

Macromolecular Crowding: Effect of high concentration of macromolecules on conformational states of proteins

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Macromolecular crowding occurs in case of high concentrations of macromolecules such as proteins (e.g. 300-400 mg/ml in *E. coli*) in the cytosol. Since these macromolecules influence the effective concentration of other molecules, they also modulate the function of enzymes and the cell metabolism. The conformational stability of proteins is also influenced by the crowded environment through the excluded volume effect. Since pressure and volume are conjugate thermodynamic variables, use of high pressure in the experiments is advantageous to reveal volume effects. Crowding circumstances are mimicked in vitro mostly by high concentrations of crowding agents like Ficoll and Dextran.

Methods: For this study Ficoll (a neutral highly branched hydrophilic polysaccharide with average molar weight of 70 kDa) was used as crowding agent, bovine serum albumin (BSA) and lysozyme as test proteins. Ficoll concentration was varied from 0 to 30%, (w/w) while the concentration of the protein was between 5 and 7 % (w/w). Self-crowding was studied using solutions with high test protein concentration (up to 25 %).

Fourier Transform Infrared (FTIR) spectroscopy was used to follow the conformation of the test protein. We analyzed the absorption bands of amide vibrations, which are sensitive to the secondary structure. By varying the pressure and temperature, we measured how the crowding condition affects the stability against heat- and pressure denaturation.

Results: From the analysis of the IR-spectroscopic data, it is shown, that concentrations of crowding agents higher than 15% have a stabilizing effect on backbone conformation of proteins. This stability of the secondary structure can be explained by the fact, that an unfolded protein needs higher excluded volume which is counteracted by the presence of the crowding agent.

Surprisingly however moderate crowding agent concentrations (below 15%) destabilize BSA against pressure unfolding. Similar effect was found in case of lysozyme. This can be explained by the effect of molecular crowding on the hydration layer at the surface of the protein. This is an important point, because the hydration layer plays an important role in the function of the proteins. Consequently macromolecular crowding is not an insignificant factor for the maintaining of the biological active state of enzymes.

none

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Application and significance of thermoregulation devices during intraoperative period

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During operation patients temperature can variate and it affects vital signs. Wide known that hypothermia can occur in operation time and in other surgical manipulations if the thermoregulation is not controlled, and that can lead down to other serious health problems. The changes of vital signs, that can occur through unstable thermoregulation can affect the operation process. That is why scrub nurse need to know the type, length of the operation and if there will be used the necessary thermoregulation devices. The base monitoring for patient observation through the operation are – electro-kardiography, the monitoring of hemodynamic and the monitoring of respiratory system. As an additional monitoring to control the status of patient through the anesthesia is thermometry, also called the measurement of patient body temperature. Thermometry is a type of monitoring that has no contraindications.

The aim of the research was to determine the use and meaning of thermoregulation devices intraoperative. In research used methods were the analysis of literature, qualitative research methods, and the research instruments were structured interview and observation protocol.

Of 43 observation protocols, the thermoregulation device is not used in 14 cases, but in 12 cases are used foley blankets, 12 cases an usual blanket and in 5 cases a device with forced air. Operations which are about 4 to 5 hours, and where the thermoregulation device is a usual blanket, in 3 from 12 cases are mentioned, that after operation the patient was shivering. 14 from 43 observations the thermoregulation device is not used, but there is a possibility to use it in operations. All 15 respondents tells, that patient monitoring intraoperative is necessary or very necessary, because the status of patient is controlled. The feeling for patient, if there is used a thermoregulation device, is better and the patient feels also comfortable, that is the meaning of all interviewed nurses.

There are no publications yet.

Supervisor(s): Liva Zdora assistant lecturer, Department of Public Health

Tissue testicular inhibin-B as A marker of spermatogenesis

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Inhibin B is one of the most important serum markers of spermatogenesis, but its testicular expression has been studied to a relatively low extent. Moreover, its sensitivity as well as our ability to forecast the level of its intensity in spermatogenesis of young males are still subject to discussion too. Aims of research: defining the role of Inhibin B in normal spermatogenesis, in case of Sertoli cell-only syndrome and in case of focal spermatogenesis (nonobstructive azoospermia). Methods: we have conducted tests on 82 males diagnosed with infertility, nonobstructive azoospermia. Furthermore, the influence of Inhibin on the germ cells of men aged 22-35 (n=10) has been analyzed using the Immunohistochemical method. The results are as follows: high expression of Inhibin can be detected both in Sertoli (98.0±2.66%) and Leydig (94.0±1.55%) cells in comparison with the men of the same age in the control group (65.9±0.44% and 12.0±0.44% respectively) when a patient suffers from focal damages of spermatogenesis (mixed atrophy); the level of Inhibin expression in spermatogonia in control group is 4.0±0.22%, whereas in cases of azoospermia it can be characterized by a substantial increase and equals 45.0±0.44%. Conclusions: through analysis of this data has proved that accumulation of Inhibin by Sertoli and Leydig cells takes place, which eliminates its compensatory effect on germ cells according to the principle of inverse relationship. The level of Inhibin expression depends on variants of the Sertoli cell-only syndrome are identified by Sertoli cell morphology, the degree of development of the seminiferous tubules, and the presence or absence of peritubular or interstitial lesions (alterations). That is why levels of tissue Inhibin expression can be used as differential diagnostic markers of azoospermia with other forms of infertility.

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2. G. Demyashkin. Morphological analysis of spermatogenesis – the basis of diagnosis of idiopathic nonobstructive azoospermia (immunohistochemical aspect)// 23rd Meeting of the EAU Section of Urological Research. – October 2016. – Parma, Italy – collected abstracts on CD.

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Prospects of poly(vinyl)alcohol scaffolds in abdominal hernia treatment. a study of mechanical properties

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Hernia is defined as protrusion or expulsion of an organ through the cavity it normally resides. Abdominal hernia is the exit of any part of the gastrointestinal tract through the abdominal cavity due a defect in the abdominal muscular wall. Current first choice treatment involves implantation of a surgical mesh, in order to close the defect and strengthen the surrounding abdominal musculature. Biomaterial science has evolved in recent years yet, currently applied surgical meshes are still accompanied with disadvantages and more common than expected complications including, mesh migration, tissue adhesion, infection and foreign body reactions.

A potential replacement of such surgical meshes is poly(vinyl)alcohol. Electrospinning is one of the techniques applied in nanotechnology used for scaffold production and tissue engineering. Furthermore PVA is a biocompatible polymer thus nanofabricated meshes produced by electrospinning, should be biocompatible. Our objective is assessing the mechanical properties of a PVA mesh as a viable implantable scaffold. Mechanical strength is essential as meshes should withstand the intra-abdominal pressure and muscle tension intrinsically created by the body.

PVA scaffolds were produced via electrospinning of 9 w% PVA and 1 M GDA solutions. Post electrospinning processing included folding, compression and cross linkage formation via scaffold immersion in 2 M HCl. After washing with ultrapure water, samples were stored in PBS while incubated at 37 OC. Two types of samples(4.5x3.5cm) were prepared, single interrupted and simple running sutured to realistically recreate surgical procedures. Polypropylene mesh samples with the same parameters were prepared serving as control measurements. Assessment of mechanical properties was performed by an Instron 5942. Samples were pulled to a maximal load of 5 N at a speed of 1 mm/s. Different measuring profiles were created examining strength, endurance and elasticity of the samples. Measurements were performed both on air and under liquid.

The samples showed gel-rubber like hybrid properties, withstanding the maximum load of 5N with minimal defects only around the suture material. Results reinforced PVA as a viable candidate for new surgical meshes showing its excellent mechanical properties with our current equipment unable to produce force high enough to tear the prepared samples.

The research group has not published an article on the topic yet.

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Topographical allocation of slow-wave activity on eeg in children. Age features

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Introduction. The paper represents activity allocation analysis of theta oscillations in occipital, central and frontal cerebral cortex in children of different age. We attempted to justify possible physiological mechanisms underlying dynamics of spectral power changes of alpha and theta range in occipital cerebral cortex in ontogenesis in children.

Material and methods. To record electrical activity electroencephalograph Neuron-Spector 4/P has been used ("Neurosoft", Taganrog, Russia). Electrodes were applied according to standard international "10-20" electrode system. We evaluated spectral power index of theta activity (SPI Θ) in central and frontal cerebral cortex of right (N4F4; F4Fp2) and left (N3F3; F3Fp1) hemispheres, as an index of morpho-functional maturity of thalamocortical correlation we appealed to index of spectral power relations (ISPR) of alpha and theta activity ISPR = ISPR α /ISPR Θ in occipital cerebral cortex.

Statistical analysis was carried out using the statistical software package STATISTICA 10.0. The children have been divided into three age groups according to the age periodization of Vygotsky L.C.: age 4 – 7 (20 children), age 8 – 12 (21 children), age 13 – 16 (21 children). The hypothesis of the equality of medians in two age groups has been checked with the help of Mann-Whitney U-test with 0,05 significance level.

Results. Statistically significant zone differences SPI Θ were determined in age groups 4–7 and 8–12 ($p < 0,01$): theta range oscillations dominate in occipital cerebral cortex. By the age of 13 – 16 SPI Θ significantly decreases both in occipital and frontal cerebral cortex ($p < 0,01$).

Conclusion and discussion. Children aged 4–7 and 8–12 have ISPR 0,7–1,2 in left hemisphere and 0,8–1,3 in right hemisphere. ISPR increase in occipital cortex in left hemisphere till 3, and in right hemisphere till 2,6 at the age of 13-16, it may indicate morphofunctional maturity of thalamocortical relations.

Sinelnikova A.N., Goldaeva A.A., Torshin D.V., Nikiforova A.E. The estimation of index spectral power of brain theta activity in occipital cerebral cortex in children. Technologies of Living Systems, 2016, vol. 13, no. 2.

Nikiforova A.E., Sinelnikova A.N. The estimation of alpha and theta activity index correlation in occipital lobe in children. VII International Conference SCIENCE4HEALTH. Moscow, 2016.

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Markers of apoptosis and proliferation in male infertility

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Background. Balance of proliferative activity and apoptosis of male gametes is important part in pathogenesis of male infertility. Here we defined indicators of some informative markers of apoptosis and proliferation (Ki-67, p53, Bcl-2 and caspases) of gametes and somatic cells in patients with non-obstructive azoospermia. In addition, we defined possible role of Sertoli cells in activation of gametes' apoptosis in Sertoli cell-only syndrome and its variants.

Methods. We have conducted tests on males diagnosed with infertility, non-obstructive azoospermia ($n=50$) and of normal men aged 22-35 ($n=10$) and 64-75 ($n=10$) using the immunohistochemical method with mouse monoclonal antibodies: Ki-67, p53, Bcl-2, caspase-9 («Leica Biosystems Newcastle Ltd», United Kingdom).

Results. In the control group, Ki-67 expression in spermatogonia nuclei was $42.0 \pm 0.34\%$ ($p < 0.05$), while apoptosis marker caspase-9 – 25.2 ± 0.44 ($p < 0.05$). On other hand, in study group (men with idiopathic azoospermia) figures of Ki-67 expression ($12.0 \pm 0.34\%$ ($p < 0.05$)), p-53 ($40.0 \pm 0.44\%$ ($p < 0.05$)) of Bcl-2 ($1.0 \pm 0.1\%$ ($p < 0.05$)) and apoptosis index ($13.0 \pm 0.22\%$ ($p < 0.05$)) indicate a predominance of death processes of gametes over their proliferation.

Conclusion. Activity of cell immunostaining on Ki-67, p53, Bcl-2 and caspase-9 in sperm cell line normally decreases in ontogenesis and indicates that during testicle aging there is no inverse relationship between activity of proliferation processes and apoptosis. Figures of p53 and Bcl-2 indicate on domination of apoptosis in seminiferous tubules of patients with unexplained infertility. Reducing the amount of immunoreactive spermatogonia does not correspond to the level of serum follicle stimulating hormone (FSH). These data show that the reduction of spermatogonia meiotic activity in infertile men is not associated with serum FSH levels.

G. Demyashkin. Morphological analysis of spermatogenesis – the basis of diagnosis of male idiopathic infertility // International Conference and Exhibition on Cytology & Histology. August 2016. Birmingham, the UK of GB and Northern Ireland.

G. Demyashkin. Morphological analysis of spermatogenesis – the basis of diagnosis of idiopathic non-obstructive azoospermia // 23rd Meeting of the EAU Section of Urological Research. October 2016. Parma, Italy.

Supervisor(s): Gregory Demyashkin senior research fellow, Department of Pathology

Molecular evolution of CCL2 chemokines – investigations of chemotactic ability of 47R, 72K and 89H pentapeptide libraries in tetrahymena

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Coevolution of chemokines and their receptors is a significant characteristic of signaling networks in chemotaxis of vertebrates. Comparison of receptor-ligand interactions in CCR-CCL and CXCR-CXCL chemokines proved a high level promiscuity in respect of ligands e.g. CCR1, CCR2 and CCR3 receptors; which is based on a varying level of homologies. Human CCR2 has a more complex crossreactivity as the same CCR2 is inducible with different ligands depending on the target cell. In our previous work we proved that fMLF and FPR have an adaptive evolution in mammals which is based on positively selected amino acids.

Objectives: (i) to evaluate contribution of phylogenetically conserved domains of CCL2 to the chemoattractant moiety of the ligand; (ii) to evaluate the GAG-binding domain (89H) chemotactic property; (iii) to measure the chemotactic ability of the penta- and nonapeptide libraries (47R, 72K, 89H); to compare their effects to the intact CCL2 chemokine (MCP-1).

CCL2 peptide evolution (positive selection) was investigated by Codeml – PAML package. The well conserved amino acid residues (47R, 72K, 89H) were determined on the basis of calculation in 34 vertebrate species. Each library was synthesized as sets of overlapping pentapeptide motives (scanned length 9 amino acids). The tested concentrations were 10^{-12} – 10^{-6} M. *Tetrahymena pyriformis* (chemotactic model cell) GL cultures were grown in 1% Bactotryptone. Chemotactic responses of cells were measured with capillary assay/ impedimetry.

