Abstracts

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Sessions

T1. RADIOPHARMACOLOGY

T1-1
SYNTHESIS A POTENT FLUORINE-18 LABELLED MCHR1 ANTAGONIST LIGAND OF [18F]FP-PEPP

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INTRODUCTION: The melanin-concentrating hormone receptor1 (MCHr1) — that is found first in the salmon hypophysis — is responsible among others for feeding behavior of mammals [1]. Intracerebral injection of this hormone increases the consumed food, starvation activates the MCH containing neurons. Many pharmaceutical companies are putting effort to develop an antagonist to control obesity. On the other hand, there are attempts to activate this receptor in animals for increased food uptake. The development these molecules necessitate the use of a tracer for positron emission tomography. Our aim was to develop a new tracer, to assist in testing forage effects on body weight of waterfowls. The molecule chosen — 4-[(4-[18F] fluorobenzyl)oxy]-1-[4-[2-(pyrrolidin-1-yl)ethoxy]-phenyl]pyridin-2(1H)-one — for labelling had already shown good brain uptake and specificity to the MCHr1 [2]. The aim of our work is to label this compound with F-18 isotopes.
METHODS: The synthesis of the precursor, 4-bromo-1-[4-(2-pyrrolidin-1-yl-ethoxy)--phenyl]-1H-pyridin-2-one (BrPEPP), took place in 3 step starting from 4-bromo-1H-pyridin-2-one. The radio-synthesis started from 2–20 GBq F-18 isotopes with the fluorination of N,N,N-trimethyl anilinium triflate (80 °C, 5 min). The resulted [18F]Fluorobezaldehyde was reduced by $NaBH_4$ on a C18 SepPak column, then was dried with He flow. The endpoint of drying was detected by measurements of the effluent gas temperature. The optimized condition for the labeling between the BrPEPP and the [18F]fluorobenzyl alcohol was found to 100°C, for 15 minutes reaction in DMF in the presence of NaH. The final product was purified on a semi-preparative Nucleodur Pyramide HPLC column, and formulated with ethanol and saline. The labeled compound was tested in healthy mice and rats, as well as on different brain slices.
RESULTS: The overall yield of the 3 step radiochemical reaction was 20 ± 10% based on the isolated product of 100–3000 MBq. The radiochemical purity was > 98%, and the molar radioactivity was found to be 112 ± 104 GBq/μmol at the end of synthesis. In the in-vivo and in-vitro investigations had shown specific uptake in the hypothalamus area of the brains. Furthermore, we had observed accumulation of the tracer in the adrenal gland, salivary glands, small intestine and in the heart.
CONCLUSION: As a result, we have a new useful tracer for investigating obesity in humans and to establish scientifically proven feeding strategies. The labeling took place on the aromatic ring, giving metabolic stability of the tracer.
Acknowledgements: This work was supported by grants FP7-PEOPLE-2012-ITN (316882 RADIOMI project), and AGR_PIAC_13-1-2013-0008.

T1-2
PRODUCTION AND QUALITY CONTROL OF 6-[18F] FLUORO-3,4-DIHYDROXY-L--PHENYLALANINE (FDOPA)

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INTRODUCTION: 6-[18F]fluoro-L-DOPA is one of the oldest PET radiopharmaceuticals. Its synthesis was first described in 1983. Earlier it was mainly used for neuropsychiatric diseases, movement disorders and malignant brain lesions. Nowadays its uses are in a wider range, for example it has been successfully used to diagnose neuroendocrine tumors. The widespread use of this tracer was inhibited, because of the only available complex electrophilic substitution reaction. An increasing number of methods were developed to implement high-yield nucleophilic synthesis in the early 2000s. Our goal was to synthetize and introduce this tracer to broaden the Hungarian radiopharmaceutical palette.
METHODS: The synthesis was performed with a cassette based synthesizer installed with the appropriate software, built and developed by TRASIS SA. The first step was the radiolabeling of the 6-nitroveratraldehyde precursor. This reaction was followed by reduction and halogenation. The forming of the whole molecule structure was achieved using a Schiff base. Then the protecting groups were removed by acid hydrolysis resulting the molecule of 6-[18F]fluoro-L-DOPA with high enantiomer selectivity. The material was purified by semi-preparative HPLC column, and it was formulated with citrate buffer. The product was sterilized by filtration on a 0.22 μm membrane. The quality control tests were carried out by gas and liquid chromatography and gamma spectrometry. In addition, pH measurements and residual phase transfer catalyst, Kryptofix 2.2.2 color spot tests were performed.
RESULTS: We manufactured pharmacopoeia compliant quality batches. The average decay corrected yield was 70%. The activity concentration of these batches were between 4.1 and 2.8 GBq/ml. The radiochemical purity was typically < 99.5%, and the enantiomeric purity was found about 97%. The product was free of organic solvents that used for the production and pH value was between 4.1–4.4. Kryptofix 2.2.2 content was below 40 μg/ml. Each batch were sterile and non-pyrogenic.
CONCLUSION: On the basis of the results obtained we had applied for a marketing authorization at OGYEI (National Institute of Pharmacy and Nutrition). Uniquely in the country 6-[18F] fluoro-L-DOPA will be available for PET-CT and PET-MR studies at PET MEDICOPUS NONPROFIT Ltd. in the second half of 2017. This would broaden the slim palette of radiopharmaceuticals for PET examinations in Hungary.

T1-3
SIGNIFICANCE OF PH CONTROL IN DETERMINATION OF RADIOCHEMICAL PURITY OF F-18 LABELED TRACERS USING LIQUID CHROMATOGRAPHY

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INTRODUCTION: Synthesis of [18F]FDG as well as [18F]FET is based on participation of [18F] fluoride ions in S_N2 nucleophile reaction. However, liquid chromatographic methods may used in quality control of these radiopharmaceuticals are not useful for detection of [18F]fluoride ions. Determination of free radioactive fluoride could be achieved using additional TLC method. The aim of this work was to examine the effect of pH of the eluent for elution of [18F]fluoride ions to determine the total radiochemical purity by single HPLC method.
METHODS: Composition of the applied HPLC system was as follows: Jasco autosampler, degasser, low pressure gradient valve, pump, radioactivity detector. Waters I-Class system was applied for UPLC measurements. The used analytical columns were Acquity UPLC, BEH Amide 1.7 μm, 3.0 × 100 mm (Waters), LiChroCART NH_2, 5 μm, 250 × 4 mm, (Merck), LiChroCART RP18, 5 μm, 250 × 4 mm, (Merck). Reference materials were prepared either on synthesis modules or manually [1].
RESULTS: In quality control of [18F]FDG the separation of active ingredient from the intermedier [18F]TAG is possible on LiChroCART NH_2 column with MeCN/H_2O (95/5 V/V%). On the other hand, the elution of [18F]fluoride ions is only possible using buffer solution with pH7. The following gradient method is could be applied for determination of total radiochemical purity of [18F]FDG. The elution started with acetonitrile/phosphate buffer (pH7; 5 mM) in the ratio of 85/15 V/V%. To elute [18F]fluoride eluent composition is to be changed to acetonitrile/phosphate buffer (pH7; 5 mM) in the ratio of 5/95 V/V%. Gradient profile: 0 min 100% *A* — 0% *B*, 2 min 100% *A* — 0% *B*, 3 min 0% *A* — 100% *B*, 7 min 0% *A* - 100% *B*. At 2 mL/min flow rate the measurement time was 7 minutes. Retention times: 1.303 min [18F]TAG, 2.485 min [18F] FDG, [18F]fluoride ion 5.143 min. The resolution between [18F]TAG and [18F]FDG was 4.2 and between [18F]FDG and [18F]fluoride was 10.2. The developed method was successfully transferred to UPLC system. In case of UPLC procedure Amide column was applied. The elution started with acetonitrile/ammonium acetate buffer (pH5; 50 mM) in the ratio of 90/10 V/V%. To elute [18F]fluoride eluent composition was changed to ammonium acetate buffer (pH10; 50 mM) in the ratio of 10/90 V/V%. Gradient profile: 0 min 100% *A* — 0% *B* 1.2 mL/min, 1.20 min 100% *A* — 0% *B* 1.2 mL/min, 1.25 min 0% *A* — 100% *B* 0.6 mL/min, 1,50 min 0% *A* — 100% *B* 0.4 mL/min, 5.00 min 0% *A* — 100% *B* 0.4 mL/min. Retention times: [18F]TAG 0.393 min, a [18F]FDG 1.024 min, a [18F]fluoride 3.045 min. The resolution between [18F]TAG and [18F]FDG was 2.8 and between [18F]FDG and [18F]fluoride was 6.9. In case of [18F]FET we implemented the elution of [18F]fluoride ions on LiChroCART RP18 column with pH7 phosphate buffer. The recovery of [18F]fluoride ions was higher than 95%.
CONCLUSION: This work gives recommendations on determination of total radiochemical purity of [18F]FDG as well as [18F]FET using liquid chromatographic technique. Single analytical method could simplify the quality control of tracers as well as to increase the productivity of Q.C. management.
1. Hamacher K, Coenen H, Stöcklin G. J Nucl Med. 1986; 27: 235–238.

