurology

**Introduction:** Aneurysmal subarachnoid hemorrhage (aSAH) is one of the most devastating neurological emergencies, with complex clinical presentation, numerous complications and often difficult choice of optimal therapeutic approach. Prevalence of intracranial aneurysms is estimated to be approximately 2-3%, while incidence of aSAH is 10/100 000. Most of IA remain asymptomatic, but as aSAH carries a relatively bad prognosis (mortality up to 50%), importance of treating unruptured aneurysms became increasingly recognized. Selecting optimal treatment plan for patient dependant and individual. Aside of known risk factors for IA growth and rutpure (hypertension, female sex, smoking, older age), there are indicators of possible genetic determination (family history of aSAH, ADPKD, MEN1 – all of which increase the risk of SAH). Based on well known vasoprotective effect of endothelial nitric oxide synthase (eNOS) on cerebral vessels, multiple studies concerning eNOS genetic polymorphysm were conducted, but results were inconsistent.

**Hypothesis:** Genetic polymorphisms of eNOS increase the risk of intracranial aneurysm growth and rupture

**Aims:** Primary aims are to test the hypothesis, investigate the genetic polymorphism distribution in Croatian populaton, and to evaulate the effect of other known risk factors. Additional informations to be gained are results of IA treatment, incidence of rupture of IA wiht diameter smaller than 5 mm, and incidence of new IA development in population tested.

**Materials and methods:** In 293 patients genetic testing was performed, analyzing eNOS polymorphisms (27VNTR, G894T, T786C) using quantitative PCR. Patients are divided in two groups (unruptured aneurysm, aSAH) with a follow up of 3-5 years consisting of both clinical and radiological examinations. Results of genetic analysis will be correlated with clinical characteristics of patients (age, sex, hypertension, smoking, IA rupture, IA symptoms) and aneurysm morphology (size, shape, location, dome-to-neck ratio, largest diameter).

**Expected scientific contribution:** Results of this study will show a possibly specific distribution of eNOS gene polymorphisms in Croatian population. Also, it will contribute to significance of genetic analysis in prediction of IA growth and rupture risk, making treatment decisions for patients with unruptured IA more precise.

**Acknowledgments:**

**MeSH/Keywords:** Intracranial Aneurysm, Subarachnoid Hemorrhage, Endothelial Nitric Oxide Synthase

**Poster code:** T-B-30-147

# Poster Title: PROFESSIONAL VALUES IN NURSING

**PhD candidate:** Hrvoje Premuž MSN, RN

**Thesis proposal:** Analysis of professional value system among intensive care nurses in Croatia

**Mentor/s:** Assistant Prof. Ana Borovečki MD, PhD, Professor Chris Gastmans, PhD

**Affiliation:** General Hospital Slavonski Brod, Croatia, Croatian ICU Nursing Comunity

**Introduction:** Societal circumstances and changes can have an impact on the professional development of healthcare workers and the quality of healthcare services. Professional value system (of physicians and nurses) has an immediate impact on all processes of healthcare delivery and their numerous outcomes. A developed professional value system allows adequate and timely reaction in demanding conditions of intensive clinical care practices, often accompanied by a number of ethical dilemmas.

**Hypothesis:** There are differences in the professional value system of nurses in intensive care units in Croatia, and NPVS - R (revised questionnaire to assess the professional values of nursing) is a reliable, valid and applicable instrument for the assessment of professional value systems of nurses in intensive care in Croatia.

**Aims:** The aim of this study is to analyse existing professional value system in everyday work of nurses in intensive care units in Croatia. The second aim of this research is to investigate the applicability of the existing instrument (NPVS-R) used at evaluating the professional values among nurses in the analysis of professional value system among intensive care nurses in Croatia.

**Materials and methods:** The research will be carried out in three phases. Phase one consist of focus group qualitative research with the aim of defining the basic set of values of professional value system among nurses working in intensive care units in hospitals in Croatia. The second phase the research will be carried out with NPVS-R instrument on sample of Croatian ICU nurses and the applicability of NPVS-R to Croatian circumstances will be analysed.

**Expected scientific contribution:** The research into professional values in nursing in different nursing fields is not common, especially when it comes to professional values that can be observed in nurses working in intensive care units. Moreover, to date there is no comprehensive analysis of the value system of nurses in intensive care in Croatia. The combination of qualitative and quantitative approach to the analysis of these issues is still in its beginnings. Understanding the value system and ethical problems in nursing care can help in better planning of education and organization of nursing staff in intensive care units. This research could lead to new methodological approach to analysis of the professional value system in the field of nursing (a combination of qualitative and quantitative analysis).

**Acknowledgments:**

**MeSH/Keywords:** nursing professionalism, nursing, nursing ethical values, survey, intensive care, ethical dilemmas

**Poster code:** T-B-31-55

# Poster Title: OPIOID DERIVATES ANALGESIA AND NONOPIOID ANALGESIA ASSESSMENT THROUGH INTERMITTENT APPLICATION AND PATIENT CONTROLLED ANALGESIA PUMP AFTER LUMBAR DISCECTOMY

**PhD candidate:** Biljana Kurtović

**Thesis proposal:** Opioid derivates analgesia and nonopioid analgesia assessment through intermittent application and patient controlled analgesia pump after lumbar discectomy

**Mentor/s:** Professor Krešimir Rotim, MD, PhD

**Affiliation:** Department of Neurosurgery, University Hospital Centre Sestre milosrdnice

**Introduction:** Pain after lumbar discectomy is a common clinical problem that greatly affects the functional status and patients' quality of life. There are several strategies that are used to relieve pain after lumbar discectomy but there is a lack of analgesic treatment systematic documentation in that population.