Results: (i) The pentapeptide reading-frame scanning of CCL2 domains resulted only partial activation of CCR2 (chemoattractant sequences: 47R – VQRLA; 72K – VAKEL, AKEIC, KEICA); (ii) reduced activity is supposed as a result of a longer or more adequate 3D structure (47R nonapeptide); however, in other domain the elongation resulted loss of activity (72K penta and nonapeptides). (iii) Neutral moiety of the only GAG-binding 89H domain in the penta- and nonapeptides points to the significance of this domain as a non-signaling but ligand attachment promoting part of CCL2. (iv) Comparison of chemotactic ability of CCL2 (MCP-1) and the penta- and nonapeptide libraries showed that the intact chemokine represents the optimal structure of conserved and non-conserved domains with a surpassing chemotactic activity (CCL2-195% vs. KEICA-160%).

Toshiaki Umemura László Kőhidai. Adaptive Evolution of Formyl Peptide Receptors in Mammals - Yoshinori Muto Stéphane Guindon. Hiroshi Ueda ; DOI 10.1007/s00239-015-9666-z

Supervisor(s): Dr. Kőhidai, László associate professor, Department of Genetics, Cell- and Immunobiology, Dr. Láng, Orsolya assistant professor Department of Genetics, Cell- and Immunobiology

Correlations between virus copy number, infectious titer and multiplicity of infection of Ebola virus Makona-C05 in Vero E6 cells

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Keywords: Ebola virus, Makona C-05 isolate, virus copy number, infectious titer, multiplicity of infection

Background: Ebola virus Makona variant is a member of the Zaire species of the Filoviridae family in the order of Mononegavirales. This virus was responsible for the Ebola disease outbreak in West Africa, in 2013-2016.

Aims: During our study we aimed to discover the correlation between virus copy number and infectious titer in case of Ebola virus Makona-C05 in Vero E6 cells. Furthermore, we wanted to find out which value of multiplicity of infection (MOI) is suitable for the infection and which day post infection is ideal for collecting the supernatant in order to obtain the highest infectious titer for further investigation of the virus.

Materials and methods: During the study, Vero E6 cell line and Ebola virus Makona C-05 isolate were used. The cells were infected with the virus using the MOI values 2.0, 0.2, 0.02, and aliquots of the supernatant were collected every day until day 10. We determined the infectious titer of the supernatants using fluorescent focus unit (FFU) assay and the virus copy number using real time PCR for Ebola virus. The titer of the mice sera used for the FFU test was determined by indirect immunofluorescence method.

Results: The number of the infectious and non-infectious viruses were proven to be similar for the three values of MOI: they showed increasing tendency until days 5-7. However, after day 7 to day 10, the infectious titer decreased with 1 log₁₀, while the copy number increased further. The infectious titer was the highest for the MOI value of 0.2. The sera of the mice could be used in dilutions of 1:40, 1:80 and 1:320.

Conclusions: It is advised to collect the supernatant on days 5-6. The MOI value of 0.2 gave the highest infectious titer, thus this value is ideal for the infection.

Analysis of Diagnostic Findings From the European Mobile Laboratory in Guéckédou, Guinea, March 2014 Through March 2015. Kerber et al, JID. 2016; Unique human immune signature of Ebola virus disease in Guinea. Ruibal et al, Nature 2016; Temporal and spatial analysis of the 2014-2015 Ebola virus outbreak in West Africa. Carroll et al, Nature. 2015; Field Evaluation of Capillary Blood Samples as a Collection Specimen for the Rapid Diagnosis of Ebola Virus Infection During an Outbreak Emergency. Strecker et al

Supervisor(s): Bernadett Pályi research fellow, National Center for Epidemiology - National Biosafety Laboratory, Budapest, Dr. Zoltán Kis research fellow National Center for Epidemiology - National Biosafety Laboratory, Budapest

Speckle-tracking echocardiography reflects both the effects of exercise training and detraining in a rat model of athlete's heart

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Recently our working group provided detailed morphologic and hemodynamic characterization on exercise-induced cardiac hypertrophy in a rat model, confirming increased contractility. In the current study we aimed to assess whether strain parameters by speckle-tracking echocardiography (STE) are able to describe the effects of training and detraining on left ventricular (LV) function. Rats were divided into trained (n=12) and control (n=12) groups. Trained rats swam 200 min/day for 12 weeks, while control rats swam 5 min/day. Trained rats remained sedentary for 8 weeks after completion of the training protocol. Echocardiography was performed at baseline, 12 and 20 weeks using a 13MHz linear transducer to obtain LV long- and short-axis recordings for STE analysis (EchoPAC). Global longitudinal and circumferential strain (GLS, GCS) and systolic strain rate (LSr, CSr) were measured. After the detraining period, LV pressure-volume analysis was performed to calculate load-independent contractility indices (i.e. slope of the end-systolic pressure-volume relationship [ESPVR]). Echocardiographic examinations showed the development of LV hypertrophy in the trained group according to wall thickness values (trained vs. control; LV mass index: 2.41 ± 0.09 vs 2.03 ± 0.08 g/kg, $p < 0.05$). This difference disappeared after detraining (2.26 ± 0.07 vs 2.40 ± 0.10 g/kg, NS), which was confirmed by post-mortem measured heart weight and histological morphometry. GCS, CSr and LSr were all increased after the training period (GCS: -19.1 ± 1.0 vs $-14.7 \pm 0.7\%$; CSr: -5.6 ± 0.3 vs -4.0 ± 0.3 ; LSr: -4.6 ± 0.2 vs -3.9 ± 0.2 Hz, all $p < 0.05$), whereas supernormal values reversed to the control level after detraining. ESPVR did not differ between the groups confirming the regression in LV function (1.82 ± 0.10 vs 1.76 ± 0.21 mmHg/ μ L, NS). Our results confirm that the morphological and functional properties of exercise-induced LV hypertrophy completely regressed after an eight week detraining period. Both changes induced by exercise training and effects of detraining reflected by the strain and strain rate parameters of STE, allowing a consecutive evaluation of LV function in rat models.

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Translocatome: a novel tool for the functional analysis of protein translocation between cellular organelles

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Localization of proteins in subcellular compartments has a key role in cellular regulation and function. In eukaryotic cells, organelles are well distinguished components with different microenvironments and specific molecular interactions. Translocation is considered as a process when functionally active proteins change their subcellular localization in a regulated manner. Although, how e.g. transcription factors translocate from the cytoplasm to the nucleus resulting in an alteration in cellular behaviour is well known, systematic analysis of this phenomenon is still missing.

During our research, we have gathered detailed information for more than 100 human translocating proteins by manual curation of related articles. We have developed a database that contains relevant localization, structural and regulation related properties of the proteins. We have named this database Translocatome, which is planned to be accessible through a user-friendly web application.

The Translocatome server communicates with our in-house developed ComPPI database (<http://compbi.linkgroup.hu>), from where interaction data for more than 13000 proteins have been imported. This data is used to create a protein-protein interaction (PPI) network that enables us to predict the probability of protein translocation with a machine learning algorithm. Further properties (such as information on biological processes from GO [<http://geneontology.org>]) are annotated for more precise predictions. Utilizing this data the algorithm is able to adjust translocation probability scores to the proteins based on the identified differences between a positive (translocating) and a negative (not translocating) training set. The predictions can be validated by manual curation or using experimental techniques.

Translocatome is a novel tool for the systematic analysis of the protein translocation process that helps to understand the role of this phenomenon in the development of certain diseases. Glioblastoma Multiforme (GBM) is a tumor with an exceptionally bad prognosis and certain protein translocations have a key role in pathogenesis. We attempt to further investigate the translocating proteins by dynamic network simulations on a GBM-specific cell model and to find possible connections between the proteins and the malignancy of the disease. With the help of our results new drug targets could be discovered.

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Supervisor(s): Prof. Péter Csermely professor, Department of Medical Chemistry, Molecular Biology and Pathobiochemistry, Dr. Dániel Veres PhD Student Department of Medical Chemistry, Molecular Biology and Pathobiochemistry

Altered complexity in eeg dynamics during cognitive challenge revealed by multifractal analysis

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Introduction. It has been shown that the brain — even at rest — exhibits a high neuronal activity, which fluctuates in a complex, scale-free (i.e. fractal) pattern that traditional EEG-analysis cannot capture. These dynamics are known as essential for higher brain functions such as cognition. Here we present a multifractal analysis of EEG to describe the complex neurodynamics elicited by cognitive challenge and to demonstrate gender-related differences.

Methods. 12 healthy students (6 ♀ & 6 ♂) volunteered in the study. Signals were recorded over 14 brain areas with a sampling frequency of 128 Hz during rest (9 minutes with eyes open) and task periods (24 minutes), respectively. Subjects were asked to recognize 36 different visual patterns (each shown for 10 seconds consecutively). Raw and filtered signals (α - and δ -band) were submitted to focus-based multifractal analysis yielding scaling functions. It was described in terms of the following parameters: focus (F) being closely related to the total variance; Hurst exponent (H) representing the degree of temporal autocorrelation and $\Delta H15$ capturing multifractality at the level of the -15th/+15th moments. These estimates were averaged for each channel and state within a subject and statistically evaluated with two-way ANOVA. Significant differences ($p < 0.05$) were confirmed with Bonferroni post hoc tests.

Results. F and $F\delta$ were the highest at rest in the prefrontal cortex (PFC) and they globally decreased during task in males, only. H and $H\delta$ — similar to F — globally decreased in males during task, while remained unchanged in females. $\Delta H15$ for PFC at rest in females exceeded the level in males, while the contrary was seen for the rest of the brain. During task: i) $\Delta H15$ decreased to a larger degree in females for PFC and in males less for the rest of the brain, ii) $\Delta H15\alpha$ changed most over the occipital cortex.

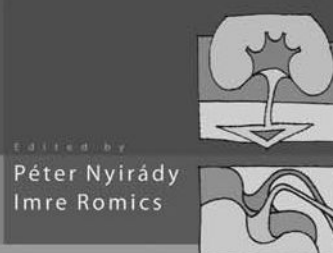
Discussion. Scale-free temporal correlation in EEG decreases in response to task. The observed gender-related differences in the multifractality of underlying neurodynamics can possibly be attributed to the gender-specific functional connectivities. Our results suggest a more interconnected PFC in females in contrast to males having higher degree of connectivity in the rest of brain. In order to support this conclusion, our future goal is to investigate the functional connectivity revealed by EEG.

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Supervisor(s): Andras Eke, MD, PhD professor, Department of Physiology, Peter Mukli, MD professor Department of Physiology

Péter Nyirády:

Textbook of Urology



TEXTBOOK OF UROLOGY

This is the 2nd revised edition of our own edited Textbook of Urology for English speaking medical students in our University. We found it essential to handle a book that contains all information in the field of urology which we find important. We hope that this book will help to learn urology for English speaking medical students not only in the Semmelweis University but also in other Hungarian medical universities as well as in Central Europe.

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High-intensity statin therapy efficacy and impact on cognitive function and quality of life in high cardiovascular risk patients

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Objective: dyslipidemia is recognized as a prominent risk factor for cardiovascular (CV) disease. High-intensity statin therapy (HIST) is indicated for high CV-risk patients(pts). Only few studies examined HIST effects on cognitive function and health-related quality of life (HRQoL).

Aim of the study: to assess HIST efficacy and impact on cognitive function and HRQoL in high CV risk pts.

Methods: in 93 pts (58 male, 63.2±9.5 years) with history of clinically evident cv disease, low-density lipoprotein cholesterol(LDL-C) >1.8 mmol/l or non-high-density lipoprotein cholesterol(non-HDL-C) >2.6 mmol/l, HRQoL and cognitive function were assessed (using the Montreal Cognitive Assessment (MoCA) and the SF-36 survey, respectively) before and 6 months after HIST (atorvastatin 80 mg/day). Dynamics of the pts' lipid profile, liver enzymes and CPK were monitored during therapy. Wilcoxon test was performed. P<0.05 was considered significant.

Results: HIST decreased lipid significantly: Total Cholesterol from 4.9±1.2 to 3.9±0.5mmol/l, LDL-C from 3.1±1.0 to 2.1±0.4mmol/l, non-HDL-C from 3.8±1.1 to 2.6±0.5 mmol/l, triglycerides from 1.9±0.6 to 1.3±0.5 mmol/l (p<0.05). Changes of HDL-C were insignificant. No side effects were observed. Only 38 (40.9%) patients achieved target LDL-C level <1.8 mmol/l after 6 month of therapy.

Mean MoCA performance was 24±3. 61 pts had cognitive dysfunction (MoCA score<26). Pts with vs without stroke (22±3 vs 25±3 scores) and older vs younger than 65 years (21±3 vs 26±2 scoores) had higher cognitive dysfunction. After HIST, mean MoCA performance was 24±3. Changes in cognitive function were insignificant.

HRQoL was significantly improved: physical functioning score from 57±27 to 63±23, physical role functioning from 40±28 to 47±26, bodily pain from 59±30 to 70±25, general health perceptions from 52±14 to 57±14, social role functioning from 63±23 to 70±25, emotional role functioning from 53±39 to 61±33, and mental health from 66±15 to 71±18.

Conclusion: HIST was effective only in 40.9% of patients, but lead to improvement in HRQoL (by most sections of SF-39 survey), had no impact on cognition.

non

Supervisor(s): Zhanna Kobalava professor, I. Department of Internal Medicine

Decorin expression in primary and metastatic colorectal cancer

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Background. Decorin is a small leucine-rich proteoglycan present in the ECM of many tissues including the colon and liver. The expression of decorin and other ECM components differs in healthy and injured or cancerous tissues. This versatile proteoglycan acts as a potent tumor suppressor through many actions including antagonizing several tyrosine kinase receptors, binding to growth factors and inhibiting angiogenesis, which are necessary for tumor growth.

Aims. As colorectal cancers are one of the most frequent tumor worldwide, our aim was to measure and compare the expression of decorin between healthy colon, primary colon cancer, liver metastasis and healthy liver of each patient. In addition to observe the correlation of decorin expression following the course of tumor progression, and finally to investigate the difference in the expression of decorin in synchronous and metachronous metastases of colon carcinoma.

Methods. A retrospective study included approximately 90 patients. From each patient sample of the normal and tumorous colon as well as metastatic and normal liver tissue were collected. From formalin-fixed paraffin embedded blocks, several tissue microarrays were assembled. Each microarray contained tissue from 2 cores of colon tumor, 2 cores of healthy colon, 2 cores of liver metastasis and 1 core of surrounding liver tissue. TMA slides were subjected to immunostaining specific for decorin. Stained sections were digitalized; the intensity of decorin was measured by the Panoramic viewer software. H-score was used to evaluate the data and statistical analysis was performed using Graphpad Prism software.