T1-4
SYNTHESIS OF F-18 LABELED N-SUCCINIMIDYL 4-[18F] TRIFLUOROMETHYLBENZOATE

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INTRODUCTION: The F-18 isotope is one of the best PET isotope with its 109.7 min half-time, low positron energy and high positron emission rate. Trifluoromethyl group is widely used in drugs as bioisostere group for stabilizing a compound or protecting a reactive methyl group. The aim of our project was to work out a synthesis method of a benzoic acid derivate with trifluoromethyl and active ester group. This derivate can be good for effective labeling compounds with amino group, such as peptides and nanoparticles.
METHODS: The synthesis of the labeling molecule was consisted multiple steps. In the first step ethyl 4-[18F]trifluoromethyl benzoate was made from ethyl 4-iodobenzoate using CuI and methyl chlorodifluoroacetate at 150°C for 20 min with a cross coupling reaction. The derivate was separated on a Macherey-Nagel Nucleodur C18 Pyramid (250 × 10 mm, 10 μm) semi-prep HPLC column. The product was hydrolyzed with tetra-methyl ammonium hydroxide at 90 °C for 5 min. The reaction mixture was passed through a C18 Sep-Pak cartridge and the benzoic acid derivate was eluted. TSTU solution was added and the mixture was heated at 90 °C for 5 min to produce N-succinimidyl 4-[18F]trifluoromethylbenzoate. The quality control was performed on Macherey-Nagel Nucleodur C18 Pyramid (250 × 10 mm, 10 μm) HPLC column with isocratic 70:30 = MeCN:H_2O (0.1% TFA) eluent.
RESULTS: The radiochemical yield of ethyl 4-[18F]trifluoromethyl benzoate was 58 ± 14% (n = 8) with the manual method, but the method was reproduced with automated synthesis, too. The separation of the production on the semi-prep HPLC column resulted pure intermediate product. The hydrolysis of the ethyl 4-[18F]trifluorometyhl benzoate to 4-[18F]trifluorometyhlbenzoic acid had 100% conversion rate. The cleaning process of the benzoic acid derivate was found effective on the C18 Sep-Pak cartridge. The radiochemical yield of the N-succinimidyl 4-[18F] trifluoromethylbenzoate was 88 ± 13% (n = 5).
CONCLUSION: The synthesis of the N-succinimidyl 4-[18F]trifluoromethyl benzoate with [18F] trifluoromethyl group was successful. The active ester group of the molecule makes possible its use for labeling peptides and amino group containing nanoparticles. We successfully worked out a fast and simple analytical process for the separation of the compounds. The automatization of the synthesis is in progress.

T1-5
DEVELOPMENT OF A STOPPED FLOW CAPILLARY SYSTEM FOR RADIOLABELING

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INTRODUCTION: The systematic variation of reaction conditions is required to determine the optimal labeling conditions in order to maximize the yield, the radiochemical purity and the specific activity of the labelled product. This procedure is often time consuming and hampered by the high deviation of experimental results, associated to non-carrier added isotopes. A stopped flow capillary system was developed on the basis of our previous experience with a continous flow system. It enables the fast optimization of labeling conditions of various chelators with 68Ga and 44Sc. The system was designed to handle small reagent volumes for scouting experimets and to be able to scaled up to larger volumes for production.
METHODS: The capillary system consists of three electronically actuated HPLC valves (Rheodyne Titan MHP) interconnected with teflon capillaries (0.25 mm i.d.) and controlled by an Arduino Mega card. The liquid is moved by the aid of a double syringe pump. The reagents are coinjected into a heated PEEK loop (0.15 mm, 25 μl) and — after the predetermined reaction time — injected onto a HPLC column for analysis.
RESULTS: The dependence of RCY on pH and chelator concentration was determined for various chelators (DOTA, NOTA, NOPO) labeled with ^{68}Ga and ^{44}Sc. DOTA and NOTA gave similarly high yields (80–85%) at pH4. 95oC, 5 min, but the NOP O chelator, which is tailored to gallium gave low RCY (20%) with 44Sc. Besides the free chelators, maleimide chelator derivatives (DOTA-, DOTAGA-, NOTA-, NODAGA-maleimide) were also tested in order to simulate the labeling of peptide conjugated chelators. In the case of gallium labeling, the difference between the chelators was small among the applied experimental conditions. Scandium labeling experiments showed more significant differences, and DOTAGA- and NODAGA-maleimide were found to be better than the DOTA and the NOTA derivatives. This can be explained by the higher stability of scandium complexes with high coordination numbers (8 for DOTAGA and NODAGA vs. 7 for DOTA and NOTA).
CONCLUSION: The developed system is more flexible than its previous version, which applied continuous flow of water to move the reagents across the system. The stopped flow operation enables the simple change of residence time and decreases activity loss caused by diffusion. 70% of the reaction mixture is injected onto the HPLC column for separation, which was only 50% for the previous system. The intra-day reproducibility of the radiochemical yield was high (1% RSD, n = 5).