**Hypothesis:** Opioid derivates analgesia through patient controlled analgesia pump more effectively reduces pain than intermittent application of opioid derivates and non opioid analgesia.

**Aims:** (1) To explore effective ways to reduce or eliminate pain after lumbar discectomy, (2) to explore whether opioid analgesia derivatives through patient controlled analgesia pump are more effective than intermittent opioid derivates analgesia and non-opioid analgesia.

**Materials and methods:** Project respodents will be patients which underwent elective lumbar discectomy of intervertebral disc extrusion level L4 - L5 established by lumbosacral spine MRI. Pain will be evaluated at regular time intervals through a shortened version of McGill pain questionnaire, in Croatian language. Minimum total sample should include at least 180 respodents. Results will be presented in tables and graphics, and in descriptive statistics with appropriate central tendency measures. Values distribution of certain variables will be determinated by Smirnov-Kolmogorovljev test. For the quantitative differences between individual values of the time measurement parametric tests will be used (independent t-test and/or ANOVA), or non parametric equivalents (Mann-Whitney U test and/or Kruskall-Wallis test). XČ2 test will establish differences in categorical variables between groups. Correlations between individual values will be determined by Pearson or Spearman correlation coefficient. To assess the impact of intravenous received opioid derivatives and non opioid analgesia intermittently or through patient controlled analgesia pump, there will be performed binary logistic regression. P values below 0.05 will be deemed as statistically significant.

**Expected scientific contribution:** Better pain control, quick patient recovery, pain associated complication prevention and shorter patient hospitalization.

**Acknowledgments:**

**MeSH/Keywords:** pain, postoperative, analgesia

**Poster code:** T-B-31-64

# 2.3.

## RESEARCH PROPOSALS
## Public Health and Health Care

# Poster Title: SIGNIFICANCE OF THE TICK-BORNE ENCEPHALITIS SEROPREVALENCE IN SENTINEL ANIMALS IN THE DETERMINATION OF NATURAL FOCI AND RISK ASSESSMENT OF HUMAN INFECTION

**PhD candidate:** Goranka Petrović, MD, Epidemiologist and Environmental Health Specialist

**Thesis proposal:** Significance of the tick-borne encephalitis seroprevalence in sentinel animals in the determination of natural foci and risk assessment of human infection

**Mentor/s:** 1. Assistant Professor Tatjana Vilibić-čavlek, MD, PhD; 2. Associate Professor Ljubo Barbić, DVM, PhD

**Affiliation:** 1. University of Zagreb School of Medicine, Croatian Institute of Public Health 2. University of Zagreb Faculty of Veterinary Medicine

**Introduction:** Tick-borne encephalitis (TBE) is the most important tick-borne neurotropic flavivirus infection occurring in natural foci in Europe and Asia. The efficiency of TBEV transmission depends on abiotic and biotic determinants, such as climatic factors, vegetation and the density and distribution of vectors and hosts within the endemic foci. Surveillance of the TBE seroprevalence in sentinel animals could be a significant predictor in the determination of natural foci, epidemiological risk assessment of the TBEV human infection as well as in the detection of those clinical cases which so far still remain unrecognized, resulting in underestimation of the importance of the problem and consequent inadequate strategy of preventive activities, both for the local population in endemic areas, as well as for travelers visiting such areas.

**Hypothesis:** The TBE seroprevalence in sentinel animals is risk predictor of TBE human infection.

**Aims:** To determine the epidemiological characteristics and possibility of risk prediction of human TBE infection by using sentinel animals.

**Materials and methods:** A cross-sectional study of asymptomatic TBE infection in humans and sentinel animals (horses and dogs) will be carried out on randomly chosen sample in the continental part of Croatia during one-year period. Based on estimated prevalence obtained by pilot study conducted in humans and animals, a sample of 707 human subjects, 656 horses and 380 dogs will be obtained. Sera of adults aged 18 and above living in continental part of Croatia will be analysed. Persons with acute nervous system infection as referral diagnosis or with history of TBE vaccination will be excluded. Horses and dogs from the same respective territory will be recruited. Human and animal samples will be analysed in laboratory in Croatian Institute of Public Health and Veterinary Medicine respectively. Commercial ELISA diagnostic tests will be used in the detection of TBEV-specific IgG antibodies. Initially positive human samples will be confirmed by commercial imunoflorescent test. Data will be analysed using the software package STATA /IC ver.11.2 (StataCorp LP, USA).

**Expected scientific contribution:** Scientific evidence of the relevance of TBEV seroprevalence in sentinel animals in TBEV natural foci detection and risk prediction of human infection would provide scientific base for the establishment of scientifically based system of risk assessment of TBEV human infection and improvement of existing TBEV infection surveillance.

**Acknowledgments:**

**MeSH/Keywords:** tick-borne encephalitis virus, natural foci, seroprevalence, sentinel animals, risk prediction

**Poster code:** T-C-1-24

## Poster Title: PREVALENCE AND RISK FACTORS OF HEPATITIS E IN CROATIA

**PhD candidate:** Pavle Jeličić, MD, MHM

**Thesis proposal:** Prevalence and analysis of risk factors for hepatitis E virus infection in continental Croatia.

**Mentor/s:** Assist. Prof. Tatjana Vilibić-Čavlek, MD, PhD, Assist. Prof. Lorena Jemeršić, DVM, PhD

**Affiliation:** Croatian Institute of Public Health, Croatian Veterinary Institute

**Introduction:** Hepatitis E virus (HEV) causes feco-orally transmitted hepatitis and is responsible for more than 50% of all acute hepatitis cases in endemic countries. There is growing evidence of HEV emergence and re-emergence with an increasing number of indigenous cases in Europe. The main reservoirs of HEV are pigs, but the virus has been isolated from other animals as well. The most common sources of infection are contaminated drinking water and contaminated, undercooked food. So far, in Croatia there were no systematic surveys on the prevalence of HEV infection or data on the risk factors associated with HEV infection. While the HEV prevalence in some animals (wild and domestic pigs) is well known, in other animals is rather unknown.