Results. Strong immunoreactivity for decorin was found in stroma of normal colon, while weak staining appeared in the stroma adjacent to tumor clusters. Decorin expression in the primary colon cancer was found to be significantly lower than in normal colon. In addition, decorin level further decreased in liver metastasis compared to the primary tumor. Decorin level in metachronous metastases was consistently higher than in the synchronous ones.

Conclusion. In conclusion, decorin acts as a tumor suppressive component in colon and liver. The fact that the more infiltrative tumors have lower expression of decorin suggests that tumor progression is linked with loss of decorin and its tumor protective function.

Response of Hepatic Stellate Cells to TGFβ1 Differs from the Response of Myofibroblasts. Decorin Protects against the Action of Growth Factor.

Proteoglycans in liver cancer.

Decorin deficiency promotes hepatic carcinogenesis.

Decorin interferes with platelet-derived growth factor receptor signaling in experimental hepatocarcinogenesis

Decorin-TGFβ axis in hepatic fibrosis and cirrhosis.

Ablation of the decorin gene enhances experimental hepatic fibrosis and impairs hepatic

Supervisor(s): Dr. Baghy Kornelia PhD, I. Department of Pathology and Experimental Cancer Research

Morphological assessment of atherosclerotic plaque after treatment by magnesium drugs

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Diseases of the cardiovascular system organs are still among the main causes of death in the world. Currently studies of atheromatous proliferation of extracellular matrix walls of the arteries, and especially its main amorphous component, are focused on the role of matrix metalloproteinases (MMP). The importance of MMP is very high in the development and nature of the atherosclerotic process, especially MMP-2 and MMP-9. Several studies have shown an increase in MMP expression levels in atherosclerotic lesions and their role in the weakening of the walls of blood vessels and the degradation of the extracellular matrix. One component of the complex in the treatment of atherosclerosis (atheromatous plaque) is magnesium. The aim of the study was to investigate changes in the atheromatous internal carotid arteries after use of magnesium-containing drugs (immunohistochemical aspect). In this clinical study, biopsies of internal carotid arteries analyzed before and after using of magnesium orotate by patients ($n = 5$) with unstable atherosclerosis bilateral internal carotid artery. Method of the morphological study is immunohistochemistry. Results. Morphological analysis of the internal carotid arteries of the two groups showed that the atheromatous changes are less pronounced, and sometimes absent in patients after using of magnesium orotate. This is confirmed by immunohistochemical reactions for MMP-9. Thus, magnesium orotate can be used as a preventive drug, prevents the development of atherosclerotic lesions, and in their presence he contributes to their reduction.

1. G. Demyashkin. Morphological analysis of spermatogenesis – the basis of diagnosis of male idiopathic infertility (Immunohistochemical aspect) // International Conference and Exhibition on Cytology & Histology. – August 2016. – Birmingham, The United Kingdom of Great Britain and Northern Ireland – collected abstracts on CD.

Supervisor(s): Grigory Demyashkin senior research fellow, II. Department of Pathology

The role of genetic predisposition in the effectiveness of exercise in type two diabetes prevention

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Introduction and aim: The risk of development of T2DM is connected with both genetic and environmental factors, but there are no studies clearly showing the effect of gene/environment interactions on this risk. The aim of our study was to evaluate whether a PA may modify the impact of the genes on the development of T2DM.

Methods: In the group of 921 subjects we have evaluated PA levels using International Physical Activity Questionnaire and genotyped 37 single nucleotide polymorphisms (SNPs). Genetic risk score (GRS) as a weighted sum of risk alleles have been calculated. To explore GRS and PA interactions, we stratified the sample according to GRS and PA levels and calculated T2DM incidents.

Results: We compared patients with low and high physical activity in high and low T2DM GRS groups separately. The incidence of T2DM was lower among physically active individuals in high GRS group (8,6% in high PA vs. 13,8% in low PA, $p < 0,03$) as well as in low GRS group (4.4% in high PA class vs. 8.7% in low PA class, $p < 0,03$).

In addition, we studied single interactions of SNPs on physical activity. We found only one significant interaction of SNPs on physical activity within ADRA2A gene (rs10885122).

Conclusions: Our study shows that the T2DM development risk is significantly diminished by physically active lifestyle, even among subjects at high genetic risk. Genetic component plays a significant role in the development of T2DM but it can be reduced by an increase in physical activity.

M. Ciborowski, E. Adamska, M. Rusak, J. Godziń, J. Wilk, A. Citko, W. Bauer, M. Górska, A. Krętowski. CE-MS-based serum fingerprinting to track evolution of type 2 diabetes mellitus. *Electrophoresis* (2015), 36(8): 2286-2293. IF: 3.028

Supervisor(s): Adam Kretowski professor, Clinical Research Centre and Department of Endocrinology, Diabetology and Internal Medicine, Maria Gorska professor Department of Endocrinology, Diabetology and Internal Medicine

Significance of the hepatic vein anastomoses in left lobe living donor liver transplantation

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Introduction: Liver transplantations are substantially limited by the worldwide shortage of organs. Living donor transplantations may cut down on the waiting list. In pediatrics, left lobe liver transplantation is already an established therapy, with either segments II-III or the entire left lobe transplanted known as "full left liver transplantation". Recently, left lobe living donor transplantation is getting more widespread in adults decreasing the burden for the donor people and cost for the donors themselves. Therefore, a more detailed examination of the surgical anatomy of the left lobe circulation is now essential.

Aim: Further investigation of the left lobe's venous circulation and searching for anastomosis between the middle and the left hepatic vein. This could be important to ensure the proper venous circulation of the recipient's liver graft in the setting of a left lobe living donor transplantation.

Materials and Methods: We developed a method where we filled the hepatic veins of 25 human livers with an extra low viscosity resin mixture and removed the parenchyma by corrosive to obtain the cast of the hepatic venous system. So far, anastomosis patterns of 5 livers have been visualized. The anatomical structure and variations were studied, analyzed and photo documented.

Results: In the prepared livers, new anastomotic venous channels were found between the left (segments II and III) and the middle (segment IV) hepatic veins.

Conclusion: We could identify till then unrecognized, new venous connections in the studied livers that may have significant impacts on liver surgery and transplantation. This knowledge is important in liver splitting as these anastomoses provide an adequate venous circulation to the transplanted left liver graft. The documented presence of such anastomoses may prevent the incidence of postoperative complications.

no publications

Supervisor(s): Zoltán Máthé professor, Department of Transplantation and Surgery, Mátyás Kiss associate professor Department of Anatomy, Histology and Embryology

Role of IDH1 gene mutation in the development of brain astrocytomas and anti-oncogene intracellular protection

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Materials and methods. Objects of retrospective study - biopsy of brain astrocytomas G II - III grade. Three groups were formed with the account of tumors variant (n = 20 cases in each group): A low proliferative activity (Ki-67 $\leq 5\%$); AB with medium proliferative activity (Ki-67 5%-10%) and B with high proliferative activity (Ki-67 $\geq 5\%$). In the second phase, in each group it was identified the percentage of cases with a mutation IDH-1 gene, which is detected by determining the product of the mutant gene atypical 2-gidroksiglutarat.

Methods: hematoxylin-eosin, immunohistochemical investigation – the monoclonal antibody Ki-67 (NovocastraTM, UK; 1: 100 dilution; two cut on glass). Evaluation of immunohistochemical reactions based on staining intensity and division of cells immunopositive as recommended by D.J. Dabbs "Diagnostic immunohistochemistry, 2010". Scale intensity of staining (expression): "-" - no expression ($\leq 1\%$ in the cells in the slice); "+" - Weak expression (1-10% of cells in the slice); "++" - Moderate expression (10-50% of cells in the slice); "+++" - Intense staining ($\geq 50\%$ in the cells in the slice).

Results. Group A.: including astrocytomas with low proliferative activity (Ki-67 $\leq 5\%$) the number of cases with the IDH-1 mutations was 83 \pm 3%. In group B with an average number of proliferative activity of IDH-1 mutations was 57 \pm 4%. Group B.: the number of cases with the IDH-1 mutations was 11 \pm 2%.

Conclusions.

1. The high degree of proliferative activity of atypical cells of astrocytomas corresponds to a low frequency of IDH-1 mutations.
2. IDH-1 – a differential diagnostic marker of astrocytomas, and in combination with Ki-67 has an important prognostic value, as it has antioncogen property.

No publications

Supervisor(s): Demyashkin G.A. college assistant lecturer, I. Department of Internal Medicine

Modifying factors of Ischemia-Reperfusion injury in a highly selected population of patients with ST elevation myocardial infarction

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Introduction: Acute restoration of coronary circulation causes a secondary myocardial injury - termed as cardiac ischemia-reperfusion injury (I/R) - which is responsible for approximately half of the final infarct size. Not only is I/R an extremely complex process, but it is heavily influenced by comorbidities (diabetes, hypertension, dyslipidemias, age), smoking, anatomical variations and length of ischemia as well. With this retrospective analysis my aim was to better understand the influencing factors of I/R.

Method: Retrospective analysis of patients who had anterior ST segment elevation Myocardial Infarction (STEMI) was performed at the Heart and Vascular Centre of Semmelweis University. Acute Coronary Syndrome patients admitted between 2011 and 2014 were screened for the following criteria: first STEMI, shorter than 6 hour duration, anterior localization and total coronary artery occlusion. Medical history, procedural characteristics, echocardiographic data (ejection fraction – EF) and laboratory results were collected. Correlation between EF and laboratory data was analyzed and patients with preserved (>50%) and decreased (<50%) ejection fraction were compared. Data sets, depending on their distribution, were analyzed with Pearson's correlation, t- and Mann-Whitney tests.

Results: Out of 3538 screened patients only 104 met all inclusion criteria and only 60 (1,7%) had sufficient data available for final evaluation. Correlations were found between high sensitive troponin T levels (hsTnT) and white blood cell count ($P<0.05$) and EF and hsTnT levels ($P<0.05$). Subgroup analysis not only showed that patients with a decreased ejection fraction had higher troponin levels (2870[1511-5813] vs 863[261-3341], $P=0.02$), but that they had more frequently a history of high blood pressure (67% vs 33%, $P=0.04$) and lower triglyceride levels (0.76 [0.54-1.1] vs 1.075[0.75-2.48], $p=0.02$) as well. Other patient characteristics such as age, BMI, history of diabetes and hyperlipidemia, smoking and creatinine and cholesterol levels were similar in this small cohort of patients.

Conclusion: Our findings show that even in an extremely selected population comorbidities like hypertension and patient characteristics like leukocyte count or triglyceride levels can have significant influence on the extent of ischemia-reperfusion injury.

J Pharmacol Exp Ther. 2016 Feb; 356(2):284-92.

Concomitant Phosphodiesterase 5 Inhibition Enhances Myocardial Protection by Inhaled Nitric Oxide in Ischemia-Reperfusion Injury. PLoS One. 2015 Oct 30;10(10). Right Ventricular Adaptation Is Associated with the Glu298Asp Variant of the NOS3 Gene in Elite Athletes.

Supervisor(s): DR LUX Arpad Clinician, Department of Cardiology

A comparison of VO_2 and RSBI in evaluating weaning readiness

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Introduction. Studies show that prolonged mechanical ventilation (MV) is associated with negative clinical outcomes such as risk of ventilator associated pneumonia, lung injury & a high mortality at 28-35% whereby MV should be discontinued as soon as possible. Tidal volume, respiratory rate (RR), minute ventilation, vital capacity, maximal inspiratory pressure & RSBI were not suggested to be used as weaning success predictors (WSP) moreover, little evidence exists on the use of CROP, IWI & CORE indices as WSP.

Objectives. To compare ΔVO_2 & RSBI as a weaning predictor during weaning.

Methods. 10 patients on MV >21 days were included in our study. Oxygen consumption (VO_2) in different stages of MV support reduction was recorded using E-COVX indirect calorimeter gas analyzer, GE. Vital signs were monitored on CARESCAPE B650, GE. Weaning algorithm was as follows: 1) Ventilation mode was set in CPAP-PSV at a comfort pressure support (PS) level. 2) Baseline reading was recorded for 2 hours. 3) Stepwise reduction in PS by 2 cmH_2O at an interval of 10 min. avoiding PS ≤ 3 cmH_2O for patients with tracheostomy tube. 4) RSBI, vitals, VO_2 , V' & arterial blood gas were recorded. If patient had active movement or tracheal suction was performed, VO_2 was considered an artefact.

Results. 6 out of 10 patients were successfully weaned. 4 patients required further MV due to weaning intolerance. ΔVO_2 was $19\% \pm 12\%$ & $47\% \pm 9\%$ in weaned and non-weaned respectively & respiratory rate (RR) 27 ± 5 & 41 ± 7 in weaned and non-weaned respectively, max RSBI 60 ± 18 & 111 ± 12 in weaned and non-weaned respectively.

Conclusion. RSBI uses RR in its calculation but VO_2 increased earlier than RR during the weaning process. To conclude, VO_2 has a better predicting value compared to RSBI.

1) The use of VO_2 & VCO_2 (indirect calorimeter parameters) to wean stroke patients from ventilatory support: VI International Scientific

Conference SCIENCE4HEALTH
2015 Peoples Friendship University of Russia

2) The use of vo_2 level changes as a predictor for weaning success in the mechanically ventilated patient: Intensive Care Medicine Experimental 2016, 4(Suppl 1):28

Supervisor(s): Rubanes Mohan scientific advisor, Department of Anesthesiology and Intensive Therapy

Quantitative assessment of acute alveolitis and fibrosis in usual interstitial pneumonia and non-specific interstitial pneumonia using his

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Background: Interstitial lung disease describes a large group of disorders characterized by progressive scarring of the lung tissue. The most common idiopathic entity is the usual interstitial pneumonia (UIP) which has a bad prognosis. UIP is characterized by active areas (acute alveolitis, AA), fibrotic areas (FA), such as honeycombing and healthy areas (HA). Non-specific interstitial pneumonia (NSIP) is characterized by better prognosis and larger ground glass areas and usually no honeycombing compared to UIP. The quantitative, proper identification of these territories is essential in the follow-up of these patients especially during therapy. Our goal was to assess the density of these areas in UIP and NSIP using histogram analysis.