T1-6
LOCAL Preparation and analysis of 68-GA-DOTA-TOC injection for clinical application

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INTRODUCTION: Preparation of radiopharmaceuticals for diagnostic and therapeutic application at the user's location provides new opportunities for the nuclear medicine laboratories.
We would like to demonstrate the requirements of the European Pharmacopeia (Pharm. Eur.8.7.,04/2016:54900) with a practical example in order to facilitate the initial activities of local preparation of radiopharmaceuticals.
METHODS: During the labelling reaction the used materials were very pure and heavy metals-free were the followings: DOTA-TOC GMP grade; Sodium acetate, highly purified water and 96% ethanol (Merck). 50 μg DOTA-TOC conjugate were dissolved in 200 μl 0.25M Sodium acetate buffer (pH 5.0) then we mixed it with the 1mL volume, 100–150MBq activities fractionated eluted 68-Ga chloride 0.05N HCl solution in the labelling vial. After mixing the reaction solution was heated at 90°C for 10 minutes, then after chilling down to room temperature it was filtered with 0.22 micrometer membrane filter. The final volume of the injection was set to 5 mL with sterile PBS solution.
After this process the analytical examinations were performed. Radiochemical purity was determined by radio-HPLC, ITLC and paper chromatography methods.
RESULTS: The radiochemical purity results of the three consecutive labelling reaction were the followings: 1) 99.1%; 2) 98.5%; 3) 98.3%.
The quantities of Impurity A and B together were in all cases around 1%. The labelled solution pH value was between 4.5–5.0. The solution for injection was clear, transparent; ethanol content was below 10%. Sterility and bacterial endotoxins tests were performed retrospectively and the results were conforming as well (sterile and less than 175 IU/mL). Organ distribution test performed on rats showed quick excretion through kidney (more than 70% I.D.) and low blood activity (less than 1.2% I.D.). We would like to continue with further examinations required by the legislations, so as the impact analysis of the heavy metal impurities (Fe, Zn) of the generator's mother element (Ge). Likewise, the integrity test of the membrane filter used for the sterile filtration is performed each time and the aseptic conditions of the preparation are check by Media-Fill.
CONCLUSION: The local ex tempore prepared 68-Ga-DOTA-TOC injections for PET/CT diagnosis of neuroendocrine tumors conforms to the prescriptions of the Pharmacopeia based on the qualifying tests we performed.
After performing and validating the additional tests with the preparation of its confirming documentation, this preparation method can support the application for the license of local preparation of radiopharmaceuticals.
The research was realized with the support of GINOP-2.1.1-15-2015-00592 project.

T2. IMAGING TECHNIQUE, IMAGE PROCESSING

T2-1
FEASIBILITY STUDY OF A HUMAN TISSUE EQUIVALENT PHANTOM

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INTRODUCTION: In the recent years the emission and transmission imaging techniques combining PET/CT and SPECT/CT hybrid devices spread rapidly. Their advantage in addition to the integration of anatomical and functional information, is the correction of radiation attenuation and scatter within the body of the patient. This could be performed using CT segmentation, and therefore, the activity-concentration of the distributed radiopharmaceutical can be measured accurately. The aim of our study was to create a phantom which can represent the entire range of attenuation coefficients specific for the human tissues. This method would be suitable to assure the quality of reconstructions using CT-based attenuation correction (PET, SPECT).
METHODS: To mimic the lung equivalent compartment, a given volume was field with Styrofoam® beads surrounded by isotope in water solution. The fat tissue was imitated by an oil-isotope mixture, and the muscle by a ballistic gel-isotope mixture. Furthermore, the bone section was a hollow shin bone of a cattle. It was possible to generate homogenous activity-distributions using the material combinations mentioned above. In case of the oil mixture, as the applied F18-FDG and TcO4 are water-based, they were firstly evaporized at high temperature, then they were diluted in isopropyl alcohol. Finally, PET/CT and SPECT/CT measurements and reconstructions of the compiled phantom were performed.
RESULTS: We measured (–650)–(–800) HU values in the lung equivalent component, (+50)–(+100) HU values in the ballistic gel, (+400)–(+800) HU values in the bone, and (–50)–(–100) HU values in the oil. The phantom covered the whole Hounsfield Unit spectrum of the tissues of the human body, measured from the lung till the bone. In addition, the measured standard uptake values and activity-concentrations fell within 10% margin of error compared to the values estimated from the known of activity, mass and volume of each compartments.
CONCLUSION: In this study, we proved successfully the introduction of ballistic gel and oil as a possible candidate of new phantom materials. Moreover, this human equivalent phantom (as an easy to create tool) can be an alternative way to support the quality assurance of hybrid devices.

T2-2
IMAGE RECONSTRUCTION OPTIMISATION FOR BRAIN PET/CT

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INTRODUCTION: Positron Emission Tomography (PET) became an essential non-invasive diagnostic imaging technique in the last two decades. Moreover, it plays an increasingly important role in terms of functional brain mapping. The image processing and writing of medical reports after a PET/CT examination needs continuous optimisation to reach more accurate results. Our aim in this study was the optimisation of reconstructions (including post-filtering) for ^{18}F-FDG and ^{11}C-MET brain PET images.
METHODS: Dynamic PET acquisition of the 3D Hoffmann phantom were performed on the MEDISO Anyscan PC and PHILIPS Gemini 64 systems. The applied total activities were primarily estimated based on the literature. The measurement of the phantom corresponded to the routine patinet examination protocol. We made reconstructions using the available options on the MEDISO Anyscan PC acquisition software: varying the number of iterations (from 4 to 16), the voxel-size (4 mm, 3 mm, 2 mm, 1 mm), and appling different post-filters (3D Gauss, 3D Bilateral etc.). During the comparison of the reconstructions, volumes of interests (VOIs) were defined based on segmentation of the CT images. Standard deviation, mean- and variability-coefficients were calculated from the applied VOIs. Furthermore, optimisation of reconstructions was made on real patient datasets, but only in the range that was restricted by the phantom. The patient records were compared based on visual assessment of experienced nuclear medicine physicians.
RESULTS: After more than 100 processed image sequences, our results showed that the dedicated brain images signify higher total counts than the frames of whole body aquisitions. This permits the use of higher number of iterations and the 1–2 mm voxel-size. In case of ^{11}C-Methionine, we received the most optimal recontruction from the raw data using high number of iterations (10–14) and properly parameterized bilateral filter (3 kernel, 1 sigma). However, in case of the ^{18}F-FDG brain examination, even a higher number of iterations led to the optimal result, while using similar filtering.
CONCLUSION: A given type of PET examination requires not only a specified aquisition, but also a dedicated reconstruction with optimized parameters to the specific radiopharmaceutical. The findings of this study made it possible to improve the quality of medical reports at our site.

T2-3

The Impact of the Q.Clear Reconstruction Algorithm on the Quantitative Evaluation of Hepatic Metastases Shown on 18F-FDG-PET/CT Studies — Preliminary Results

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INTRODUCTION: PET/CT scans are routinely reconstructed by iterative algorithms, where a well-known limitation is the worsening of the signal-to-noise ratio when increasing the number of iterations. A novel Bayesian penalized likelihood reconstruction algorithm (Q.Clear) has allowed more iterations without simultaneously significantly increasing noise levels that results in a better signal-background ratio. The aim of our study was to compare this algorithm with the conventional OSEM reconstruction by investigating 18F-FDG-PET/CT studies.

METHODS: We investigated the 18F-FDG-PET/CT studies of 9 patients (6 women, 3 men) and a total of 24 FDG-avid hepatic metastases were included in our sample. The raw data of each patient were reconstructed by both the OSEM and the Q.Clear algorithm. A spheric VOI of 3 cm diameter was placed in the normal hepatic tissue as reference and a spheric VOI was manually adjusted to the metastases, both in an identic location in the two differently reconstructed studies of each patient. The size of the lesions were calculated by the largest axial diamater measured on the CT scans. Standardized uptake values (SUV) based on body weight were calculated, including SUVmax and SUVmean. Noise was defined as the standard deviation of the normal liver parenchyma SUV. Signal-to-noise ratio was given as SUVmean in the normal liver parenchyma divided by the noise. Signal-to-background ratio was defined by SUVmax in a lesion divided by the SUVmean in the normal liver parenchyma. Two-tailed paired sample t-tests were calculated to compare the datasets.