**Hypothesis:** Occupational exposure to animals is a risk factor for hepatitis E infection.

**Aims:** 1. Assess the HEV prevalence in the population of professionally exposed and non-exposed to animals in continental Croatia. 2. Assess the HEV prevalence in dogs and horses in continental Croatia. 3. Analyze the risk factors for the HEV infection in Croatia. 4. Determine the possible association between the source of infection in humans and animals (molecular epidemiology).

**Materials and methods:** 295 human (hunters, forest workers, veterinarians, general population) and 666 animal (horses, dogs) sera will be collected and analyzed. Data on sociodemographic characteristics and possible risk factors will be collected using a questionnaire. Serum samples will be tested for HEV IgM and IgG antibodies using the commercial ELISA tests. Initially reactive results will be confirmed using a commercial immunoblot test. All samples with positive HEV antibodies will be tested for the presence of HEV RNA using a quantitative real-time RT-PCR method. Positive RT-PCR samples will undergo the sequencing and phylogenetic analysis of HEV strains. Serological diagnostics will be carried out at the Reference Center Ministry of Health for Diagnosis and Surveillance of Viral Zoonoses at Croatian Institute of Public Health, while the molecular diagnostics will be carried out at the Department of Virology at Croatian Veterinary Institute.

**Expected scientific contribution:** Data on HEV prevalence and potential risk factors for HEV infection have been inconsistent. Knowledge about the prevalence and risk factors of HEV in specific target population groups, as well as the prevalence in animals and their phylogenetic relation represent original scientific contribution to the epidemiology of HEV infection in Croatia and the world.

**MeSH/Keywords:** Prevalence, risk factors, hepatitis E virus, Croatia

**Poster code:** T-C-1-68

## Poster Title: EPIDEMIOLOGIC CHARACTERISTICS OF PRIMARY HEADACHES AMONG UNIVERSITY OF APPLIED HEALTH SCIENCES STUDENTS IN ZAGREB

**PhD candidate:** Lukrecija Jakuš, MA

**Thesis proposal:** Epidemiologic characteristics of primary headaches among University of Applied Health Sciences students in Zagreb

**Mentor/s:** Assist. Prof. Darija Mahović Lakušić, MD, PhD

**Affiliation:** University of Applied Health Sciences

**Introduction:** Primary headaches,the most common disorders of the nervous system, cause substantial levels of disability. The percentages of the adult population with an active headache disorder are 46% for headache in general, 11% for migraine, 42% for tension-type headache and 3% for chronic daily headache. Headache disorders are into the ten most disabling conditions for the two genders and into the five most disabling for women. The burden of headache is large, but knowledge of it is incomplete and needs to be gathered. Published studies have used variable methodology, which has influenced findings and made comparisons difficult.

**Hypothesis:** The one-year prevalence of primary headaches among University of Applied Health Sciences students in Zagreb is in line with similar studies. Headaches impose a great burden on the individual in terms of lower quality of life and headache impact.

**Aims:** Aim is to determine the prevalence of primary headaches and their clinical characteristics at University of Applied Health Sciences students in Zagreb, and to estimate the individual and socioeconomic burden of primary headaches according to quality of life, disability and health-care resource consumption.

**Materials and methods:** Cross-sectional study will be conducted on full-time students at University of Applied Health Sciences in Zagreb, aged 18 to 25. Students will complete the Headache-Attributed Restriction, Disability, Social Handicap and Impaired Participation (HARDSHIP) questionnaire, a validated instrument incorporating demographic enquiry, diagnostic questions based on ICHD-3 beta criteria, and enquiries of headache-attributed burden. The questionnaire will be translated into Croatian using the Lifting the Burden translation protocols, cross-culturally adopted and validated. The general and specific characteristics will be analysed. Correlation between quality of life and wellbeing level and headache intensity and frequency will be observed.

**Expected scientific contribution:** The methods developed for population-based burden of headache studies will be applied in Croatia. The methodology and validation of the HARDSHIP questionnaire, adapted from those used by Lifting the Burden in similar studies will be presented and findings will be comparable. Findings in this study will improve knowledge about socioeconomic burden and the headache quality of life impact. According this findings appropriate management program with young adults who suffer from headache can be planed in order to prevent chronic headache disorders and disability in later life.

**Acknowledgments:** I would like thank my mentor Assist. Prof. Darija Mahović Lakušić, MD, PhD for her help and support.