Methods: HRCT scans of 42 ILD patients (23 UIP, 19 NSIP) were analysed using Philips interspace portal version 7. The scans were obtained during inspiratory phase using Philips Brilliance 16. Histogram data (mean, standard deviation, maximum, minimum and skewness) were obtained using circular area (ROI ~ 50mm). Three measurements were performed in fibrotic areas (FA), active (AA) and healthy (HA) and their average was used in the statistical analysis (t-test).

Results: Mean and minimum density of fibrotic areas was significantly decreased in UIP patients compared to NSIP (-354 vs. -434 HU, $p=0.007$ and -734 vs. -800 HU, $p=0.03$), while skewness showed a borderline significance (0.43 vs. 0.00 $p=0.06$). No significant differences were detected between healthy and AA areas between UIP and NSIP.

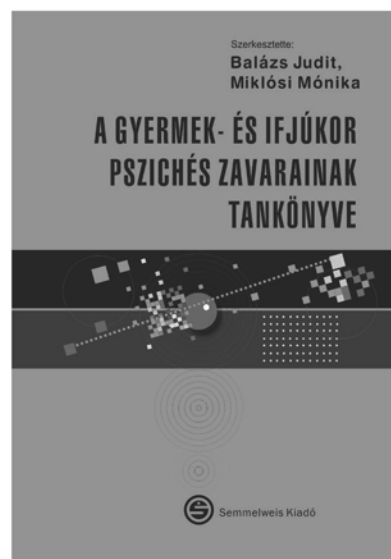
Significant differences were observed among the three groups in mean value (NSIP: FA>AA>HA: -712±51 vs. -434±84 vs. -893±28 HU, $p=0.000$, UIP: FA>AA>HA: -703±47 vs. -355±91 vs. -886±58 HU, $p=0.000$). Standard deviation, minimum and maximum densities showed also significant differences in both groups ($p=0.000$) and skewness in NSIP. No significant differences were found between the skewness of AA/FA ($p=0.630$) and FA/HA ($p=0.523$) in UIP patients but in case of AA/HA in UIP ($p=0.000$).

Conclusions: Histogram analysis seems to be useful for the differentiation of areas of acute alveolitis, fibrosis and healthy lung tissue in NSIP and UIP. These results can be useful to stimulate further studies on the volumetric assessment of these areas in

Pubmed

Supervisor(s): Adam Domonkos Tarnoki, assistant lecturer, Department of Diagnostic Radiology and Oncotherapy, David Laszlo Tarnoki assistant lecturer Department of Diagnostic Radiology and Oncotherapy

MEGJELENT!



Balázs Judit, Miklósi Mónika

A GYERMEK- ÉS IFJÚKOR PSZICHÉS ZAVARAINAK TANKÖNYVE

A pszichés zavarok nagy terhet rónak arra, akinek ilyen problémával kell élnie, legyen szó gyermekről vagy felnőttéről. Gyakran nemcsak a mentális betegséggel előre jelenthet ez terhet, hanem a környezetére is, és ezen keresztül az egész társadalomra. Mindezek miatt kiemelt jelentősége van a pszichés zavarok prevenciójának, korai felismerésének és kezelésének. A pszichiátriai problémák jelentős része gyermekkorban kezdődik, a megelőzésnek már erre a korosztályra is fokozott figyelemmel kell lennie. Fontos továbbá, hogy az olyan gyermekek és felnőttek, akiknél pszichés probléma áll fenn, időben eljussanak szakemberhez és megkapják a megfelelő, korunk tudására épülő, evidenciákon alapuló segítséget, és így életminőségük, funkcionalitásuk javuljon, tehát a pszichés zavar miatt rájuk és az egész társadalomra eső betegségteher csökkenjen. Ez a tankönyv ehhez igyekszik segítséget nyújtani.



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Our experience in the heart echinococcosis (hydatid disease)

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Heart echinococcosis is an uncommon disease (0.01-2% from all registered echinococcosis cases). However it is causing to many discussion among the scientists with its dangers. Echocardiography is a relatively simple and very reliable method to diagnose echinococcus. Tactics of the treatment of the heart echinococcosis can be divided into two groups: conservative (antibiotic treatment and chemotherapy) and surgical. The surgical treatment can also be divided into two group: cystectomy by using cardiopulmonary bypass and cystectomy on the beating heart. The most dangerous complication of the heart echinococcosis is cyst perforation. Frequency of intracardiac perforation is very high. Our experience in surgical treatment of the heart echinococcosis is based on 12 cases. the age variety of the patients was from seventeen to fifty three years. The cysts were localized mostly in the right ventricle. Seven patients underwent a cystectomy from the heart using cardiopulmonary bypass and the other five patients underwent a cystectomy from the heart using off-pump operation techniques. After the operation all patients underwent three or more courses of antibiotic treatment. Treatment of the patients with heart echinococcosis should be complex: both surgical intervention and conservative therapy should be undergone at the same time. chemotherapy and antibiotic treatment in the post-operative period is able to decrease the recurrence of the disease in many instances. As well as, staying in a hospital in the post operative period is lesser in patients who were operated on the beating heart than those who were operated on the beating heart than those who were operated by using cardiopulmonary bypass.

Summary, from our investigation there are some benefits of the method of cystectomy on the beating heart. 1. The patients may recover from surgery more quickly than those who operated "on pump". 2. The second advantage is reduced injury to the heart, that is to say there are fewer heart rhythm problems and fewer post-operative complications by patients.

Myxoma of the heart, innovative method of mitral implantation, endocarditis, implantation of the electric cardio stimulation in diabetic patients

Supervisor(s): *Xamidullo Abdumajidov omonullaevich professor, Department of Experimental and Clinical Surgery, Abdunosir Turgunov Ismoilovich senior lecturer Department of Cardiac Surgery*

Prospects of poly(vinyl)alcohol scaffolds in abdominal hernia treatment. A study of bio-adaptability in small and large animals

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Background: Abdominal hernias are one of the most frequent disorders treated in general surgery. First choice treatment in such cases is hernioplasty but intraperitoneal positioning of currently applied non-biodegradable surgical meshes may cause serious complications including, chronic post-operative pain, mesh migration, adhesion, infection and foreign body reactions. Biocompatible poly(vinyl)alcohol meshes may also have potential biodegradable properties, thus could prevent such complications. Purpose of the following experiments is to examine in vivo biological adaptation to our tissue engineered PVA meshes.

Methods: Non-woven, nanofabricated PVA scaffolds were produced via electrospinning and were sterilized with ClO_2 . Two series of experiments were performed. First, wistar rats ($n=60$) were randomly sorted into four groups of 15 animals each. In Group I, PVA scaffolds were placed on the peritoneum and fixed upon the abdominal musculature via four corner single interrupted sutures. Group II and III received a PVA mesh (2.5cm in Diameter D) to repair artificially created abdominal wall defects ($D = 2\text{cm}$) and were fixed with absorbable and non-absorbable thread (5/0) respectively. Lastly Group IV was a control group were only an incision on the skin and muscle was made. A preliminary study on large animal was then performed on swine ($n=2$). Scaffolds ($D=8\text{cm}$) were implanted laparoscopically and fixed intraperitoneally without creating a defect upon the right side anterior abdominal wall. Concurrently polypropylene meshes were also implanted on the left side serving as a control measurement. Rats in each group were dissected after 7th, 14th, 28th, 90th and 180th postoperative days, the swine were terminated on the 5th week. Implants were evaluated macroscopically and histologically.

Results: Infection or other complications were not found in the environment of the PVA meshes in none of the animals. Macroscopical findings showed significantly more adhesion formation along the suture line than PVA scaffold itself proving its biocompatibility. Histological examination showed that all of the meshes were integrated to the host tissue and kept their structure until the end of the experiments.

Conclusion: Our results proved that a PVA nanofabricated mesh is biocompatible and could be a promising biomaterial for the prevention of future incisional hernia formation.

Abdominal hernia repair with poly (succinimide) and with its cysteamine crosslinked nanofiber hernia meshes. A preliminary experimental study Andrea Ferencz, Daniella Fehér, Györgyi Szabó et al., International Journal Of Bio-Technology And Research 6:(2) p. In press.6p.(2016)

Tissue engineered nanofiber poly(vinyl alcohol) mesh for the treatment of abdominal wall hernia Daniella Fehér, Andrea Ferencz, Györgyi Szabó et al., International Journal Of Bio-Technology And Research 6:(2) pp. 7-14. (2016)

Supervisor(s): *Daniella Fehér research fellow, Department of Experimental and Clinical Surgery, György Wéber professor Department of Experimental and Clinical Surgery*

Evaluation of the results of treatment of children after caustic burns of the esophagus

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1. *Introduction.* Caustic burns of the esophagus are very topical issue of Pediatric Surgery. Severe and deep injuries of esophageal induce extended esophageal stenosis, requiring surgical treatment in 98% cases of esophageal caustic burns. Nowadays there isn't common algorithm of treatment and predicting the outcome of the disease is extremely difficult so the choice of treatment is a challenge.

2. *Aim of the study.* To examine the results of treatment of children, who received burns of esophagus with substances containing alkali. To determine the indications for preventive bougienage, the duration of bougienage for the alkali burns of the esophagus.

3. *Materials and methods.* The retrospective review has been carried out for 57 children with esophageal caustic burns treated in Filatov Children Hospital for the period 2010-2015. We used different methods of bougienage: peroral bougienage of the esophagus, bougienage on thread in the presence of gastrostomy and string guide bougienage under general anesthesia. Average time of bougienage ranged from 4 to 18 months. Bougienage on thread was used in 16 (28%) cases. Among children admitted in Filatov Children Hospital in the acute period, gastrostomy was not carried out. Preventive peroral bougienage of the esophagus or string guide bougienage was used in 31 (54,4%) cases. 2 patients (3,5%) underwent extirpation of the esophagus on an emergency basis due to perforation of the esophagus. 23 (40,4%) patients required esophageal replacement using stomach or colon.

4. *Results.* In long term results dysphagia was not marked in 48 (84,2%) cases after a course of esophageal bougienage. Gastro-esophageal reflux was diagnosed in 9 cases (15,8%), 2 children underwent laparoscopic fundoplication. 1 children was operated due to hiatal hernia. 23 patients who underwent esophageal replacement also didn't have dysphagia nor diet limitations. 2 patients (3,5%) have dysphonia due to laryngeal paresis. 1 patient have some dietary limitations.

5. *Conclusion.* There is a high probability of necessity in esophagoplasty (40,4%). In most cases (84,2%) esophageal bougienage is effective method of treatment, but the period of bougienage should continue at least 8 months. String guide bougienage can help to avoid gastrostomy. In addition to esophageal stenosis, esophageal caustic burns can lead to gastroesophageal reflux or to hiatal

A miniinvasive method for the treatment of congenital lobar emphysema in children.

Surgical treatment of children with biliary atresia.

Evaluation of the results of treatment in children after alkali burns of the esophagus.

Supervisor(s): Stepanenko Nikita Sergeevich scientific advisor, I. Department of Surgery

Gene polymorphisms as predictors of aortic dissection in Marfan syndrome

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Background: Gene polymorphisms (SNPs) of folic acid cycle enzymes are evidenced to be responsible for elevated plasma homocysteine levels, which correlate with aortic dissection. Marfan patients are genetically prone to this severe condition and aortic diameter is insufficient for risk stratification. We aimed to identify SNPs of folic acid cycle enzymes that predict aortic dissection in Marfan patients.

Methods: We studied 71 Marfan patients and divided them into groups based on the severity of cardiovascular involvement: none (group A, n=27); moderate requiring prophylactic aortic-root surgery (group B, n=17); severe requiring acute aortic-root surgery (group C, n=27) subdivided into: patients presenting with annuloaortic ectasia (subgroup C1, n=14) and aortic dissection (subgroup C2, n=13). Besides, 117 control subjects were examined. Among the study subjects, we evaluated plasma homocysteine, folate, vitamin B12 levels and polymorphisms of the folic acid cycle enzymes: methylenetetrahydrofolate reductase (MTHFR), methionine synthase (MTR) and methionine synthase reductase (MTRR). We also provided a novel SNP score system for risk stratification.

Results: Marfan patients with aortic dissection (C2 subgroup) had significantly higher plasma homocysteine level together with SNP score and significantly lower plasma folic acid and vitamin B12 compared to other groups (all $p < 0.02$). Plasma homocysteine level was an independent risk factor for severe cardiovascular involvement (group C; OR 1.85, 95% CI 1.28-2.66, $p = 0.001$) and especially for aortic dissection (subgroup C2; OR 2.49, 95% CI 1.29-4.78, $p = 0.006$). A negative correlation was found between plasma levels of homocysteine and folic acid and vitamin B12 (all $p < 0.001$).

Conclusion: Our novel SNP score system correlated strongly with plasma homocysteine levels and the occurrence of aortic dissection in Marfan patients, and thus is appropriate for cardiovascular risk stratification of such high risk patient groups, enabling closer follow-up and optimization of prophylactic aortic-root surgery. Supplementation of folic acid and vitamin B12 may be reasonable for Marfan patients in order to prevent adverse cardiovascular events.

Benke K*, Sayour AA*, ... Radovits T, et al., Gén polimorfizmusok, mint rizikó faktorok a Marfan-szindróma kardiovaszkuláris manifesztációinak előrejelzésében. *Cardiol Hung* 2016; 46:76-81.

Benke K, ... Radovits T et al., Gene polymorphisms as risk factors for predicting the cardiovascular manifestations in Marfan syndrome. Role of folic acid metabolism enzyme gene polymorphisms in Marfan syndrome. *Thromb Haemost* 2015; 114:748-756.

*Equally contributed to this study.

Supervisor(s): Tamás Radovits, MD PhD associate professor, Department of Cardiology, Kálmán Benke, MD cardiac surgery resident Department of Cardiac Surgery

Targeted therapy patients with metastatic renal cell carcinoma

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Background. Over 200 thousand of new renal cell carcinoma (RCC) patients (pts) with registered every year in the world. A quarter of them has metastatic RCC (mRCC) and 20-40% pts after radical surgical intervention subsequently has progression disease with appearance of metastases, therefore, the incidence of mRCC remains high. Tyrosine kinase inhibitors (TKI) demonstrated efficacy in treatment MRCC in randomized trials.

Goals and objectives. The aims of our study were assessment of results of TKI treatment of mRCC pts and analysis of prognostic factors of 1st line targeted therapy.