RESULTS: The average size of the lesions was 18 ± 8.85 mm (range: 10–53 mm). The Q.Clear algorithm resulted in significantly higher SUVmax and SUVmean values in the lesions ($p < 0.001$): ΔSUVmax 2.12 ± 1.75; ΔSUVmean 0.50 ± 0.48. The signal-to-background ratio was significantly better with Q.Clear (3.33 ± 2.45 vs. 2.87 ± 2.26; $p < 0.001$) while signal-to-noise and SUVmean-to-noise ratios were not significantly different. The latter can be explained with the (nonsignificantly) higher levels of noise by using Q.Clear.

CONCLUSION: Our study showed that the Q.Clear reconstruction algorithm resulted in better signal-to-background ratios without the decrease of the signal-to-noise ratio in FDG-avid hepatic metastases which leads to better recognition and characterization of the lesions.

T3. ONCOLOGY — PET

T3-1

INCIDENTAL LESIONS IN FDG-PET/CT SCANS

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INTRODUCTION: The modern oncological diagnostics are unimaginable without FDG-PET/CT. During the metabolic information gaining process we often discover different, incidental lesions, which aren't connected to the primary tumours. Our goal in the study was to retrospectively specify the origins of these freshly discovered, independent FDG-avid lesions in „routine" FDG PET/CT scans.

METHODS: We revised 326 FDG-PET/CT exams' results, which are asked by the most different oncologic indications, from 2006 February to 2012 January (229 men, 97 women; average age: 57.4 year). According to the written results we classified the PET findings and separate those FDG-avid lesions, which aren't connected to the primary malignancies. Under the 2 years follow up we could define the incidentalomas exact locations, states and malignancies. The correct histological identifications and the long follow up time were essential in our study, because we could accurately isolate and evaluate the benign and malignant diseases from each other.

RESULTS: 119 abnormal, unexpected, focal lesions were confirmed in 112 patients out of 326. All in all 18 (5.5%) newly detected, separate, primary malignancies were certified, while 19 (5.8%) metastases and 82 (25.1%) benign diseases have been described as well. Locationally, greater part of the incidental lesions were found in the gastrointestinal system and in the head and neck region (35–35), while the respiratory- and urogenital system, the skin and other locations contained the remaining part (30%). In point of the digestive tract the most focal, FDG-avid findings were in the colon (24/42), but none of them was malignant, on the other hand the findings in the stomach and pancreas were decisively more aggressive. The head and neck lesions were often proved to the primary disease's metastasis (10/13). Surprisingly no histological confirmed malignant lesion was detected in the thyroid gland. The other findings in the suprarenal gland and in the lung were equally metastases and newly discovered, primary malignant tumours.

CONCLUSION: In summary, we can detect unexpected, incidental lesions in the third of the FDG-PET/CT scans. Most of them are benign, although significant part of these FDG-avid lesions, approximately and another third part of the all suspicious findings are progressive, malignant, pathological diseases, which raise the patients' mortality. The most false positive signs can be detect in the gastrointestinal system.

T3-2

PREDICTIVE ROLE OF FDG PET/CT IN HEAD AND NECK CANCER TREATED WITH RADIOTHERAPY — PRELIMINARY RESULTS

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INTRODUCTION: FDG PET/CT provides crucial information for the proper staging assessment and radiotherapy planning (RTP) of head and neck cancer patients. Our aim was to search for therapeutic outcome predicting parameters in the pre-treatment functional imaging data.

METHODS: Retrospective evaluation was performed using PET/CT image datasets of 21 head and neck cancer patients. PET/CT was acquired before the therapy, used for RTP and repeated 3–6 months after the completion of therapy for response evaluation. From the pre-treatment image datasets we assessed the SUVmax, SUVmean, Metabolic Tumor Volume (MTV) and Total Lesion Glycolysis (TLG) parameters of the primary tumor. According to the results of the therapeutic response evaluation PET/CT and the clinical follow up two patient subgroups were created in relation to the presence or absence of viable primary tumor tissue. Subgroup related metabolic parameter evaluation was performed (Wilcoxon test).

RESULTS: After radiotherapy in 10/21 cases viable residual tumor tissue was detected on the restaging PET/CT image dataset and 11/21 subjects reached complete remission. For the therapeutic success prediction assessment we were unable to find any correlation with pre-treatment SUVmax and SUVmean values ($p = 0.55$ ill. $p = 0.32$). MTV and TLG parameters however provided statistically significant differences between the two patient subgroups [MTV ($p = 0.008$), LTG ($p = 0.020$)], as a summary MTV proved to be the most useful parameter for therapeutic response prediction.

CONCLUSION: Simple metabolic data provided by FDG PET/CT were unable to predict therapeutic response, while according to our preliminary results complex volume information containing parameters proved to be more useful for this purpose, thus their inclusion to risk stratification may have of additional value. Survey is planned to be followed with more subject and parameter inclusions.

T3-3

EVALUATION OF HEPATIC FDG UPTAKE DURING LYMPHOMA RESPONSE ASSESSMENT PET/CT

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INTRODUCTION: For the FDG PET/CT based visual therapy response assessment of lymphoma liver became the most important reference organ recently. The aim of the current project was to assess the stability of hepatic tracer uptake during chemotherapy treatments and to evaluate the potential change characteristics.

METHODS: Retrospective analysis was performed using the imaging data of 55 lymphoma patients (19 Hodgkin's disease, 36 Non-Hodgkin's lymphoma). All subjects underwent PET/CT for initial staging, after 2–4 cycles of chemotherapy for early response assessment and after completion of 6–8 cycles of therapy for restaging purposes. Hodgkin's disease patients received ABVD therapy, for Non-Hodgkin's lymphoma patients CHOP-based therapeutic regimen was administered. Mean and maximal hepatic standardized tracer uptake values (SUV) — using body weight, lead body mass and body surface area related normalization — were calculated with PERCIST liver reference ROI auto-segmentation tool of Syngo.via image processing application. The average hepatic Hounsfield values (HU) were also calculated using the same VOI on the low-dose CT images. For the evaluation of treatment associated hepatic SUV and HU changes one and two way Tukey's post hoc test was used after analysis of variance. One-way model was used when the type of lymphoma was ignored, and two-way method was assessed when the changes were examined within the two lymphoma subgroups.

RESULTS: None of the performed tests could reveal statistically significant alteration for any of the investigated SUVmax and SUVmean or average HU parameters. Further analysis was performed after creating 3 subgroups from the subjects according to the hepatic HU value changes. In the first group the reduction of hepatic average HU was larger than 10% (17 people), for the 2. group the HU value alteration was less than 10% (29 people). The 3. group contained the subjects with more than 10% increase in HU values (9 people). For the 1. group the reduction of HU values were found to be significantly lower during and after the treatment with $p < 0.0001$ than the value before the treatment. However, changes in SUV values were not found to be significant within this subgroup, as patients with increased and decreased SUV values were also occurred. The other two (2–3) subgroups had no statistically significant HU change, due to small changes (2. subgroup), and as a consequence of low subject number (3. subgroup).

CONCLUSION: The survey, containing the data of our own patient population reassuringly confirms the stability of liver activity during lymphoma response assessment FDG PET/CT examinations, we were unable to demonstrate any significant alteration restricting the further use of liver as a visual reference organ.