**MeSH/Keywords:** primary headache, epidemiology, migraine, tension type headache, burden of disease, quality of life

**Poster code:** T-C-1-135

## Poster Title: ATTACHMENT MODEL RELATED TO BODY-ESTEEM AND RISKY BEHAVIOUR

**PhD candidate:** Marija Posavec, MD, school medicine specialist

**Thesis proposal:** Attachment model related to body-esteem and risky behaviour in first year college students

**Mentor/s:** Professor Darko Marčinko, MD, PhD, psychiatry specialist, Marina Kuzman, MD, PhD, school medicine specialist

**Affiliation:** Andrija Stampar Teaching Institute of Public Health

**Introduction:** Adolescents are considered to be vulnerable population for risky behaviour due to intensive development, experimenting, and lack of experience. Risky habits of younger adolescents are extensively investigated. However, risky choices of older adolescents have been less studied. Risky eating habits, risky sexual behaviour and problematic internet use in late adolescence seem to be related to at least two psychosocial factors: body self-perception and perception of oneself in relationships. Body-esteem proved to be related to eating disorders, whereas results on its association with sexual behaviour and internet use are inconsistent. Attachment model, secure and insecure (avoidant, anxious, disorganized), is the base for behaviour in close relationships. Insecure attachment models are positively associated with eating disorders and negative body-esteem in patients with eating disorders. Results on attachment model related to sexual behaviour are inconsistent and to internet use, to the best of our knowledge, not investigated.

**Hypothesis:** Insecure attachment models are positively associated with negative body-esteem, risky eating habits, risky sexual behaviour, and problematic internet use.

**Aims:** Main goal of the study is to investigate association of attachment model components with body-esteem and risky behaviour. Avoidant and anxious dimensions of insecure attachment related to body self-perception, risky eating habits, risky sexual behaviour and problematic internet use are to be evaluated. Association of body-esteem with risky behaviour will be explored.

**Materials and methods:** A total sample of 2000 first-year college students studying at the University of Zagreb will be randomly selected. Self-administered anonymous questionnaire consisted of six sections (general/medical data, Body-Esteem Scale for Adolescents and Adults, Vulnerable Attachment Style Questionnaire, risky eating habits, risky sexual behaviour, problematic internet use) will be obtained. Survey will be conducted during 2016 in school health offices of Andrija Stampar Teaching Institute of Public Health, Zagreb, Croatia. During regular systematic check-up students will be invited to participate up till sample size is met.

**Expected scientific contribution:** Evaluating association of attachment model with risky behaviour and body-esteem will contribute to better understanding of risky choices in older adolescents. Results will be useful for creating adequate intervention programs in college-based settings.

**Acknowledgments:** I would like to thank doctors and nurses from School and adolescent medicine department, Andrija Stampar Teaching Institute of Public Health, for their technical support in conducting the survey and students for participating.

**MeSH/Keywords:** adolescents, risky behaviour, body-esteem, attachment model

**Poster code:** T-C-2-8

## Poster Title: IODINE INTAKE AND THYROID FUNCTION IN LACTATING WOMEN AND BREASTFED INFANTS AT THE REGION OF ZAGREB

**PhD candidate:** Marina Prpić, MD

**Thesis proposal:** Iodine intake and thyroid function in lactating women and breastfed infants at the region of Zagreb

**Mentor/s:** Professor Zvonko Kusić, MD, PhD, Associate Professor Maja Franceschi, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre Sestre Milosrdnice, Zagreb, Croatia

**Introduction:** Iodine is essential for the synthesis of thyroid hormones. Lack of iodine during pregnancy and early childhood can induce thyroid dysfunction and consequently cause permanent damage on growth and disorders in fetal brain development and impaired mental function in young child. Universal salt iodization (USI) is the most effective preventive measure to ensure optimal population iodine status. New law on USI has been introduced in Croatia in 1996 with 25 mg of potassium iodide per kg of salt. Herewith, Croatia successfully solved the problem of iodine deficiency as shown in studies in school children, as shown in nationwide studies in 2002 and 2009.Lactating women and infants are one of the most vulnerable groups that may be affected by the long lasting consequences of iodine deficiency. Finally, iodine deficiency in these population groups is hasn't been investigated yet.

**Hypothesis:** USI that exists in Croatia when is properly applied to all salt, allows optimal iodine intake in lactating women and infants in accordance with the WHO/UNICEF/ICCIDD recommendations.

**Aims:** 1.assess if the of Croatian model of USI can meet physiological dietary requirements of iodine,2.assess thyroid function through determination levels of thyroid hormone, TSH and thyroglobulin in relation to iodine concentration in urine and iodine intake

**Materials and methods:** Participants will be divided into two population groups: 1. lactating women (between 18-44 years) 2.infants (between 2-26 months).Inclusion criteria: 1. for lactating women generally healthy women, without chronical drug therapy and thyroid diseases 2. for infants: born at full-term (in pregnancy week 38-42),birth weight(≥2500g-4200g) and completely breastfed. Methods: 1.Questionnaire for lactating women- to assess the inclusion criteria, history of use of iodized salt in home, consumption of processed foods containing iodized salt and foods rich in native iodine and consumption of iodine containing dietary supplements and specialized food products. Questionnaire for infants - birth data and infant feeding practice. 2.Collection biological samples(blood, urine, breastmilk)in order to assess laboratory levels of thyroid hormones, TSH, thyroglobulin as well as iodine concentration in urine and breast milk.

**Expected scientific contribution:** Results of the study will try to answer on questions whether the model of universal salt iodination is sufficient to allow a sufficient amount of iodine to the target groups-lactating women and infants.