Methods. We included 27 mRCC pts received TKI therapy in oncurology department Moscow Scientific Oncology Institute n.a. P. A. Hertzen. Mean age was 61.9±9.9 years. Related with TKI treatment arterial hypertension was registered in 7 (25.9%) pts, local symptoms were detected in 8 (29,6%) pts and systemic manifestations of mRCC was in 6 (22,2%) pts. Most of the pts was clear cell mRCC 18 (66,6%) pts, papillary mRCC was diagnosed in 5 (18,5) patients with, 1 (3,7%) patient with chromophobe mRCC, one (3,7%) with mixed mRCC and one (3,7%) with Bellini collecting ducts carcinoma. All included pts undergone nephrectomy. Pts received first-line targeted therapy including Sunitinib, combination Avastin with Interferon and Sorafenib. We assessed the progression-free survival (PFS) and impact of pathological characteristics of tumor and laboratory tests on survival.

Results. Median progression-free survival (PFS) was 12 months. Median overall survival was 21 months. Multivariate Cox regression analysis revealed high correlation only with histological type of mRCC ($p = 0.03$), presence of necrosis in tumor ($p = 0.01$), number of poor MSKCC prognosis criteria, $p = 0.04$; Karnofsky performance status ($p = 0.006$), time from diagnosis of RCC to progression of less than 1 year ($p = 0.004$), thrombocytosis ($p = 0.003$), neutrophilia ($p = 0.01$) and PFS.

Conclusion. PFS of mRCC pts received first-line targeted therapy was comparable with results of large randomized trials and goes to 12 months. Identified predictors of effective targeted therapies in population of our pts include histological type of mRCC, presence of necrosis in primary tumor, number of poor MSKCC criteria, including Karnofsky performance status, time to progression less than 1 year, thrombocytosis and neutrophilia.

not represented

Supervisor(s): Kalpinskiy Alexey Sergeevich scientific advisor, Department of Urology

Anti-Infliximab Antibody Interferences in Immunological Assays

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Background: The aim of the study was to evaluate the possibility of anti-infliximab antibody interference in commercial immunoassays.

Method: Five patients' serum samples were collected from each of 3 groups: Crohn's disease patients undergone infliximab therapy with detectable anti-infliximab antibody levels, Crohn's disease patients undergone infliximab therapy without detectable of anti-infliximab antibody level, and subjects without Crohn's disease and infliximab therapy. After evaluation of available product descriptions of Roche, Beckman-Coulter, Diasorin and Abbott immunoassays, Abbott tests were selected as possible subjects of interference. Percentage recovery was measured on Architect i2000SR for HE-4, CA-125, FSH, and LH immunoassays after spiking the samples with calibrators of different levels.

Result: Percentage recovery did not differ between different groups.

Conclusion: The presence of anti-infliximab antibodies had no effect on tested Abbott immunoassays. Therefore, any interference of immunoassays with anti-infliximab antibodies is unlikely.

Keywords: Anti-infliximab antibody; interference; immunoassay; infliximab therapy

None

Supervisor(s): Professor Barna Vásárhelyi professor, Department of Laboratory Medicine

Concepts of lower limb reconstruction in patients with pvd

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In Germany between 50,000 and 80,000 patients, of whom about 70% are diabetics, will develop limb ischemia each year. Thereby the biggest challenge of avoiding major amputations is an interdisciplinary approach and involves angiologists, radiologists, vascular and plastic surgeons.

Classically in patients with critical limb ischemia, revascularization is first target, debridement and defect closure are dated later. In patients with chronic ischemia and tissue necrosis additional one stage reconstruction with revascularisation and defect closure can be done.

Plastic surgeons armamentarium for covering lower limb defects are skin grafts, local flaps (local tissue transfer) and free flaps (free tissue transfer). The use of skin grafts is limited to soft tissue defects with vascularized wound bed, in other cases local or free flaps are needed. Local flaps use vascularized tissue surrounding the defect and in absence of suitable tissue nearby the defect, free flaps are needed.

Examples for local flaps are muscle based local flap as the M. gastrocnemius muscle flap or perforator pedicled propeller flaps (PPP).

In contrast to the skin grafts and local flaps, free flaps are transposed from a donor side to the receipt area including their blood vessels named artery and vein. Using microsurgical techniques the flaps artery and vein are End-to-End or End-to-Side anastomosed to the receipt vessels.

Examples for free flaps used in pvd patients are the antero-lateral-thigh (ALT), latissimus dorsi, medial sural artery perforator (MSAP) and superficial-circumflex-iliac-artery-perforator-flap (SCIP)

In this study we want to present our techniques and a preview of results in delayed and one stage reconstruction with free flaps in pvd patients.

Muenker AV:

2012: Current Developments of Rehabilitation after Hip- and Knee-Joint Replacement in Germany

2013+2014: Current guidelines for diagnostics and rehabilitation treatment of low back pain in Germany

2015: Lower limb reconstruction with free flap in patients with pvd

2016: Post-treatment following shoulder endoprothesis

2016: All problems solved in regular subacromial decompression?

Jandali Z:

various publications 2008-2016

Supervisor(s): Dr. Zaher Jandali Dissertation supervisor,
Evangelisches Krankenhaus Oldenburg

Evaluation of the cardiosecur pro telemetric ecg system in acute cardiac care patients

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Introduction and aim: Computerized forms of electrocardiography (ECG) transmitted over the internet are widely used for telemetric diagnostics. The aim of the investigation was to compare the CardioSecur tablet-based ECG system and the widely used Philips EASI M2601B ECG readings. The former is based on the Dower orthogonal lead derivations, which can be represented by the traditional 12-lead ECG system, or even by the newly developed 22-lead ECG with the complementary V7-V9 and RV1-RV9 right-sided thoracic derivations. The diagnostic performance could be evaluated through waveform comparisons obtained during every day intensive care use on patients with arrhythmias, conduction abnormalities, and acute coronary syndromes.

Methods and materials: The study investigated the medical diagnostic accuracy of the two systems based on 41 individuals, followed by a technical comparison in ECG signals generated with a reduced lead system. The clinically obtained ECGs were verified by two independent cardiologists, where orientation of the P, Q, R, S, and T waves were evaluated. Subsequently, technical waveforms of healthy and pathological conditions were stimulated between 30-180bpm with an ECG emulator to ensure identical electrical input for both systems. These were also compared with respect to morphology and amplitude.

Results: The diagnoses were clinically identical in the ECGs measured with both CardioSecur and the Philips device. A Pearson correlation coefficient was calculated for the collected data, indicating a strong positive correlation. The additional 10-leads of the CardioSecur were not analyzed, as the Philips device does not permit this setting. Moreover, the technical subset of the study revealed that the CardioSecur showed an absolute 10% higher R peak than the Philips device. This discrepancy can be explained by the difference in device filter settings. Morphologically, all ECGs (patient and stimulated) showed identical orientation in the measured parameters.

Conclusion: This study has shown that the CardioSecur device is identical to the ECGs recorded by the Philips device with equal diagnostic capabilities. Morphologically, the orientation of all recorded ECGs were clinically identical in the measured data. Focus of future studies can investigate the advantages of an additional 10-leads applied to the CardioSecur device.

“Comparison Study Philips M2601B vs. CardioSecur pro”

David Triebel, Peter Kenedi, Istvan Preda, Adam Szekely, Marcus Skribek, Markus Riemenschneider.

Personal MedSystems Frankfurt, Central Hospital of the Hungarian Defence Forces Budapest.

Supervisor(s): Istvan Preda Prof. emer., MD, PhD, DSci, FESC,
Department of Cardiology, Adam Szekely MD, PhD
Department of Cardiology

Benefits of the minimally invasive operative methods in children with purulent-inflammatory diseases of the cerebrum

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Introduction. Purulent-inflammatory diseases of the cerebrum in children are very serious issue in the world. Frequency of fatal outcome in these patients is high; it can be between 10 and 30%. There are some ways to treat these diseases such as minimally invasive methods and radical method. The radical method of treatment leads with many complications including the cerebral protrusion. The minimally invasive methods could be a better decision in children with purulent-inflammatory diseases.

Materials and methods. 54 patients aged between 1.5 months and 14 years old with purulent-inflammatory diseases of the cerebrum were included in research study and got operated from 1990 to 2015 in Morozovskaya Children's City Clinical Hospital. Duration of disease anamnesis was between 5 days and 3 months. Many diseases were diagnosed in children for example: 26 patients had singular encephalopyosis, 8 patients had multiple encephalopyosis, 11 patients had subdural empyema, 5 patients had osteomyelitis of a frontal bone with formation of abscess in an epidural cavity and 4 patients had encephalopyosis with subdural empyema. All the children had non-focal neurological, meningeal, pyoinflammatory symptoms. We used a sonography of the brain and computer tomography (CT) to diagnose the case.

Results. 54 minimal invasive operations were made in patients with purulent-inflammatory diseases of the cerebrum. 19 double-barreled drainages were implanted in the abscess cavity, 31 punctures were made for abscess emptying and 4 bone resections with an epidural empyema emptying. We assess the efficacy of the treatment on clinical neurologic evidences and by using dynamic check-out of the sonography of the brain and CT. None of the patients needed total lancing of encephalopyosis. Postoperative lethality was 7,4% (4 patients). Sequelae of pyoinflammatory occurred in 7 patients: 2 patients had hydrocephalus, 4 patients had bone defect and 1 patient had epilepsy. 5 homogenous bone grafting were made after inflammation elimination.

Conclusion. The minimally invasive methods such as double-barreled drainage and punctures in combination with antibacterial therapy in children with purulent-inflammatory diseases are effective methods of treatment.

Goncharova A.Y./Short-term and long-term results of the occluder "Watchman" implantation in patients with atrial fibrillation/Semmelweis International Students' Conference/Hungary, 2016

Goncharova A.Y., Fayed Afsoon A.R./Benefits of the occluder "Watchman" implantation over prolonged-action anticoagulants in patients with atrial fibrillation/7th International scientific conference Science4health/Russia, 2016

Supervisor(s): P.I. Manzhos associate professor, I. Department of Surgery, A.G. Faibushevich associate professor I. Department of Surgery

Personal Health Practices of International Medical Students in Germany and Hungary: A Cross-Sectional Study

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Introduction. Recent studies have demonstrated a positive correlation between physicians' personal health practices and frequency and efficacy of patient health counseling. Students with healthy personal habits, especially those planning to specialize in family medicine, report counseling their patients about prevention more frequently. By analyzing the health practices of medical students, we might find correlation between certain health behaviour elements and future specialty preference of family medicine.

Methods. A multicenter, cross-sectional survey (n=2935) was performed across four universities in Germany (Dresden, Munich; only German students) and Hungary (Budapest, Pécs; Hungarian, Norwegian and German students). All students in the 1st, 3rd and 5th years were asked to voluntarily and anonymously complete a survey covering various aspects of health behavior and future specialty preference. Data collection took place during classes in 2014 (overall response rate = 56.2%). Subgroup analysis focused on the three largest groups: German (n=1289), Hungarian (n=1057) and Norwegian (n=148).

Results. Of the 2375 survey participants who specified their desired specialty, 164 (6.9%) answered family medicine (FM). These students represented 11.2% of Germans studying in Germany, 10.3% of Germans studying in Hungary, 4.5% of Norwegians and 2.2% of Hungarians (p<.001). Overall 7.1% of females and 6.6% of males selected FM as a specialty (non-significant difference). Study semester demonstrated a marginal significance with 8.0% of those in 2nd semester, 5.0% in 6th and 7.6% in 10th selecting FM specialization (p=0.051). FM students reported cannabis use in 10.5% and excessive drinking in 16.87% while those preferring other specialties reported cannabis use in 15.9% and excessive drinking in 22.77% (marginal significance, p=.067 and p=.084, respectively). Religion, smoking habits, physical activity and BMI showed no significant correlation with specialty preference.

Conclusion. Our results indicate that those planning to choose a more preventive field of medicine also follow a healthier lifestyle. Counselling practices can be learned and fortified during medical studies if proper health promotion is included in the curriculum. Promoting healthy behaviour among medical students might enhance the efficacy and increase the frequency of their future counselling efforts.

Do socio-cultural factors influence medical students' health status and health-promoting behaviors? A cross-sectional multicenter study in Germany and Hungary

Henna Riemenschneider, Péter Balázs, Erika Balogh, Axel Bartels, Antje

Bergmann, Károly Cseh, Nora Faubl, Zsuzsanna Füzesi, Ferenc Horváth,

István Kiss, Jörg Schelling, András Terebessy and Karen Voigt
BMC Public Health (2016) 16:576

Supervisor(s): Dr. András Terebessy senior lecturer, Department of Public Health

Parotid gland's cholesteatoma – review and report of an unusual case

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Background. Cholesteatoma is a non-neoplastic, keratinizing lesion, characterized by the proliferation of epithelium into the middle ear or mastoid cavity. The exact pathogenic molecular mechanisms behind the formation and propagation of cholesteatoma remain unclear. An acquired origin is hypothesized in patients with a previous history of an inflammatory process of the external or middle ear. Without timely detection and intervention, cholesteatomas can result in numerous intracranial and extracranial complications.

We report an extremely rare case of parotid gland's cholesteatoma in 23 years old male patient. The parotid gland's cholesteatoma is an uncommon entity. It has been mentioned in the literature, but never discussed as a main subject of a study.

Case report. In 2006 the patient was diagnosed with chronic suppurative otitis media (CSOM) and right ear conductive hearing loss of 55 dB. Consequently the middle ear cholesteatoma was observed, which was operated on and the tympanic cavity was radically cleared. In 2009 and 2012 recurrent cholesteatomas were diagnosed and radically operated on. In March 2016 a control MRI incidentally revealed an hyperintensive tumor in the right parotid gland. It has become painful since July 2016. Since September 2016 patient presented with dropping of the mouth corner on the side of the tumor. In October 2016 pre-operative examination of ear showed a dry and clear of cholesteatoma postoperative tympanic cavity. While operated the cholesteatoma-like tumor expanding from the styloidmastoid foramen was excised. It lay on facial nerve trunk, in between superficial and deep lobes of parotid gland. Histologic examination confirmed cholesteatoma. In tympanoscopy the tympanic cavity was clear of cholesteatoma.