T3-4
CORRELATION BETWEEN METABOLIC ACTIVITY AND CLINICOPATHOLOGICAL FACTORS IN BREAST CANCER

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INTRODUCTION: Breast cancer is the most common malignancy among women. Therefore, correlations between the clinicopathological prognostic factors of breast cancer and numerous parameters obtained by ^{18}F-FDG PET/CT (e.g. SUVmax) are well studied issues. However, there are still discrepancies in the literature.
Our aim is to examine correlations between SUVmax values and the clinical status of the patients as well as immunohistochemical characteristics of primary breast tumors.
METHODS: We assessed the baseline ^{18}F-FDG PET/CT scans and histological reports of 96 breast cancer patients. Only patients with a primary tumor diameter larger than 2 cm were included in this study to minimize bias caused by partial volume effect. Mann-Whitney U test and Spearman's correlation were performed to find associations between SUVmax and the following clinicopathological prognostic factors: size of the primary tumor, histological type, grade, estrogen, progesterone and HER2 receptor status, MIB-1 proliferation index, and the presence of local lymphatic and distant metastases.
RESULTS: We found connections between SUVmax values of the primary tumor and the following parameters: estrogen ($p = 0.003$), progesterone ($p \leq 0.001$) and overall hormone receptor status ($p = 0.001$), HER2 receptor status ($P = 0.002$), grade ($p \leq 0.001$), triple negative phenotype ($p = 0.013$), and presence of regional ($p \leq 0.001$) metastases. SUVmax values were higher in hormone receptor negative, HER2 receptor positive, triple negative or high-grade tumors, and in patients with local lymphatic dissemination. A positive relationship was found between SUVmax and MIB-1 proliferation index ($r = 0.573$, $p \leq 0.001$) and tumor size ($r = 0.681$, $p \leq 0.001$) by Spearman's correlation. The presence of distant metastases and histological type did not show significant association with SUVmax.
CONCLUSION: Our results are mainly in concordance with other studies. However, the literature is contradictory in the case of HER2 receptor status as many articles found no correlation between HER2 status and SUVmax. Our findings confirmed the theory that higher SUVmax is associated with bad prognostic factors.

T3-5
EVALUATION OF 11C-CHOLINE PET/CT FOR RESTAGING OF PROSTATE CANCER

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INTRODUCTION: ^{11}C-Choline PET/CT is one of the most sensitive diagnostic tools for detecting locally recurrent and metastatic prostate cancer. ^{11}C-Choline PET/CT has been available in human care since 2014 in our country.
Our aim was to determine the diagnostic role of ^{11}C-Choline PET/CT in patients with biochemically recurrent prostate cancer who initially underwent radical therapy.
METHODS: This retrospective study enrolled 100 prostate cancer patients initially treated with radical prostatectomy (followed by radiation and/or hormone therapy) or radiotherapy (with or without hormone therapy). The median age of the patients was 66.3 years (49 to 87 years). Patients with unknown PSA level and those who received only hormone therapy were excluded. The average pretest PSA level was 6.91 ± 10.26 ng/ml (median: 3.27 ng/ml, 0,008 to 50 ng/ml) and the median Gleason score was 7 (4–10).
The PET/CT acquisition (6 to 8 frames each for 120 sec) started 5 minutes after the iv. injection of 700–850 MBq ^{11}C-Choline. For attenuation correction and anatomical localization low dose CT was done (120 keV, 150 mAs).
Statistical analyses were performed both, on a patient and lesion basis to assess the relationship between PET positive findings and PSA level, type of initial treatment and tumor grade.
RESULTS: Seventy-two patients underwent radical prostatectomy, while 28 patients were initially treated with radiation and 50% of the overall patient population received hormone therapy as well. We found a significantly higher PSA level in the PET positive patient group, the median level of the PSA was 5.25 ng/ml and 0.95 ng/ml in the PET positive and PET negative patient subgroup, respectively (Mann-Whitney U test, $p = 0.000$). Significantly higher Gleason score was characteristic for PET positive patients (Mann-Whitney U test, $p = 0.04$). The lesion based analysis showed significant difference in PSA level (Kruskall-Wallis test, $p = 0.000$).
CONCLUSION: ^{11}C-Choline PET/CT is a sensitive study in the setting of locally recurrent or metastatic prostate cancer. The strong correlation of this method with the PSA test results is helpful in determining the timing of imaging.

T4. THERAPY, RADIATION PROTECTION

T4-1
30 YEARS OF RSO IN HUNGARY

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The first publication about Radiosynoviorthesis (RSO) appeared in 1952 by the author Fellinger. In Hungary the first RSO was performed in 1985 in the National Institute of Rheumatology and Physiotherapy. From 2000 the RSO is performed at BIK. The treatment was introduced in Kecskemét and in the Uzsoki Hospital in 2000. and later in Szeged and Debrecen as well.
THE ACHIEVED RESULTS IN THE SUBJECT:
We were the first to introduce radiosynoviorthesis (RSO) in our country.
We compiled a points system for the evaluation of RSO.
We proved the efficiency of the method by following up many patients (8000) for a long period of time.
Using multifactorial regression analysis we proved that efficiency of RSO is influenced primarily by the local x-ray stage of the joint and the diagnosis of the main disease.
We proved that the best results can be expected in Steinbrocker stage I.–II., local stage I.–II. of RA.
We proved that among patients with SPA the ratio of excellents and goods together is only 46.8% but 70.6% of the patients don't need further punction.
We proved that the treatment is also useful in inflamed patients with OA.
We proved that in case of synovitis of traumatic origin when the synovitis persists after the proper surgical treatment of the change maintaining only the synovitis, the usage of this method should be weighed.
We proved that in patients who underwent orthopedic surgical operation earlier the result of this is as good as in those without previous operation.
We proved that the efficiency of RSO is not influenced by the duration of synovitis, the number of punctions preceding RSO, the number of intraarticular steroid injections before RSO, the gender and the age of the patient.
For objective following up of RSO we elaborated arthroscopic and histologic method.
AFTER 2000: We elaborated and proved by animal experiments, toxicologic, clinical, ultrasound and isotope examinations that Holmium-166 phytate is a suitable isotope for RSO.
With draining examinations, we proved that radiation exposure by 166-Holmium-phytate is minimal.
With chromosome examinations, we proved that 166-Ho-IHPP does not cause chromosome damage.
We have the 166-Ho-IHPP registered.
The HBCS made for the usage of 166-Ho-IHPP has come into force.
We proved that RSO is also effective for the treatment of chronic synovitis beside biologic therapy.
We proved that the efficiency of RSO can be measured by the following: dynamic knee joint scintigraphy; following up with ultrasound, arthroscopy, and histology; our objective scoring system; and the necessity of punctions after RSO.