**Acknowledgments:**

**MeSH/Keywords:** iodine, thyroid, iodine deficiency disorders, iodine nutrition

**Poster code:** T-C-2-105

# Poster Title: HEALTH INSPECTORATE AS A TOOL FOR QUALITY IMPROVEMENT IN PUBLIC HEALTH INSTITUTIONS OF PRIMARY HEALTH CARE IN KOSOVO

**PhD candidate:** Ardita Baraku, MD, Spec. Public Health, MSc Public Health

**Thesis proposal:** Health inspectorate as a tool for quality improvement in public health institutions of primary health care in Kosovo

**Mentor/s:** Prof. Gordana Pavlekovic (1), Assoc. Prof. Merita Berisha (2)

**Affiliation:** (1) University of Zagreb, School of Medicine, Croatia, (2) National Institute of Public Health, Prishtina, Kosovo

**Introduction:** Primary health care institutions in Kosovo are legally obliged to implement basic standards of quality of health care (BSQHC), while Health Inspectorate has a mandate to request improve if they are not implemented. There is a need to know if and what is being done right during external supervision, in order to make necessary changes and improve work processes

**Hypothesis:** Health Inspectorate is an efficient tool in implementing basic standards of quality of health care provided by the public institutions of primary health care in Kosovo.

**Aims:** The aim of this research is to analyse if Health Inspectorate of Kosovo is an efficient tool in implementing basic standards of QHC by the PIPHC, by specifically 1) evaluating the compliance level of the PIPHC with the legally set basic standards of QHC, on initial and follow up health inspection, 2)determining the level of improved compliance of the PIPHC with the legally set basic standards of QHC, during follow-up health inspection, and 3)dentifying and comparing factors influencing PIPHC to meet the legally set basic standards of QHC.

**Materials and methods:** Initial and follow up inspections will be conducted, unannounced and check list based, in purposefully selected PIPHC to evaluate the initial situation and the progress upon the provided recommendations. Quality Coordinators from the same institutions will be divided in two groups: experimental and control. Experimental group will be trained to evaluate and ensure the quality in the PIPHC. Qualitative part of the research consists of structured interview with the Coordinators on experiences, motivation, factors and proposals for improve of the system. Quantitative and qualitative data will be analysed in time, by differences of the institutions and by experimental and control group.

**Expected scientific contribution:** This research will assess the impact of Health Inspectorate on improving the quality of health care (QHC). It could add new information to previous researches and, support development of new methods and tools in QHC. In practice, the results could guide the Ministry of Health in taking further actions to increase the QHC, and in increasing the support for the Health Inspectorate to assist this process. This research could be used as a benchmark study for countries in development and transition.

**Acknowledgments:** To my mentor Prof. Gordana Pavlekovic for endless support and motivation to prepare this project

**MeSH/Keywords:** public health care, quality of health care, Health Inspectorate, Kosovo, primary health care

**Poster code:** T-C-2-37

## Poster Title: SENSE OF COHERENCE, HEALTH AND QUALITY OF LIFE IN ADOLESCENTS DURING SECONDARY EDUCATION

**PhD candidate:** Ivica Matić, MSN

**Thesis proposal:** Sense of coherence, health and quality of life in adolescents during secondary education

**Mentor/s:** Professor Vesna Jureša, MD, PhD

**Affiliation:** School of Nursing Mlinarska

**Introduction:** Adolescence is marked by numerous developmental tasks and constant adaptation to stressful situations. One such situation is the beginning of high school that many adolescents successfully overcome, while some experience health problems and a lowered quality of life. The factors that help an individual stay healthy despite challenging situations are explained by salutogenesis based on the sense of coherence, a characteristic which is important in dealing with stressors. Thanks to the life orientation that determines one's perception of events in a logical manner even if the events are out of control, persons with a higher degree of sense of coherence become more resistant to stress. Numerous studies have shown that a strong sense of coherence is a health-promoting factor. However, there are no many studies of adolescents' health and life quality related to the sense of coherence, and the issue of adolescents' adaptation to school context and life in dormitories has not been investigated at all.

**Hypothesis:** Adolescents staying in dormitories have a lower sense of coherence, poorer health and life quality as compared to those living with parents.

**Aims:** To determine a degree of the sense of coherence, subjective health and life quality, and to research their correlation and stability in adolescents staying in dormitories and those staying with their parents during a two-year period.

**Materials and methods:** The research is conceived to be a longitudinal prospective cohort study on a stratified random sample of 400 adolescents divided into two groups according to whether they stay in the dormitories or with their parents. Participants will complete a survey regarding their life orientation, health status and life quality at the beginning of their schooling and during the third grade. Collected data will be processed based on relevant statistical methods. The results will be interpreted at the 5% significance level.

**Expected scientific contribution:** This research expands knowledge in the field of the sense of coherence, health and life quality. The existing studies do not provide information on their relatedness when it comes to the adolescents who live in dormitories. This research proposal contributes to the expansion of new scientific knowledge and it is a step toward the promotion of health because it identifies potentially protective personal health factors in adolescents. Based on this research results, interventions promoting adolescents' health by improving work processes in educational institutions could be planned.

**Acknowledgments:**

**MeSH/Keywords:** adolescence, sense of coherence, health, quality of life

**Poster code:** T-C-2-46

## Poster Title: HOW MANY SPECIALISTS DOES CROATIA REALLY NEED?

**PhD candidate:** Danko Relic, MD

**Thesis proposal:** Development of a model for planning of specialist education of medical doctors in Croatia

**Mentor/s:** Prof. Jadranka Bozikov, PhD

**Affiliation:** University of Zagreb School of Medicine, School of Public Health Andrija Stampar

**Introduction:** Lack of proper policy planning and human resources management in many countries has resulted in an imbalance with multiple effects on employees in health care. Although the determination of the real ratio between the number of health workers and population size has become an aim of national policy on the human resources development in health care, in most cases remains a gap between plans and their realization. Croatia is a country which does not have enough medical doctors and it needs another 2500 to reach the EU average. Croatian Medical Chamber reports that, since Croatiažs accession to the EU, more than 1300 medical doctors were issued certificates confirming their qualifications in order to work abroad. Long term systematic planning is absent at both, the total number of medical doctors and at the level of individual specialties.