Conclusion. Although parotid glands cholesteatoma is rare, we should keep in mind the possibility of its presence. The earlier it is discovered, the easier it is to perform surgical removal and to lower the chance of facial nerve involvement. This case was unusual as the disease had extended beyond the ear and we therefore wish to alert clinicians to cholesteatoma as a possible cause of facial nerve palsy or parotid gland's tumors. Also, searching for predictors of aggressiveness might give help to determine the proper timing of intervention and prevent occurrence of complications.

Assessment of BRAF V600E (VE1) protein expression and BRAF gene mutation status in codon 600 in benign and malignant salivary gland neoplasms.

The incidence of laryngeal cancer in Europe with special regard to Poland in last 2 decades.

Do we need a new classification of parotid gland surgery?

Sialendoscopy and sialendoscopically-assisted operations in the treatment of lithiasis of the submandibular and parotid glands: our experience of 239 cases.

Letter to the Editor of European Archives of Otorhinolaryngology about a paper "Classification of parotidectomies: a proposal of the European Salivary Gland Society"

Supervisor(s): Malgorzata Wierzbicka professor, Department of Experimental and Clinical Surgery

Can Serious Games like The Kheiron Training System Enhance Skill Acquisition from Traditional Box Trainers?

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Background: Studies have shown that simulation training can significantly enhance the complicated skill set required for minimally invasive procedures; however, access to such trainings is limited and expensive. Newer studies have evaluated the benefit of video- and Serious Games in acquisition of basic surgical skills. The main objective of the Kheiron Training System (KTS) is to offer medical students and novel surgeons with an innovative ICT-based approach for training basic key psychomotor skills in minimally invasive surgery.

Methods: Third-year Hungarian students of the Basic Surgical Techniques course were given the opportunity to practice with KTS prior to the laparoscopic training module. Volunteers (n=21) trained for 45 minutes, completing six levels of the game. Later, students were timed on three tasks using a traditional box trainer: Paper Cluster - reclassification of small rolls of paper according to color (Paper), placing a medical needle into its cap mid-air (Needle) and Peg Transfer. Results of the volunteers (KTS) were gathered along with results of 30 randomly selected students with no previous laparoscopic experience (Control). Results: Data are mean \pm standard deviation and mm:ss. Task completion time (TCT) was used to compare the two groups. For Paper, an independent-samples t-test was run to determine TCT differences. TCT for KTS was faster (00:46 \pm 00:19) than Control (00:53 \pm 00:16), however, the mean difference (00:07) was not statistically significant (95% CI, 00:00 to 00:18), $t(39)=1.231$, $p=.226$. A Mann-Whitney U test was run for both Needle and Peg Transfer. For Needle, TCT for KTS (mean rank=20.50) and Control (mean rank=21.26) were not statistically significantly different, $U=182$, $z=-.193$, $p=.860$. For Peg Transfer, TCT for KTS (mean rank=17.96) and Control (mean rank=22.57) were not statistically significantly different, $U=146.5$, $z=-1.169$, $p=.246$. Our preliminary analysis and re-analysis with higher significance levels confirmed there is insufficient evidence to reject the null hypothesis for all three tasks.

Conclusion: There is not sufficient evidence to support the claim that KTS training yields faster task completion time on tasks performed on a standard pelvitrainer. However, we believe sufficient support may be acquired by increasing the amount of time spent training with KTS and increasing the sample sizes of both groups.

Publications: around 220 scientific papers and more than 148 conference publications (57 invited lecture) IF: 202,599.
(<https://vm.mtmt.hu/www/index.php?AuthorID=10004445>)

Supervisor(s): György Weber M.D., Ph.D. Director, Department of Surgical Research and Techniques, Dr. Juhos Krisztina scientific advisor Department of Surgical Research and Techniques

Evaluation of HIV-1 drug resistance spreading in Russia in 2011-2015

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Introduction. Since 2006 in Russian Federation highly active antiretroviral therapy (HAART) became widely available. For 10 years the number of HIV-infected people under treatment has increased more than 10 times. WHO and UNAIDS Program "90-90-90" implies a further increase of patients on effective therapy. The aim of the study was the analysis of HIV-1 drug resistance mutations (DRM) spreading in Russian naïve and therapy experienced patients with diagnosis date 2011-2015.

Material and methods. We analyzed the nucleotide sequences of HIV-1 samples genome isolated from 143 patients receiving HAART, and from 391 naïve patients by on-line tools CPR V.6.0 and HIVdb Program v.7.0.

Results. 5.88% (23/391 samples) of naïve patients were infected by drug resistant viruses and 43.36% (62/143 samples) of viral samples from treated patients harbored DRM. The most frequent mutation in viruses among naïve patients was K103N (8 /23 samples-34.78%), on the second place in this group was M184V (5/23 samples 21, 74%). Another 3 samples (13, 04%) contained G190S mutation. In viral samples from treated patients there was another frequency of occurring mutations. The most frequent mutation was M184V (50/62 samples-80, 65%). K103N mutation was found in 15 samples (24, 19%); G190S-in 12 samples (19, 35%). In both groups of patients we found the low frequency of DRM to protease inhibitors.

Conclusion. The prevalence of DRM in Russia from 2011 to 2015 among naïve patients was 5, 88% and among treated patients 43, 36%.

The most frequent mutation in samples from naïve patients was K103N (34, 78%); and in samples from treated patients – M184V (80, 65%).

The highest level of drug resistance was found to drugs commonly used in first-line regimens of HAART, according to national protocols of HIV-1 treatment (EFV, NVP, 3TC).

Low prevalence of drug resistance to protease inhibitors in both groups of samples shows, that this class of antiretroviral drugs is high effective in Russia.

Discussion. Despite HIV-1 DRM spreading in Russia HAART schemes used in our country are effective, because they includes drugs belonged to different antiretroviral classes and may successfully suppress viral replication. However, monitoring of HIV-1 drug resistance in Russia should be ongoing and the results of this monitoring are important for choosing first-line regimens of HAART.

no publications

Supervisor(s): Pokrovskaya Anastasia Vadimovna assistant lecturer, Department of Infectious Diseases of RUDN, Kireev Dmitry Evgenevich research fellow Central Research Institute of Epidemiology

Technical challenges to integrating ICT approaches into laparoscopic training

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Background: Minimally invasive surgeries are increasing worldwide creating a large need for effective and cost effective training methods for novel surgeons and medical students. I will describe some of the available technology and the different challenges with each. Not only the training but the evaluation of the training is important, and I will outline some basic approaches utilized. Finally I will recommend what I think is the best solution for a ICT approach to training for laparoscopic procedures.

Methods: Pubmed searches for "laparoscopic training methods" and supervisor recommended articles to read.

Conclusions: There are two main approaches to utilizing ICT in laparoscopic training. 1) simulate a virtual surgery using an advanced tracking system. 2) use laparoscopic tools to train psychomotor skills in a 3D virtual environment. The kheiron training system (KTS) is an example of the latter where a serious game is controlled using a laparoscopic training box with real laparoscopic graspers being tracked by a webcam. Other serious gaming systems such as "Underground" game by grendel use a specialized gaming system with custom made controllers to control the virtual environment. Both have their advantages and disadvantages. Simulating real laparoscopic surgeries have required more advanced controllers and more complex simulations. Because of their complexity they are prohibitively expensive and therefore availability is an issue. To mediate the gap between these two categories I have started the process of developing a laparoscopic controller that is very cheap to build, yet precise enough to be used in laparoscopic surgery simulations. In an ICT training solution, much more statistical data is available and we can measure skill based on many more metrics than classical training affords us. Classical training usually gives us feedback on end-result and the time taken, whereas ICT can describe the economy of movement, the errors made during the procedure, and many other metrics as well.

around 220 scientific papers and more than 148 conference publications (57 invited lecture) IF: 202,599.
(<https://vm.mtmt.hu/www/index.php?AuthorID=10004445>)

Supervisor(s): Dr. Weber György Director, Department of Surgical Research and Techniques

Incidence of markers of atherosclerosis and arteriosclerosis in patients with arterial hypertension and type 2 diabetes mellitus

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Objective. We aimed to study the degree of atherosclerosis and arterial stiffness in patients with arterial hypertension (HTN) and type 2 diabetes mellitus (DM).

Materials and methods. The cross-sectional study included 55 patients with HTN and DM (19 (38%) male, mean age 61.6±12.7 years, mean office blood pressure (BP) 141.7±25.7/84.0±10.9 mmHg, heart rate 75.4±10.2 beats/min), mean aortic BP 136.0±21.2/76.4±11.2, glomerular filtrate rate 64±18.4 ml/min/1.73m², low-density lipoprotein 3.4±1.19 mmol/l). Target HbA1c levels were reached in 6 (10.9%) patients. All participants were treated with ACE inhibitors, 12 (21.8%) with beta-blockers, 51 (92.7%) calcium channel blockers, 35 (63.6%) - thiazide diuretics, 4 (7.27%) patients received statins. Target BP <140/85 mmHg was reached in 29 (52.7%). Carotid-femoral (CF) and carotid-radial (CR) pulse wave velocity (PWV), Sphygmocor, AtCor), cardio-ankle vascular index (CAVI) and ankle-brachial index (ABI) (VaSera 1500, Fukuda Denshi) were measured. Increased arterial stiffness was defined as pulse pressure (PP) > 60 mmHg, PWV >10 m/s, CAVI >9.0, atherosclerosis - as ABI <0.9. ABI >1.3 indicated noncompressible arteries. Aortic-to-peripheral arteries stiffness gradient was assessed by CF-PWV/CR-PWV ratio with values >1 indicating its the loss.

Results. Mean PP values were 61.0±14.3 mmHg; 10 (18.1%) patients had PP > 60 mmHg. Mean CR-PWV was 7.7±1.18 m/s, mean CF-PWV – 10.3±2.0 m/s, CF-PWV >10 m/s was noted in 15 (27.2%) patients. Mean stiffness gradient was 1.3±0.37, CF-PWV/CR-PWV >1 were found in 51 (92.7%) patients. Mean CAVI was 8.5±1.8, CAVI > 9.0 – in 23 (49%) patients. Mean ABI was 1.03±0.1, ABI < 0.9 was present in 5 (9%), ABI >1.3 in 2 (3.6%) patients.

Conclusions. In patients with HTN and DM receiving effective antihypertensive treatment in 52.7% of cases markers of arterial stiffness are more prevalent than markers of atherosclerosis. The prevalence of arterial stiffness depends on the diagnostic method used: the highest number of patients is diagnosed with increased arterial stiffness by CAVI measurement, and the lowest number – by PP measurement. This may reflect the greater sensitivity of PP to antihypertensive therapy. Typically patients with HTN and type 2 DM present with an early loss of stiffness gradient from aorta to peripheral arteries that may reflect early vascular aging.

Don't have.

Supervisor(s): Kobalava Zhanna Davidovna professor,
Department of Internal Medicine

Shift in relative contribution of longitudinal and radial motion to global right ventricular function in heart transplant patients

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Longitudinal shortening is considered to be the most important motion determining right ventricular (RV) function. However, the radial direction (“bellows” effect) can gain particular importance in certain conditions.

Our aim was to quantify the longitudinal and the radial components of RV performance using three-dimensional (3D) echocardiography in patients after heart transplantation (HTX) and assess their relative contribution to RV function in time.

Fifty-one HTX patients and 35 age- and gender matched healthy volunteers were enrolled. Fifteen HTX patients also completed one-year follow up. Beyond conventional echocardiographic protocol, full volume datasets were acquired using multi-beat reconstruction from 4 or 6 cardiac cycles. Using dedicated software for RV 3D and speckle-tracking analysis (4D RV-Function 2), 3D beutel model was created and exported volume-by-volume throughout the cardiac cycle. Beside end-diastolic volume (EDV) and total ejection fraction (TEF), we quantified longitudinal (LEF) and radial ejection fraction (REF) by decomposing the motion of each vertex of the reconstructed 3D beutel model along three orthogonal axes and omitting the other two directions.

EDV was higher, EF was mildly decreased in HTX patients compared to controls (HTX vs. control; EDV: 96±27 vs. 80±26 mL, EF: 47±7 vs. 51±4%, both p<0.01). In normal subjects, EF was mainly determined by longitudinal motion (LEF β=0.64, REF β=0.54, R²=0.52, p<0.001), however, in HTX patients the radial motion became far dominant (LEF β=0.49, REF β=0.84, R²=0.87, p<0.001). After one-year follow up, EDV and EF did not change significantly (EDV: 96±27 to 101±21 mL, EF: 47±7 vs. 52±9%, both p=NS). Notably, longitudinal function improved in time (LEF: 12±4 to 15±5%, TAPSE: 14±3 to 17±3mm, free wall longitudinal strain: -19±6 to -26±5%, all p<0.05). Nevertheless, radial function remained dominant (LEF β=0.48, REF β=0.66, R²=0.65, p<0.001). TAPSE and free wall longitudinal strain correlated with the time elapsed after HTX (r=0.57 and r=-0.48, respectively, both p<0.001).

Our software allows to quantify longitudinal and radial motion of the RV separately using 3D analysis. Current results confirm the empirical phenomenon on the superiority of radial motion in determining RV function in HTX patients. In time, longitudinal function may recover, however, radial motion remains dominant.

Orv Hetil. 2016 Jul;157(29):1139-46. doi:
10.1556/650.2016.30491.

Assessment of the right ventricular anatomy and function by advanced echocardiography: pathological and physiological insights [Article in Hungarian] Lakatos B, Kovács A, Tokodi M, Doronina A, Merkely B

Supervisor(s): Attila Kovács MD PhD medical resident in cardiology, Department of Cardiology, Bálint Lakatos MD PhD student

Department of CardiologyNeurological manifestations of acute rheumatic fever

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Rheumatic chorea is one of the main diagnostic criteria of acute rheumatic fever (ARF). It's delayed manifestation of the disease.

Objective: to determine the frequency, the structure of the clinical manifestations of rheumatic chorea and approaches to therapy in Moscow children.

Methods: 56 children 4-17 years old with rheumatic fever, hospitalized in the Morozovskaya Children's Clinical Hospital in 2001-2015 were included in the study, among them – 24 with chorea. The following methods were used: clinical and medical history, laboratory and instrumental (ECG, echocardiogram, CT scan and MRI of the brain, EEG, electroneuromyography).