T4-2
TREATING PAINFUL BONE METASTASES OF PROSTATE TUMORS WITH A-RADIATING ISOTOPES

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INTRODUCTION: 223-radium-dichloride (Xofigo) is an α-particle emitting radionuclide with an advantageous toxicity profile, which is recommended for treating bone metastases causing symptoms in castration-resistant prostate cancer patients when no visceral metastases are present. It can be used following Docetaxel therapy for achieving extended survival time in patients experiencing progression of the disease. The study was undertaken to find out about the effectiveness of the treatment.
PATIENTS AND METHODS: In our Department 33 interventions in 7 patients were performed from July 2015 through December, 2016. The mean age of the patients was 70 years (range 61–78 years). Four patient received treatment on 6 occasions each, one patient received treatment on 5 occasions and another one patient received Xofigo treatment on 3 occasions (the third one was performed in another department.)
RESULTS: An average of 4.7 treatments were performed in our patients, i.e. treatment was provided in 78 percent of the cases. Significant results were found in terms of the treatments performed. Patients receiving treatment on 6 or 5 occasions reported significant decrease of the bone pain, in 2 patients the pain even stopped. In another 2 patients the 10 value on the pain scale dropped to 0 and in 3 patients it dropped to 3, which means that the change can be called significant. Remarkable improvement in our patients' quality of life could also be observed. The evaluation of the treatment received by a low number of patients revealed findings similar to those of the ALSYMPCA study and the international EAP analyses, i.e. full survival time (OS) was longer and the bone pain intensity significantly decreased in patients having received 5–6 treatments as opposed to those who could receive the injection only 1–4 times. The majority (68%) of patients having received 223 radium dichloride treatment also got 5–6 injections. Median OS was 16 months in the whole cohort.
CONCLUSION: In addition to prolonged survival time the preservation of the quality of life is also important. In early-stage bone metastases Xofigo improves both the survival time (OS) and quality of life. The maximum advantages of 223 radium dichloride treatment can be enjoyed by patients having received treatment on 5–6 occasions. We should do our best for our patients to access all possible therapies, which makes effective cooperation with the other specialties indispensable.

T4-3
INICIAL EXPERIENCE WITH XOFIGO ($^{223}RaCl_2$) THERAPY

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INTRODUCTION: Prostate cancer is one of the most common malignant tumor in men. The disease prognosis is poor, metastases are common, which develop 85–90% in the bones. In bone involvement treatment the Ca analog $^{223}RaCl_2$ (Xofigo) is the first alpha emitting product not only relieves bone pain, but also improves the overall survival of the patients.
METHODS: From August 2014 to February 2017, 30 patients were treated with Xofigo. 141 times were given $^{223}RaCl_2$ by us [mean activity was: 4.37 (± 1.3) MBq] Haematological parameters of the patients were tested before each treatment. For the first treatment patients arrived with medical referral and bone scintigraphy result. To follow-up the pain intensity changes the patients was asked to fill out a Visual Analog Pain Scale (Pain Assasment Scales, NIPCTM) each treatment. We compared the bone scintigraphy results of the patients, which were made within 3 months before and after the therapy.
RESULTS: There were no difficulties in the radiopharmaceutical preparation and injection. We followed the general rules of radiation safety, there wasn't detected significant changes in background radiation by surface mesurments [the avarage value before treatment: 0,125 (± 0.03) uSv, after treatment: 0,135 (± 0.03) uSv]. The 30 patients hematological parameters were monitored throughout the therapy. There were no significant changes in red blood cell, hemoglobin and platelet counts. In the number of red blood cell 0.7 (± 0.18), T/L, in hemoglobin 10 (± 4.56) g/L, and in platelet 90 (± 17.37) g/L average decrease was observed. Haematological changes was slightly more significant in white blood cell and neutrophil granulocyte count, in white blood cell 3 (± 1.031) g/L, in neutrophil count 1.8 (± 0.6) g/L average decrease was observed. 16 patient got the full six cycle treatment. Due to major haematological changes the therapy was suspended in 3 cases. In those cases when patient received less than 6 cycle from the treatment, the oncologyst or urologyst doctor indicated the treatment suspension by some other reason, which was not proven to associate with Xofigo therapy (like visceral progression). The bone pain intensity of the patients were gradually decreased during the treatment, most of the cases after the fourth cycle the bone pains were almost completely gone. Based on the numeric pain scale the pre-treatment mean value 6.4 (± 2) was decresed to 1.2 (± 1) post-treatment mean value. Comparing the pre and post therapy bone scintigraphy results of the patients, in most cases regression were occurred, means the number and/or the intensity of the bone metastases were reduced.
CONCLUSION: The alpha-emitting $^{223}RaCl_2$ is safely used for the treatment of castration-resistant prostate cancer with bone metastasis. Compliance with the general rules of radiation safety, increased background radiation was not observed. The condition of the patients usually were improved, their bone pains were decreased, almost in every case completely disappeared. Bone scintigraphy is suitable to follow-up the treatment effectiveness.

T4-4
TREATMENT OF METASTATIC PROSTATE CANCER PATIENTS WITH RA-223 DICHLORIDE (XOFIGO)

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INTRODUCTION: Ra-223 dichloride is approved for the treatment of patients with castration-resistant prostate cancer suffering from symptomatic bone metastases and no evidence of visceral metastatic disease. Ra-223 dichloride is the first alpha-particle emitting radiotherapeutic drug for systemic use. As calcium analogue, it forms complexes with hydroxyapatit crystals especially in the areas of increased bone turnover. In our study we analysed efficacy of the therapy on bone pain and on the survival of the patients treated with Ra-223 dichloride.
METHODS: We treated 51 patients (mean age 68.51 year, 44–89 y) with 271 cycles of Ra-223 dichloride therapy matching the approved inclusion criteria for the treatment. The mean follow-up period was 15 months (6–29 months). The time from the diagnosis of bone metastases to the therapy was mean 3.3 years (1–16 y). Every patient had at least 3 bone metastases especially in the axial skeleton. 50 kBq/kg Ra223 dichloride was administered iv. in 6 cycles, with 4-week intervals. During the follow-up we controlled the hematological status with lab tests and the intensity of the pain using 10-point visual scale. 22 patients got chemotherapy (Docetaxel) before Ra-223 therapy. All statistical calculations were carried out by IBM SPSS statistics software.
RESULTS: 36/51 patients completed 6 cycles of radioisotope therapy. We had to discontinue the treatment in 15 cases. The median overall survival after Ra-223 therapy was 11 months. Kaplan-Meier analysis proved that there is no significant difference in survival time between patients who underwent chemotherapy prior to Ra-223 therapy or did not (12 months vs. 11 months). The significance was calculated by Breslow (Generalized Wilcoxon) test, $p = 0.506$. We could not find significant changes in laboratory parameters (Mann-Whitney test) during the therapy. Jonckheere-Terpstra test was applied to examine trends in pain response during the treatment. The $p = 0.000$ indicated the differences in pain (the median of pain value changed from score 6 to score 2).
CONCLUSION: Radium-223 dichloride is the first systematic α-emitter therapeutic agent that has shown significant benefits to soothe bone pain in prostatic cancer patients having bone metastases.