**Hypothesis:** Gap between supply and the needs for medical doctors of various specialties by 2035 can be corrected by using simulation models with previously known parameters further exploits and those that will be potentially significant new parameters while trying to create a model.

**Aims:** To develop a model for simulation of the needed number of specialists of different specialties in the Republic of Croatia by the year 2035 based on the expected changes in size and age structure of population and experts' estimates of the needs.

**Materials and methods:** The model will be implemented in the form of a computer program based on the estimated most potent predictors. The developed model will be used as a tool for the simulation of different schemes for specialist education along with different scenarios of specialists' migration flows in order to compare different possibilities and options for the renewal of the Croatian healthcare personnel.

**Expected scientific contribution:** Results will enable the development of recommendations for the adoption of a rational plan of referral to specialist training. Indirectly, developed model will be useful for needs assessment and simulation and planning of workforce renewal of other health professionals and for other countries.

**Acknowledgments:**

**MeSH/Keywords:** medical doctors, modelling, specialisations, needs and demands for medical specialists

**Poster code:** T-C-2-127

# 3. LIST OF CANDIDATES

# List of Candidates and Abstract Titles

| PhD Candidate | Poster Title | Page |
|---|---|---|
| Blažeković, Antonela | GENETIC MECHANISMS OF LYSOSOMAL DYSFUNCTION IN PARKINSON'S DISEASE | 15 |
| Bogdanović Dvorščak, Matea | THE EFFECT OF INTRAOPERATIVE APPLICATION OF MANNITOL IN HEMODYNAMICALLY UNSTABLE RECIPIENTS ON THE DEGREE OF POSTREPERFUSION HEMODYNAMIC INSTABILITY AND GRAFT´S ISCHEMIA-REPERFUSION INJURY DURING LIVER TRANSPLANTATION | 125 |
| Bojanić, Katarina | SURVIVAL PREDICTION OF HIGH-RISK OUTBORN NEONATES WITH CONGENITAL DIAPHRAGMATIC HERNIA FROM CAPILLARY BLOOD GASES | 79 |
| Bolanča, Ivan | SONOGRAPHY-BASED AUTOMATED VOLUME COUNT FOLLICLE (SONOAVC) METHOD FOR PREDICTION OF OOCYTE YIELD IN A STIMULATED OVARIAN CYCLE | 127 |
| Bujan Kovač, Andreja | THE SIGNIFICANCE OF THE POSTPROCESSING BRAIN MRI (MAGNETIC RESONANCE IMAGING) IN THE PREOPERATIVE DIAGNOSIS OF PATIENTS WITH PHARMACORESISTANT EPILEPSY | 92 |
| Crnošija, Luka | CORRELATION OF THE VEMP SCORE, AMBULATION AND UPPER EXTREMITY FUNCTION IN CLINICALLY ISOLATED SYNDROME | 91 |
| Čalušić, Martina | PERIOPERATIVE MULTIMODAL MANAGEMENT AND OXIDATIVE STRESS IN LAPAROSCOPIC CHOLECYSTECTOMY | 124 |
| Čaržavec, Dubravka | ACOUSTIC FEATURES OF VOICE ANALYSIS FOR ASSESSMENT OF FATIGUE IN PATIENTS WITH MYELOFYBROSIS | 64 |
| Čulav Košćak, Ivana | ASSOCIATION OF THE CLINICAL PRESENTATION AND VIRAL GENOTYPES IN GENITAL INFECTIONS WITH HUMAN PAPILLOMAVIRUS IN MEN | 126 |
| Davidović, Maša | GENETIC AND ENVIROMENTAL FACTORS IN CONGENITAL HEART DISEASE DEVELOPMENT | 80 |
| Dediol, Iva | ITCHY AND PAINFUL DERMATOSES CARRY THE HIGHEST PSYCHOLOGICAL BURDEN AMONG DERMATOVENEROLOGICAL PATIENTS | 36 |
| Dembitz, Vilma | THE ROLE OF AUTOPHAGY IN DIFFERENTIATION AND SURVIVAL OF LEUKEMIA CELL LINES | 13 |
| Djaković, Ivka | CERVICAL ELASTOGRAPHY IN TERM PREGNANCIES | 132 |
| Dominko, Kristina | THE ROLE OF ALTERED CHOLESTEROL METABOLISM ON RETROMER (DYS)FUNCTION IN NEURODEGENERATIVE DISORDERS | 19 |
| Dragičević, Maro | THE ROLE OF MARKERS OF ENDOTHELIAL DYSFUNCTION: ASYMMETRIC DIMETHYLARGININE AND NITRIC OXIDE IN THE ASSESSMENT OF CARDIOVASCULAR RISK AFTER LIVER TRANSPLANTATION – PRELIMINARY RESULTS | 55 |
| Drvar, Željko | PULMONARY VASCULAR PERMEABILITY INDEX AND EXTRAVASCULAR LUNG WATER IN PATIENTS WITH SEPSIS SYNDROME | 31 |
| Dumić Čule, Ivo | EFFECTS OF BONE MORPHOGENETIC PROTEIN 2 AND 7 ON BONE METABOLISM IN RATS WITH REMOVED THYROID AND PARATHYROID GLANDS | 5 |
| Đuran, Nataša | GROUP SUPPORTIVE PSYCHOTHERAPY EFFICACY IN TREATMENT OF SCHIZOPHRENIA | 86 |
| Ejubović, Emina | THE INFLUENCE OF PREOVULATORY AND POSTOVULATORY PROGESTERONE SERUM CONCENTRATION ON THE OUTCOME OF THE IN VITRO FERTILIZATION | 129 |
| Ercegović, Nela | IDENTITY IMPAIRMENTS IN ADOLESCENTS WITH NON-SUICIDAL SELF-INJURY BEHAVIOR AND SUICIDAL ATTEMPTS | 169 |
| Fila, Branko | VEIN DIAMETER AFTER INTRAOPERATIVE DILATATION WITH VESSEL PROBES AS A PREDICTOR OF SUCCESS OF HEMODIALYSIS ARTERIOVENOUS FISTULAS | 65 |
| Flegar, Darja | INDUCTION OF JOINT-ASSOCIATED MYELOID LINEAGE CELLS BY CHRONIC INFLAMMATION IN COLLAGEN INDUCED ARTHRITIS | 17 |