Results: In pre-hospital period chorea has been the most difficult to diagnose. The mistaken diagnoses in chorea (30%) were reported as: acute ischemic stroke, the brain tumor, stem encephalitis, convulsions. The high incidence of chorea in rheumatic fever patients was revealed (43% - 24 patients): the isolated form of chorea - 12.5% (7), the combined form - 30.4%(17) Chorea clinically was manifested as choreiform movements, muscle weakness, hypotonia, (chorea paralytica in 2 patients), gait disturbance, difficulty in writing and speaking, hyperreflexia, autonomic, emotional lability. The neurological manifestations in ARF were significantly more frequent in children with a history of neurological anamnesis ($p < 0,05$). A history and laboratory confirmation of streptococcal infection in rheumatic fever occurs much less frequently ($p = 0,02$) in patients with isolated chorea (45.8%) compared with patients without damage of the nervous system (69%).

Conclusion: The problem of rheumatic fever remains an urgent and requires attention from the medical community. Chorea is the most difficult for the differential diagnosis among all manifestation of rheumatic fever. Even isolated chorea may later result in chronic rheumatic heart disease. Corticosteroids (prednisone) must be included in chorea treatment in addition to antibacterial drugs and drugs that affect the metabolism of dopamine.

Novikova Yu.Yu., Lapshin A.A. Modern frequency and clinical features of extracardiac manifestations of acute rheumatic fever in children.

M.G. Kantemirova, O.A. Korovina, V.A. Artamonova, Yu.Yu. Novikova, V.D. Rusakova, A.A. Shokin, D.Yu. Ovsyannikov, Lapshin A.A. The difficulties in diagnostics of rheumatic chorea in children (case report)

Supervisor(s): Yu.Yu.Novikova scientific advisor, I. Department of Pediatrics

Final results on immunogenicity profile and predictors of ADA development of biosimilar infliximab during the first 12 months of the therapy

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Introduction: Biosimilar infliximab CT-P13 received EMA approval in June 2013 for all indications of the originator product. In the present study we aimed to prospectively evaluate the immunogenicity profile of the biosimilar infliximab and predictors of TDM in IBD during the first year of therapy in a nationwide, multicentre cohort.

Methods: Demographic data were collected and a harmonized monitoring strategy was applied. Clinical and biochemical activity were evaluated at weeks 14, 30 and 54. Routine therapeutic drug monitoring (TDM) was applied. Trough level (TL) and anti-drug antibody (ADA) concentration were measured by ELISA (LT-005, Therdiag, France) at baseline and at 2,6,14,30 and 54 weeks right before anti-TNF administration.

Results: 353 consecutive IBD patients (209 CD and 144 UC patients) were included in the present cohort. 23.4% of CD patients and 19.4% of UC patients had received previous anti-TNF therapy. None of the patients had received infliximab within 12 months prior to initiation of the biosimilar infliximab. 60/51% of CD/UC patients received concomitant immunosuppressives at baseline. Mean TLs were 18.9, 17.3, 7.4, 4.3 and 5.3 $\mu\text{g/ml}$ at weeks 2, 6, 14, 30 and 54 in CD and 19.1, 11.8, 5.0, 3.9 and 4.5 $\mu\text{g/ml}$ UC. Previous anti-TNF therapy was associated with lower early TL-s in both CD (week 2, 14, and 30, $p < 0.05$) and UC (week 2 and 6, $p = 0.03$). ADA positivity rates were 4.3%, 12.0%, 20.9% and 28.6% in naïve patients at weeks 0, 14, 30 and 54 (ntotal= 266, 312, 290 and 210). ADA positivity at week 14 was associated with lower TLs in all CD (week 2, 14 and 30, $p < 0.007$ for all) and UC (week 6, 14 and 30, $p < 0.001$ for all) patients. Concomitant IS use prevented ADA formation in anti-TNF naïve patients (week 14, 30 and 54, $p = 0.01, 0.02$ and 0.004) in CD but not in UC and did not affect clinical remission or response rates. 32 (8.9%) patients had infusion reactions during induction or maintenance treatment, of which 16 patients had received previously infliximab.

Conclusions: Drug TLs and ADAs in IBD patients until week 54 were in line with results reported for the originator in previous studies. Patients with previous exposure to anti-TNFs had lower early TL coupled with ADA positivity and were more likely to develop infusion reactions. Concomitant IS use prevented ADA development in anti-TNF naïve patients.

Supervisor(s): Dr. Lakatos Péter László associate professor, I. Department of Internal Medicine

High incidence and negative prognosis of residual congestion assessed by bioimpedance vector analysis in decompensated heart failure

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Introduction: Systemic congestion is the main cause of hospital readmissions of patients with decompensated heart failure (DHF). The aim of the study was to evaluate changes of hydration status assessed by clinical criteria and bioimpedance vector analysis (BIVA).

Material and methods: In 97 patients admitted with DHF, 68±10 y.o., arterial hypertension 89%, ischemic heart disease 78%, myocardial infarction 45%, atrial fibrillation 59%, diabetes mellitus 42%, known chronic kidney disease 26%, left ventricular ejection fraction (EF) 44±12%. Hydration status was assessed according ESC 2010 Scientific statement and by BIVA using resistance (R) and reactance (Xc), standardized by height (h). Results: 85 (88%) patients discharged with clinical compensation, but only 33 (34%) patients attained compensation of hydration status by BIVA. Patients without vs with compensation by BIVA had lower baseline 6-minute walk distance, lower EF, more pronounced edema, higher NT-proBNP level at discharge (3927±1314 vs 1253±756 pg/ml), lower rate of in-hospital therapy with beta-blockers (75 vs 100%), higher rate of thiazide diuretics (50 vs 18%) and shorter duration of hospitalization. Independent predictors of subclinical congestion according to BIVA were NT-proBNP>1337 pg/ml, Furosemide dosage >90 mg/day, ejection fraction <40%, evidence of congestion on X-Ray. Subclinical congestion by BIVA at discharge was associated with higher rate of hospital readmission and death in 6 month.

Conclusion: Despite the regress of clinical symptoms, at the time of discharge 66% of patients had signs of subclinical congestion according to BIVA. Subclinical congestion was associated with negative prognosis. Discussion: Assessment congestion by BIVA help to achieve adequate fluid balance status in patients with DHF and can be used to identify high-risk patients in order to optimize treatment and reduce the incidence of complications.

Don't have

Supervisor(s): Kobalava Z.D. professor, Department of Propaedeutics of Internal Medicine

MIT TEGYEK, HA BETEG A GYERMEKEM?

„A felnőttek mindent előre tudnak. Azt is, hogy leesem onnan, azt is, hogy öszszetöröm, azt is, hogy felgyújtom, azt is, hogy kiöntöm, azt is, hogy megfázom, azt is, hogy tönkreteszem, és azt is, hogy nem lesz ennek jó vége.”

– írta Janikovszky Éva.



DE VAJON TUDJÁK-E, HA MINDEZ BEKÖVETKEZIK, MIT TEGYENEK?

A Cseh Áron, Krivácsy Péter és Szabó Attila szerkesztésében megjelent könyv segít eldönteni, hogy betegség, baleset esetén mekkora a baj, kell-e szakemberhez fordulni. Praktikus tanácsok, útmutatók beteg gyermekünk otthoni ellátásával kapcsolatban.

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Strategy for use of different dorsal instrumentations in children with adolescent idiopathic scoliosis

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It's well known that Heuter-Volkman law contributes to progression of spinal deformity forcing vertebrae to turn into wedge-shaped. Not all of the dorsal instrumentations for AIS treatment studied for influencing on post-op spinal growth.

The aim of study is to define indications for use of different dorsal instrumentations in children with AIS according to post-op spinal growth assessment.

We studied the results of treatment 258 children with AIS. Patients were divided into 3 groups: 1st group (198) instrumented with hook instrumentation with sliding rods (HISR). 2nd group (22) instrumented with hook instrumentation with locked rods (HILR). 3rd group (44) instrumented with transpedicular screw fixation (TSF). Complex analysis of all scoliosis deformity parameters was carried out with mean follow-up of 27,9±0,7 months. Spinal growth assessment made on plain AP radiographs by evaluation of some absolute and relative parameters of major curve, such as concave-convex spinal height ratio (CCS), concave-convex vertebral body height ratio (CCVB) and others. Statistical analysis was made in Statistica 10.0 using K-W, Wilcoxon test, Spearman criteria and Pearson Chi-Square for appropriate variables.

Highest correction rate (CR) early after operation were obtained in 1st group (76,6±0,9%, p<0,001), however the highest rate of rod breakage/migration (10,9%, p=0,0009) and reoperations (15,5%, p=0,008) mostly in age of 15-17 (67% migrations and 50% breakages) noticed. Highest CR increase on final follow-up was obtained in 3rd group (+2,3±0,4%, p=0,000), while loss of CR obtained in 2nd group (-1,7±1,3%, p=0,000). CCS and CCVB increased from early post-op period to final follow-up in 1st group (CCS +0,02±0,001; CCVB +0,04±0,001) and in 3rd group (CCS +0,01±0,004; CCVB +0,03±0,003) due to decreasing of pressure on both concave and convex sides of terminal vertebral growth plates in contrast with inversion of Hueter-Volkman law in 1st group.

HISR can be used in children with AIS before 13 years old and Risser 0-3 with changing instrumentation to TSF before age of 16 due to a high complications risk. It's preferably to use TSF in children aged more than 13 even with Risser 1-3 due to physiological vertebral bodies remodeling. HILR should be used only in children reached Risser 4 after age of 13 if there are contraindications for using TSF due to a loss of correction.

Koroteev VV, Kretyashin VM, Malchenko OA, Tarasov NI;
Complex approach to operative correction of dysplastic progressive scoliosis in children; J. Ped. Surg. 2012#2; p16-19; ISSN 2412-0677

Semenov AV; Arthroscopy as the main method in diagnostics and treatment of osteochondropathy of the knee-joint area in children; 2014

Supervisor(s): Vladimir Koroteev scientific advisor,
Department of Orthopedics

Assessment of left ventricular reverse remodeling by cardiac CT after transcatheter aortic valve implantation using CT angiography.

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Background: Aortic stenosis (AS) instigates pressure overload of myocardial chambers and in particular the left ventricle (LV), resulting in LV hypertrophy and remodeling. This process entails structural and functional changes leading to poor clinical outcomes. Transcatheter aortic valve implantation (TAVI) has rapidly emerged as a safe and effective treatment option for high risk patients with severe AS. CT provides reliable and reproducible assessment of structural anatomical data as well as remodeling processes. Therefore, we aimed to assess the impact of TAVI procedure on the LV remodeling manifested by measurable LV mass changes based on CT.

Methods: We performed retrospectively gated CT angiography for the planning and follow-up of TAVI procedure in 20 patients. We measured LV mass and volume on serial CT images using a semi-automated software. Epi- and endocardial contours were manually adjusted. All measurements were performed in random order blinded to the scan data and patient data to reduce retrospective bias. Binary variables are reported by percentages, continuous variables are reported as mean ± SD or median with interquartile range as appropriate. Pre- and post-procedural left ventricular mass and volumes were compared using Wilcoxon signed rank test.

Results: A total of 20 patients were included in our study: mean age was 76.5 ± 14.1 years, 55% were male and BMI was 25.3 ± 3.6 kg/m². We found significant reduction in LV mass after TAVI procedure: 179 [239.9-157.6] grams for pre- and 129 [150.2-104.5] grams for post-TAVI, respectively, p<0.01. LV end-diastolic volumes increased significantly: baseline LV volume: 85.4 [127.3-59.3] ml, post TAVI LV volume: 122.2 [159.4-108.5] ml respectively, p<0.01. The average time since implant was 1.2 ± 0.8 years for the follow-up scans.

Conclusion: Significant regression of LV mass was observed after TAVI procedure that is presumably associated with the reverse remodeling of the left ventricular structure.

No other publications in this field at the time.

Supervisor(s): Bálint Szilveszter senior research fellow,
MTA-SE Cardiovascular Imaging Research Group, Heart and Vascular Center, Semmelweis University, Pál Maurovich-Horvat senior lecturer MTA-SE Cardiovascular Imaging Research Group, Heart and Vascular Center, Semmelweis University

Hereditary breast and ovarian cancer management

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Introduction. The problem of hereditary breast and ovarian cancer is coming more and more up to date. BRCA1 mutation carriers have a risk of 40-85% to develop breast cancer lifetime and 25-65% to develop ovarian cancer. BRCA2 mutation carriers have a 40-85% risk of developing breast cancer and 15-20% for ovarian cancer. ATM mutation carriers have a 60% risk of breast cancer development through the life. There are several other gene mutations associated with high risk of breast and ovarian cancer development. Therefore, there is a high need to find the best option of clinical management for these patients.

Methods. During the research we have analyzed several strategies of hereditary breast and ovarian cancer patients management suggested in the world's literature and compared them with our strategies in National Cancer Institute of Ukraine.

Results. As for chemoprevention, in premenopausal patients tamoxifen is an approved option to reduce breast cancer risk, especially ER-positive cancer (50%). In postmenopausal women, aromatase inhibitors seem to be more efficient, however there is no evidence regarding their use because of bone loss. Surgical strategies give a lot better reduction rates: bilateral prophylactic mastectomy gives more than 90% reduction in breast cancer development risk, and prophylactic salpingo-oophorectomy gives 80-90% risk reduction of ovarian cancer and 40-50% risk reduction of breast cancer. In breast cancer department of National Cancer Institute we noticed an increase of prophylactic subcutaneous mastectomies with implant-based reconstruction for the last several years. Patients find this option as the most effective oncologically and with the best esthetic outcome.

Conclusion. Although there is a need of further research with a higher amount of patients, so far we can conclude that there is a tendency of increase in providing a surgical prophylactic treatment for patients with hereditary breast and ovarian cancer. This strategy gives an approved higher cancer risk reduction result and a good esthetic view after reconstructive surgery.

Keywords. BRCA mutations, bilateral prophylactic mastectomy

No former publications.

Supervisor(s): Igor Motuzyuk associate professor, Oncology Department, Bogomolets National Medical University, Oleg Sydorchuk associate professor Oncology Department, Bogomolets National Medical University

Detailed segmental anatomy of intrahepatic biliary system for advanced liver surgery and partial liver transplantation

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Introduction: In the last couple of decades liver surgery has improved greatly. New techniques were developed such as laparoscopic and/or parenchyma sparing liver surgery, partial-, segmental or living donor liver transplantation. In the new era of advanced liver surgery the precise knowledge of intrahepatic anatomical variations of bile ducts are particularly important in the light of the high incidence of postoperative complications in the bile duct system.