T4-5
BIOLOGICAL THERAPY AND RADIOSYNOVIORTHESIS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS

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INTRODUCTION: The treatment of patients with rheumatoid arthritis (RA) has been spectacular changed since the 1950's. Introduction of the steroid compounds and their local application, the chemical and radionuclide synovectomy, surgical synovectomy, use of non-steroid drugs, the basic treatment and the spread of biological therapy are the most important steps. Introduction of the biological therapy has changed the quality of life for these patients.
OBJECTIVES: During biological therapy sometimes 1 or 2 joints could be affected by inflammation. In this cases always the question is how to solve the problem. Change of the biological or basic therapy, use surgical synovectomy or radiosynovectomy (RSO)?
METHODS: In our reumatological department 2100 patients with RA and PA were treated with biological therapy between 2002 and 2015. In 100 patients we applied RSO because of the inflammation of the knee joint during biological therapy. We made a long term follow-up in 72 patient.
All participants provided written informed consent.
62 participants inflammatory knee joint disease was diagnosed on the basis of the American College of Rheumatology. 55 of 62 patients with rheumatoid arthritis were seropositive, 7 seronegative. Steinbrocker functional stadium II was observed in 52, stadium III in 10. 10 patients were psoriatic arthritis. Mean age of 11 male and 61 female patients was 51.4 years (range 24–79) years. In 38 patients the right knee, in 34 the left knee was treated by radiosynovectomy. Mean duration of disease was 7.3 years (range 0.5–25), of synovitis (6.3 month (range 3–8). Mean number of punctions of the treated joint prior to radiosynovectomy was 4.2 per patient and of steroid administrations prior to radiosynovectomy 3.0. In 12 patients a systemic steroid therapy has been performed.
RESULTS: During the study period, inflammation decreased. In the first two years excellent and good results were recorded in 82.2%. Two years after radiosynoviorthesis 83.3% of patients did not need another punction.
Before the knee inflammation patients were in complete remission which status has been achieved after RSO as well. DAS: 2.4 ± 0.4.
CONCLUSIONS:
1. RSO is an effective method to treat the inflammation of the knes.
2. The RSO performed during biological tehrapy is as effective as in the case of patients without biological therapy.
3. In case of a successful RSO there is no need for biological or basic therapy neither for surgical synovectomy.
4. However an intraarticular injection has a low risk for infection it is recomended to avoid the biological therapy during the RSO.

T5. PRECLINICAL STUDIES

T5-1
SYNTHESIS OF NOVEL ^{68}GA-LABELLED 2-NITROIMIDAZOLE-NOPO RADIOTRACER FOR TUMOR HYPOXIA IMAGING

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INTRODUCTION: Positron emission tomography (PET) is suitable for visualizing hypoxic regions in tumors. Tumor hypoxia can play essential role in malignant progression and resistance to anticancer treatment. 2-Nitroimidazole-based radiopharmaceuticals are used for the imaging of hypoxia since 2-nitroimidazole derivatives accumulate in hypoxic cells. Recently, the use of the radiometal chelates as a radiotracer has been intensely investigated. The aim of this project is the preparation of the new ^{68}Ga-labelled 2-nitroimidazole-NOPO radiotracer and to evaluate its potencial for tumor hypoxia imaging.
METHODS: Firstly, the commercially available 2-nitroimidazole was N-alkylated by 2-(t-butyloxycarbonylamino) ethyl bromide. After the removal of the t-butyloxycarbonyl protecting group the obtained 2-nitroimidazole derivative was coupled with NOPO chelating agent. The synthesized 2-nitroimidazole-NOPO precursor was labelled with ^{68}Ga, which was obtained from a ^{68}Ge/^{68}Ga generator. Solid phase extraction afforded the novel ^{68}Ga-labelled 2-nitroimidazole-NOPO and the radiochemical purity was determined by radio-RP-HPLC. A small animal PET/MRI study was performed in a KB tumor-bearing and a BALB/c mouse. Images were obtained at 90 mins after tail vein injection of radiotracer.
RESULTS: We successfully synthetized a new ^{68}Ga-labelled 2-nitroimidazole-NOPO radiotracer. According to PET/MRI study the ^{68}Ga-labelled radiotracer uptake was intense. Mean SUV was 0.42 ± 0.04 and the tumor to muscle SUV ratio was 14 ± 1.38.
CONCLUSION: The preliminary biological study confirmed that ^{68}Ga-labelled 2-nitroimidazole-NOPO could be a promising new radiotracer for the evaluation of tumor hypoxia.

T5-2
PRECLINICAL ANALYSIS OF MELANOMA WITH GA-68 LABELED PROCAINAMIDE DERIVATIVES

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Introduction: Malignant melanoma is the most aggressive form of skin cancers. Although, only 3–5 percent of the skin cancer is melanoma, it possesses the worst prognosis. Nowadays one of the most efficient methods in tumor diagnostics is PET imaging; several recent studies focus on the development of melanoma specific tracer. Previous researches have shown that benzamide derivatives were proven to be specific markers for detection of melanoma. The aim of this study was to radiolabel the NODAGA and HBED-CC chelator conjugated PCA derivative with Ga-68, and in order to PET imaging, to apply the labeled compounds on animal models of melanoma. Moreover, we aimed an extensive testing of the compounds under in vitro and in vivo conditions.
Methods: The procainamide was conjugated with NODAGA and HBED-CC chelators. The complete ligands were purified with RP-HPLC and then were lyophilized. The product was characterized by ESI-MS and ^{1}H-NMR. The ^{68}Ge/^{68}Ga generator (Eckert-Ziegler, Obninsk) was eluted by using 0.1 M with 5 mL HCl. The labeling was accomplished on pH = 4.5–4.6 in NaOAc buffer at room temperature and at 95 °C for five minutes. The melanin specificity of ^{68}Ga-HBED-CC-PCA and ^{68}Ga-NODAGA-PCA was investigated in vitro and in vivo using amelanotic (MELUR and A375) and melanin containing (B16-F10) melanoma cell lines. Tumour-bearing animals were prepared by subcutaneous injection of B16-F10, MELUR and A375 melanoma cells into C57BL/6 (n = 10) and SCID (n = 9) mice.
Results: Procainamide derivatives conjugated with two different chelators were prepared successfully. The compounds possessed excellent radiochemical purity (≥ 98%). The octanol-PBS partition coefficients (LogP) of the two radiolabeled compounds were determined. Based on the results of the in vitro measurements the ^{68}Ga-NODAGA-PCA showed significantly ($p \leq 0.01$) higher accumulation than the ^{68}Ga-HBED-CC-PCA on the B16-F10 cell line.
Conclusion: Two ^{68}Ga labelled PCA derivatives were developed, which could selectively accumulate in melanin producing melanoma cells. The uptake values of the compounds are diverse and the in vivo preclinical measurements have confirmed, that the ^{68}Ga-NODAGA-PCA possessed higher uptake on tumour models. Therefore, it was proven that the heterobifunctional chelators also served as pharmacokinetic modifiers, and by their selection the distribution profile of the radioligands within the organism can be considerably modifiable.