| PhD Candidate | Poster Title | Page |
|---|---|---|
| Jandroković, Ivana | COULD ABNORMAL GENERAL MOVEMENTS IN INFANCY INDICATE LATER NONMOTOR DISORDERS? | 114 |
| Jeličić, Pavle | PREVALENCE AND RISK FACTORS OF HEPATITIS E IN CROATIA | 176 |
| Jerković Gulin, Sandra | BIOLOGICAL PROPERTIES OF T-CELL LYMPHOMA (Mycosis fungoides) IN CORRELATION WITH THE CLINICAL PICTURE, STAGE AND PATIENT OUTCOME IN CROATIA – TEN-YEAR FOLLOW-UP | 35 |
| Jurić, Dunja | THE ROLE OF PSYCHOSOCIAL FACTORS IN OUTCOMES OF IN VITRO FERTILIZATION METHODS | 168 |
| Karadža, Vjekoslav | ASSESSMENT OF BODE INDEX AS INDICATOR OF CARDIORESPIRATORY FUNCTION IN LUNG RESECTION FOR BRONCHIAL CARCINOMA | 145 |
| Karanović, Boris | ASSOCIATION BETWEEN ACE GENE POLYMORPHISMS AND SEVERITY OF SYSTEMIC SCLEROSIS | 68 |
| Kardum, Vedran | WNT PATHWAY IN OVARIAN CANCER | 128 |
| Kašnik, Katarina | EFFECT OF PENTADECAPEPTIDE BPC 157 ON COLLATERAL CIRCULATION IN ACUTE OBSTRUCTION OF THE ABDOMINAL AORTA | 103 |
| Katalinić, Lea | EXPRESSION OF WNT4, FGF23 AND KLOTHO PROTEIN IN THE WALL OF INFERIOR EPIGASTRIC ARTERY OF PATIENTS WITH END-STAGE RENAL DISEASE | 141 |
| Kekin, Ivana | THE RELATIONSHIP BETWEEN NEUROCOGNITIVE STATUS AND PSYCHOPATHOLOGY, TREATMENT RESPONSE AND VARIANTS OF GENES MTHFR AND ZNF804A IN PATIENTS WITH THE FIRST PSYCHOTIC EPISODE | 84 |
| Kelava, Iva | WIDEBAND TYMPANOMETRY IN OTOSCLEROTIC EARS | 160 |
| Knežević, Mario | LIGATION OF SUPERIOR MESENTERIC ARTERY AND VEIN IN RAT: STABLE GASTRIC PENTADECAPEPTIDE BPC157 BENEFICIAL EFFECT | 104 |
| Kontić, Maša | ALVEOLAR MANOEUVRE PROCEDURE AND USAGE OF END-EXPIRATORY PRESSURE DURING GENERAL ENDOTRACHEAL ANAESTHESIA | 123 |
| Kos, Jelena | BIOMARKERS OF PROXIMAL TUBULE INJURY IN ENDEMIC NEPHROPATHY | 44 |
| Koshi, Rreze | COMPARISON OF CLINICAL CHARACTERISTICS AND OUTCOMES IN PATIENTS WITH ST-ELEVATION MYOCARDIAL INFRACTION IN KOSOVO AND CROATIA | 49 |
| Kovač Bilić, Lana | METHYLATION LEVEL OF ASC/TMS1 AND MyD88 GENES IN HEALTHY LARYNX AND LARYNGEAL SQUAMOUS CARCINOMA | 107 |
| Kovačević, Vinka | HISTOLOGICAL, MRI AND TRANSCRIIPTOME ANALYSIS OF THE REORGANIZATIONAL PROCESSES IN THE DEVELOPING HUMAN HIPPOCAMPUS | 115 |
| Kovačević, Maja | ASSOCIATION OF SERUM CONCENTRATIONS OF INTERLEUKINS IL-18, IL-19, IL-21 AND IL-22 WITH THE ETIOPATHOGENESIS AND ASSESSMENT OF CLINICAL ACTIVITY OF NONSEGMENTAL FORM OF VITILIGO | 37 |
| Kralj, Tamara | THE EFFECT OF PENTADECAPEPTIDE BPC 157 ON EPISCLERAL VEIN CAUTERIZATION MODEL IN RATS | 105 |
| Kraljičković, Iva | PROLONGED VERSUS STANDARD INFUSION OF PIPERACILLIN/TAZOBACTAM – A PROSPECTIVE, RANDOMIZED, CONTROLLED STUDY IN CLINICAL HOSPITAL CENTRE ZAGREB | 150 |
| Krasniqi, Xhevdet | PREDICTION OF MAJOR ADVERSE CARDIAC EVENTS BY APELIN LEVEL FOLLOWING ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION | 47 |
| Krečak, Ivan | CLINICAL SIGNIFICANCE OF YKL-40 AND CHITOTRIOSIDASE IN PATIENTS WITH PHILADELPHIA-NEGATIVE CHRONIC MYELOPROLIFERATIVE NEOPLASMS | 138 |