Aim: Our aim was to provide the best ever detailed description of variations in the intrahepatic bile duct branching system at segmental level to improve safety in liver surgery.

Materials and Methods: 50 human liver preparations were made with our specially designed corrosion cast method. The biliary casts were studied, analyzed and photo documented.

Results: With this study we provide the most detailed data recording on the segmental anatomy of intrahepatic bile duct system in the Hungarian population. Among the anatomical variations and their sub variations were described and some of these are not known in the international literature.

Conclusion: By the improved knowledge on intrahepatic biliary variations we may contribute to a safer hepatic surgery resulting in less intra- and postoperative bile duct complications. Thus a careful preoperative planning according to the actual biliary variation/s is mandatory.

no publications

Supervisor(s): Zoltán Máthé professor, Department of Transplantation and Surgery, Mátyás Kiss associate professor Department of Anatomy, Histology and Embryology

Surgery treatment for Synchronous Neuroendocrine Tumors Liver Metastases (SNTLM)

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Background. The aim of this study was to estimate postoperative outcomes of patients with SNTLM treated with simultaneous primary tumor resection and hepatectomy.

Methods. Patients underwent simultaneous surgical resection for SNTLM from any primary were identified from a prospective database at our institution between May 2005 and September 2016. Clinicopathologic, operative, and perioperative data, complications, and grade of complications were reviewed to evaluate selection criteria, operative methods, and perioperative outcomes.

Results. Thirty-nine patients were identified. The median of age was 51.5 years (range 3 – 64.5 years). 46,2% of patients were female. Nine patient (23%) had NETs of pancreas, 11 (28,2%) had gastric NETs, 21% - colorectal primary and 12,8% - jejunum, and 6 (15,4%) - other localizations. Liver surgical procedures included major liver resection in 11 cases: 7 hemihepatectomy, 1 meso-hepatectomy, 3 extended hemihepatectomy. The mean postoperative hospital stay was 13.5 days (range,7-28 days). Six patients (15,4%) had postoperative complications. There were no operative deaths. The mean follow-up period was 6.5 years (range 18 days to 10 years); 36 patients (92,3%) are alive, 3 died of progressive tumor, and 24 (61,5%) are disease-free. The actuarial overall survival rate is 82% at 5 years.

Conclusions. Surgical management of hepatic metastases from neuroendocrine tumors is associated with significant long-term survival rates. Simultaneous resection is an acceptable option in patients with synchronous neuroendocrine tumors metastasis.

Keywords: neuroendocrine, carcinoid, synchronous liver metastases, simultaneous liver resection

No former publications.

Supervisor(s): Olena Kolesnik professor, Abdominal Oncology Department, National Cancer Institute, Andrii Lukashenko associate professor Abdominal Oncology Department, National Cancer Institute

Validation of different implant stability measurements in vitro using three different implant macro designs

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Introduction: It is a challenge to rate the large variations of dental implants used in hard tissue reconstruction. Insertion torque measurements are particularly important, since torque parameters provide a lot of information about implantation procedure. The aim of the present study was to validate and compare the sensitivity of different stability measurements of intraosseous implants using 3 different implant geometries in polyurethane artificial bone blocks (D1-D5).

Materials and methods: Polyurethane artificial bone blocks were utilised with different densities from D1 to D5. Custom-made implants were designed in three shapes: full threaded (FTh), half threaded (HTh), without threads (NTh) (divided in three groups). Instron 5960 – PTS system were used to measure torque insertion and pull-out values (peak values, Newton [N]). Periotest device (Periotest value [Pt] and Osstell resonance device (Implant stability Quotient [ISQ]) were used for non-invasive measurements. Each implant geometry in each bone density were measured 5 times.

Results: We found significant differences between the different implant macro designs by the pull-out tests. In each bone density we got a significant difference between pull out values. For bone density D3 the pull-out force is 52.6 ± 18.3 N for FTh group, 2.6 ± 0.8 N for NTh, in D4 bone the pull out force values are as follow: 41.7 ± 4.0 N, 21.4 ± 2.6 N and 0.8 ± 0.3 N for FTh, HTh and NTh respectively. On the other hand, we found that Osstell measurements are less sensitive to implant type. Using Osstell test, we only find significant difference between FTh and HTh values in D3 bone (22.9 ± 4.2 ISQ vs 5.3 ± 1.9 ISQ). The Periotest evaluation showed also significant differences between three implant geometries in D2 (FTh vs. HTh: -0.4 ± 0.5 Pt vs. 2.2 ± 0.5 Pt; FTh vs. NTh: -0.4 ± 0.5 Pt vs. 2.3 ± 0.3 Pt) and D5 (FTh vs. NTh: 11.1 ± 3 Pt vs. $24.1 \pm 2,5$ Pt; HTh vs. NTh: 9.8 ± 0.6 Pt vs. $24.1 \pm 2,5$ Pt) densities.

Conclusion: Our results show that different implant designs and bone-densities substantially affect implant stability in artificial bone. Our complex methodology using both torque force, RFA and pull-out measurements offers a reliable and inexpensive tool for quantitative in vitro testing of new implant designs.

Supervisor(s): Sándor Farkasdi PhD student, Department of Oral Biology, Dávid Pammer assistant lecturer, BME Department of Materials Science and Engineering

The prevalence of molar-incisor hypomineralisation in hungarian population and the main etiological factors

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Background: The Molar-Incisor Hypomineralisation Syndrome (MIH) is a developmental defect caused by enamel matrix malformation of the permanent first molars and incisors. The malformation is due to multifactorial ameloblast cell dysfunction. There has been a wide variation in MIH prevalence to be reported. It seems to differ with regions and various birth cohorts. Following tooth eruption hypomineralised dental hard tissues with high porosity are quickly lost with rapid caries development. Hypersensitivity and the moderate adhesion capacity to dental materials make the clinical management harder. Complications for clinicians include complexity in treatment planning and treatment implementation, poor prognosis of the restorations, difficulty in achieving pain control during treatment and behaviour management problems.

Aim: This research aims to provide a picture of the prevalence of MIH in Hungary. Furthermore, the study highlights on the most probable etiological factors of the disease and according to family history.

Design: Patients age groups of 7 to 12 years arriving at Semmelweis University, Department of Paediatric Dentistry and Orthodontics for general dental examination between 2014 and 2016 were included in the study. The criteria for acceptance were the presence of MIH of the first permanent molars and incisors. Following photo documentations and detailed anamnesis, special attention was given to proper nutrition, oral hygiene and individualized dental prevention, thus eliminating the environmental factors. Statistical analysis was made by using Fisher's exact.

Results: A total of 573 patients were examined, male/female ratio 0.9. 17 of the girls (5.86%) and 10 of the boys (3.53%) presented MIH, for a total prevalence of 4.7%. In the main etiological factors there was no statistically significant difference ($p \leq 0.05$).

Conclusion: Global prevalence rates are highly variable in the literature, ranging from almost 2 up to 40%. The MIH prevalence found in this study was lower compared with other countries. Both, prevalence results and those from the analysis of the etiological factors could be due to the low number of the participants. For MIH patients early diagnosis and treatment are essentially important. Therefore, the applied treatment methods should follow the principles of minimal invasive dentistry.

Arresting progression of molar-incisor hypomineralisation (MIH) syndrome on permanent first molars - Case presentation

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Supervisor(s): Dr. Rózsa Noémi Katinka PhD, Msc associate professor, Department of Pedodontics and Orthodontics, Dr. Mlinkó Éva clinical specialist Department of Pedodontics and Orthodontics

Comperative enantioseparation of neutral drugs using polysaccharide-type chiral stationary phases in polar organic mode

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Direct liquid chromatographic resolution using chiral stationary phases is the golden standard in chiral separations and polysaccharide-based columns are the most commonly used in this field.

In the current study the enantioseparation capabilities of four polysaccharide-type chiral columns (Chiralpak AD, Chiralpak AS, Chiralcel OD and Chiralcel OJ) were investigated in polar organic mobile phase mode using pure methanol, acetonitrile, ethanol and isopropanol as mobile phase. Seven neutral drugs including - lenalidomide, praziquantel, racecadotril, tolvaptan, tofisopam, guanfacine and its prodrug guanfacine ethyl carbamate – with various structural and pharmacological properties were chosen for investigation. Screening was performed at 0.5 ml/min flow rate and over the temperature range of 5-40 °C. Among the investigated stationary phases the cellulose tris(3,5-dimethylphenylcarbamate) showed the best results by delivering enantioseparation for all of the seven investigated compounds. Between the amylose based columns the amylose tris(3,5-dimethylphenylcarbamate) containing Chiralpak AD exhibited higher chiral recognition ability compared to amylose tris[(S)- α -methylbenzyl carbamate containing Chiralpak AS.

Among the tested mobile phases, alcohol type solvents were superior over acetonitrile. Classical van't Hoff analyses were applied for the characterization of thermodynamic parameters and revealed that enantioseparations were mainly enthalpy controlled, however in few cases, unexpected, entropy controlled separations were also observed. Enantiopure standards were applied for the determination of the elution order. The study revealed that the polysaccharide backbone and the nature of the substituents can also influence the elution order, moreover in the case of lenalidomide, a solvent dependent reversal of elution order was also observed. After optimization our methods were validated according to the ICH guidelines in terms of linearity, precision, accuracy, limits of detection and quantification. Applications of methods were tested by analysis of pharmaceutical formulations or determination of 0.1% chiral impurity. The developed methods further underline the ease of use of polar organic mobile phase mode with polysaccharide-based stationary phases.

Szabó ZI, Foroughbakhshfasae M, Szócs L, Nagy J, Komjáti B, Noszál B, Tóth G: Stereoselective interactions and liquid chromatographic enantioseparation of thalidomide on cyclodextrin-bonded stationary phases J Incl Phenom Macro 85:(3) pp. 227-236. (2016)

In former research cyclodextrin based columns were used for separation of thalidomide enantiomers, however in the recent study polysaccharide based columns were used in order to separate enantiomers of seven different neutral compounds.

Supervisor(s): Gergő Tóth associate professor, Department of Pharmaceutical Chemistry

Validation of Higuchi's facilitated dissolution method for the solubility measurement of poorly soluble compounds

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Solubility of a substance is of particular importance in pharmaceutical science. This parameter is the rate-limiting factor in oral absorption and its knowledge is essential in the formulation during drug development. Up to now the saturation shake flask method (SSF) is the "gold standard" despite the numerous limitations when dealing with poorly soluble compounds with low dissolution rate.

Facilitated dissolution method (FDM) was first proposed by Higuchi to overcome the extremely long equilibration time for solubility measurement by practically insoluble compounds. He suggested using a small amount (~1%) of water immiscible organic solvent dissolving the compound 200 times better than water, thereby increasing the surface area available for dissolution.

The aim of our work is to perform a systematic validation of FDM and to come across a probable standard protocol in the experimental conditions.

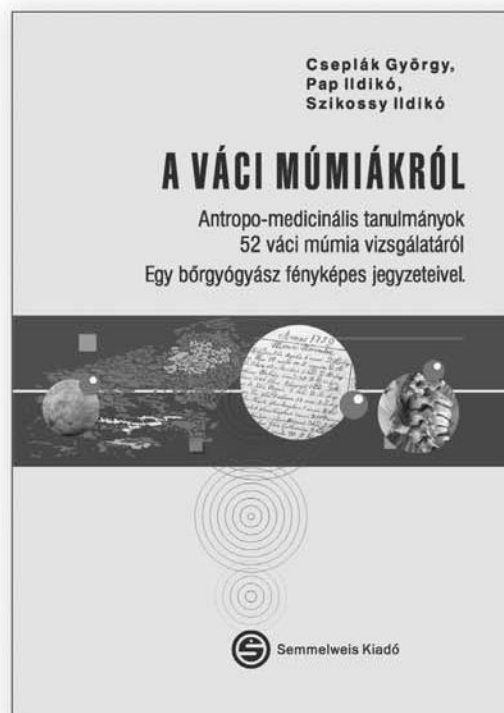
Progesterone (neutral, UV active) was chosen as the model compound. First the solubility was investigated by the SSF method with changing parameters like buffer system, equilibration time and phase separation technique. The solubility of progesterone was found: $S_0 = 7.95 \pm 0.21$ [µg/ml] and used as reference data further in the study. Next progesterone was measured by FDM. The following parameters were changed: type (dodecane, octane, hexane) and volume (0.5-2%) of organic solvent, equilibration time (6-120h) and solid excess. The obtained result by FDM was: 8.00 ± 0.79 [µg/ml] proving the validity of the method. Further we tested other poorly soluble compounds with slow dissolution rate to see whether the FDM could reduce the equilibration time. Experiments showed that octane could not be used as a general solvent since the majority of the compounds tested (14/15) did not dissolve 200 times better than in water. The search for other possible organic solvents continued; dichloroethane and octanol showed to be good solvents and the applicability of these solvents with progesterone was proven. Additionally FDM was applied for digoxin, a compound known to have extremely low dissolution rate.

In the presentation we will introduce these results and the final conclusions.

No previous publications concerning this topic.

T Supervisor(s): *Krisztina Takács-Novák professor,*
Department of Pharmaceutical Chemistry

Cseplák György, Pap Ildikó, Szikossy Ildikó



A VÁCI MÚMIÁKRÓL

Antropo-medicinális tanulmányok
52 váci múmia vizsgálatáról
egy bőrgyógyász fényképes
jegyzeteivel

A könyvben számos, a kutatók számára is meglepőnek bizonyult érdekesség olvasható. A leírt, lefényképezett megfigyelések hozzájárulnak a titokzatos 18. század megértéséhez. Például a hang színét meghatározó pajzsporc méretéből következtetni lehet a múmia hangjának hangszínére. A súlyos betegségben szenvedők ápolatlan körmei a betegség elhúzódását bizonyítják. A már akkor is lyukasztott fülcimpákon a lyukak vannak a lyukasztás a halál előtti időpontjáról. Megfigyelhetjük a korabeli kötszerek minőségét, a kötözések módjait. Olvashatunk a könyvben a ritkán előforduló, méhen belüli keresztelésről is, amely a közelgő, vagy beállt anyai halál miatt válhat szükségessé. Azt is bizonyítani lehetett, hogy császármetszéses szülést is végeztek.

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