| PhD Candidate | Poster Title | Page |
|---|---|---|
| Kruljac, Ivan | INCIDENCE OF DIABETIC KETOSIS AND KETOACIDOSIS IN PATIENTS WITH CLINICAL FEATURES OF TYPE 2 DIABETES MELLITUS | 63 |
| Kryeziu, Kaltrina | MASSETER AND TEMPORALIS MUSCLES ACTIVITY IN MANDIBULAR CONDYLE AND ANGLE FRACTURES | 146 |
| Kurtović, Biljana | OPIOID DERIVATES ANALGESIA AND NONOPIOID ANALGESIA ASSESSMENT THROUGH INTERMITTENT APPLICATION AND PATIENT CONTROLLED ANALGESIA PUMP AFTER LUMBAR DISCECTOMY | 172 |
| Lončar, Andrija | ACUTE CHANGES OF BRAIN ACETYLCHOLINESTERASE ACTIVITY IN THE MOUSE AND RAT MODEL OF SPORADIC ALZHEIMER'S DISEASE | 12 |
| Lulić, Fabijan | A NEW METHOD FOR PARAMETER IDENTIFICATION IN A LUMPED MODEL OF PULMONARY CIRCULATION | 144 |
| Ljevak, Josip | ROLE OF GENETIC POLYMORPHISM OF ENDOTHELIAL NITRIC OXIDE SYNTHASE IN THE ASSESMENT OF RISK OF INTRACRANIAL ANEURYSM GROWTH AND RUTPURE | 170 |
| Majić, Višnja | DEVELOPMENT OF THE STRUCTURAL BASIS OF THE SOMATOSENSORY THALAMOCORTICAL SYSTEM IN THE HUMAN FETAL BRAIN: CYTOARCHITECTONIC AND MOLECULAR MARKERS | 111 |
| Mance, Marko | SPORT INJURIES, TREATMENT METHODS, RECOVERY PREDICTORS AND OVERALL SATISFACTION AMONG PROFESSIONAL ICE HOCKEY PLAYERS: A 6 YEAR RETROSPECTIVE – PROSPECTIVE STUDY | 39 |
| Mandić, Krešimir | ATROPHY PROGRESSION OF ELLIPSOID ZONE IN DRY FORM OF AGE RELATED MACULAR DEGENERATION | 69 |
| Marković, Ivan | CONTINUOUS SYSTEMIC INFLAMMATION AND ARTERIAL DYSFUNCTION IN RHEUMATOID ARTHRITIS | 142 |
| Matić, Ivica | SENSE OF COHERENCE, HEALTH AND QUALITY OF LIFE IN ADOLESCENTS DURING SECONDARY EDUCATION | 181 |
| Matković, Zinka | EVALUATION OF NUTRITIONAL STATUS AND PHYSICAL PERFORMANCE IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE | 58 |
| Miklić Bublić, Martina | COMPARISON OF ROCURONIUM ADMINISTRED IN MULTIPLE SEPARATE DOSES WITH ROCURONIUM GIVEN IN CONTINUOUS INFUSION ON INTRAOPERATIVE CONDITIONS AND THE QUALITY OF RECOVERY AFTER GENERAL ANESTHESIA FOR LUMBAL DISCECTOMY | 121 |
| Mioč, Marina | OBSTRUCTIVE SLEEP APNEA SYNDROME AND AUTONOMIC NERVOUS SYSTEM | 90 |
| Miovski, Zoran | CORRELATION OF ESTROGEN RECEPTOR ALFA AND INTERLEUKIN 6 POLYMORPHISM WITH ENDOTHELIAL FUNCTION IN ASYMTOMATIC DESCENDANTS OF PATIENTS WITH EARLY CORONARY DISEASE AND ACUTE CORONARY SYNDROME – EARLY RESULTS | 51 |
| Mrazovac, Danijela | RETINAL NERVE FIBER LAYER CHANGES IN PATIENTS WITH CHRONIC OPTIC NEURITIS | 70 |
| Muhaxhiri, Fatos | COMPARISON BETWEEN GnRH AGONIST VERSUS hCG AS OVULATION TRIGGER IN THE MILD STIMULATED IVF CYCLES | 40 |
| Murgić, Jure | MRI IN PROSTATE HIGH-DOSE-RATE BRACHYTHERAPY | 155 |
| Nikić, Ines | EFFECT OF BODY POSITION ON CEREBROSPINAL FLUID VOLUME IN CRANIAL AND SPINAL COMPARTMENTS | 116 |
| Ostojić, Vedran | INCREASED SPECIFIC IMMUNOGLOBULIN G4 ANTIBODIES INDUCED BY NATURAL EXPOSURE TO AMBROSIA POLLEN IN PATIENTS WITH ALLERGY | 16 |
| Pajtak, Alen | THE ROLE OF PENTADECAPEPTIDE BPC 157 ON INCISIONAL VENTRAL HERNIA PREVENTION AND WOUND TENSILE STRENGTH IMPACT | 6 |