T5-3
PET/MR IMAGING OF APN/CD13 EXPRESSION OF EXPERIMENTAL TUMORS USING 68GA-LABELLED NGR DERIVATIVES

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INTRODUCTION: Aminopeptidase N (APN/CD13) plays an important role in neo-angiogenic process and metastatic tumor cell invasion. Our previous studies have already shown that ^{68}Ga-labelled NGR peptides specifically bind to APN/CD13 expressing tumor cells. The ^{68}Ga labelled NGR peptides were enabled to investigate the neo-angiogenic process with Positron Emission Tomography (PET). The aim of this study was to investigate and compare the ^{68}Ga-NOTA-c(NGR), ^{68}Ga-NODAGA-NGR (tioether) and ^{68}Ga-NODAGA-NGR (sarcosine) specificity of APN/CD13 in hepatocellular carcinoma (He/De) and mesoblastic nephroma (Ne/De) tumor models using PET/MRI.
Methods: He/De (hepatocellular carcinoma) and Ne/De (mesoblastic nephroma) cells were used for the induction of heterotopic transplanted [subcutaneously (n = 4) and under the left kidney capsule (n = 4)] tumor models in Fischer-344 rats. Whole body PET/MRI (nanoScan PET/MRI, Mediso Ltd, Hungary) scans and ex vivo biodistribution studies were performed using tumor-bearing and control (n = 3) animals 90 min after intravenous injection of 6.9 ± 0.2 MBq ^{68}Ga-NOTA-c(NGR) or ^{68}Ga-NODAGA-NGR (tioether) or ^{68}Ga-NODAGA-NGR (sarcosine) and two weeks after tumor cell implantation. The imaging of neoangiogenetic process with ^{68}Ga-NOTA-c(NGR) was compared with ^{68}Ga-NODAGA-NGR (tio) and ^{68}Ga-NODAGA-NGR (sar) tracer. Aminopeptidase N receptor expression of He/De and Ne/De tumors was verified by western blot analysis.
Results: In control animals using ^{68}Ga-NOTA-NGR high SUVmean values were observed in abdominal organs, however, in the case of ^{68}Ga-NODAGA-NGR (tio) and ^{68}Ga-NODAGA-NGR (sar) it was much higher. SUVmean and Tumor/Muscle(SUVmean) ratios were found higher after injection of ^{68}Ga-NOTA-NGR, than the administration of ^{68}Ga-NODAGA-NGR (tio) or ^{68}Ga-NODAGA-NGR (sar) in Ne/De tumor bearing animals. In the case of He/De tumor bearing animals comperable SUVmean and Tumor/Muscle(SUVmean) values were detected. Higher SUVmean and Tumor/Muscle(SUVmean) ratios were measured after the injection of ^{68}Ga-NOTA-NGR, than after that of the ^{68}Ga-NODAGA-NGR (tio) or ^{68}Ga-NODAGA-NGR (sar). The APN/CD13 receptors attendance was demonstrated with Western blot analysis.
Conclusions: Among the investigated radiopharmacons the ^{68}Ga-NOTA-c(NGR) showed the highest binding affinity to APN/CD13 positive tumors by PET/MRI imaging. Therefore, ^{68}Ga-NODAGA-NGR (tio) showed sufficient and ^{68}Ga-NODAGA-NGR (sar) showed the worst properties for the detection of APN/CD13 expression.
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T5-4
INVESTIGATION OF MSH RECEPTOR EXPRESSION USING GA-68- AND SC-44-LABELED MOLECULES

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INTRODUCTION: Alpha melanocyte stimulating hormone (alpha-MSH) enhances melanogenesis in melanoma malignum by binding to melanocortin 1 receptor (MC1R). Earlier studies demonstrated that MSH analogues (e.g. NAPamide) specifically binds to MC1R receptor. Radiolabeled NAPamide is a promising radiotracer for the detection of melanoma tumors by Positron Emission Tomography (PET). In this present study the MCR1 selectivity of the newly developed Sc-44-labeled DOTA-NAPamide was investigated using melanoma tumors.
METHODS: MC1R positive (B16-F10) and negative (A375) melanoma cell lines were used. Cells (1×10^6/ml tube) were incubated for 30 or 60 min in the presence of 0.74 MBq of Sc-44- or Ga-68-labeled DOTA-NAPamide. After the incubation time samples were washed and the radioactivity was measured with calibrated gamma counter. For the induction of tumor models 1×10^5 A375 or B16-F10 tumor cells were injected subcutaneously into the left shoulder area of CB17 SCID or C57BL/6J mice, respectively. For imaging studies mice were injected intravenously with 13 ± 1.2 MBq of Sc-44/Ga-68-labeled DOTA-NAPamide 15 ± 1 days after tumor cell inoculation. 20-min static whole body PET scans were acquired 60 min after radiotracer injection using preclinical PET/MRI. Radiotracer uptake was expressed in terms of standardized uptake values (SUVs).
RESULTS: In vitro and in vivo imaging experiments showed that Ga-68- and Sc-44-labeled DOTA-NAPamide specifically bind to MC1 receptors of B16-F10 cell and tumors. B16-F10 cells showed significantly ($p \leq 0.01$) higher in vitro radiotracer accumulation than that of A375 cells. In animal experiments, significantly ($p \leq 0.01$) higher Ga-68-DOTA-NAPamide (SUVmean: 0.38 ± 0.02), and Sc-44-DOTA-NAPamide (SUVmean: 0.52 ± 0.13) uptake was observed in subcutaneously growing B16-F10 tumors, than in A375 tumors, where the SUVmean values of Ga-68-DOTA-NAPamide and Sc-44-DOTA-NAPamide were 0.04 ± 0.01 and 0.07 ± 0.01, respectively. We found that the tumor-to-muscle (T/M SUVmean) ratios were approximately 15-fold higher than the T/M ratios of A375 tumors, and this difference was also significant ($p \leq 0.01$) using both radiotracers. No difference was observed between Ga-68- and Sc-44-labeled DOTA-NAPamide uptakes.
CONCLUSION: The investigated Sc-44-labeled DOTA-NAPamide, as a newly developed PET radiopharmaceutical specifically binds to MC1 receptors of melanoma cells. Due to its high specificity Sc-44-DOTA-NAPamide is a promising PET radiotracer for the detection of melanocortin 1 receptor positive melanoma tumors in the clinical routine.

T6. CLINICAL NUCLEAR MEDICINE

T6-1
CARDIAC 18F-FDG PET/CT IN CONNECTIVE TISSUE DISEASES

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INTRODUCTION: Cardiac involvement is a common complication in connective tissue diseases particularly in systemic sclerosis (SSc). In SSc the immuno-inflamatory damage leads to myocardial fibrosis and consequent myocardial dysfunction. The development of overt myocardial manifestation is recognized as powerful adverse prognostic factor. 18F-FDG PET/CT has increasing role in inflammatory diseases with myocardial manifestation. The aim of this study was to assess the diagnostic utility of cardiac 18F-FDG PET/CT in patients with SSc, and to evaluate simultaneously results of 2Dimensional Speckle Tracking Echocardiography (STE).
METHODS: 17 patients with connective tissue diseases (13 patients with SSc and 4 patients with suspected arteritis, age: 57.3 ± 10, 13 female, 4 male) where enrolled in the prospective study. After low carbonhidrate-diet (previous 24 hours) and extended fasting (6 hours) cardiac ^{18}F-FDG-PET/CT acquisition was performed in 2D mode and short-whole-body in 3D mode. Within 24 hours all patients underwent comprehensive echocardiography focusing on left ventricular myocardial mechanics applying STE. The recommended 17 segment model was used to assess the 18F-FDG activity and for the calculation of myocardial strain as well. On -FDG PET/CT the segmental myocardial 18-FDG uptake in kBq/cc by PMOD software was calculated. The strain values were measured offline by speckle tracking EchoPAC software.
RESULTS: Among 17 patients 5 patients (29%) showed significantly increased 18F-FDG uptake (18.6 ± 6.8 kBq/cc vs. 7.77 ± 3.4 kBq/cc, $p < 0.01$) in the myocardium. In patients where the 18F-FDG uptake was increased, measured global left ventricular longitudinal strain values (19.4 ± 2.7% vs. 13.4 ± 8%, $p < 0.01$) was decresed. There was a negative correlation between myocardial strain and 18F-FDG uptake ($p < 0.05$, $r = -0.54$) In 4 patients with arteritis, the 18-FDG uptake was not increased (4 ± 0.2 kBq/cc), and left ventricular strain values were also in physiological range (21.5 ± 2%).
CONCLUSION: 18F-FDG PET/CT is a promising imaging tool to detect myocardial manifestation of SSc. In the active condition of the myocardial involvement STE provides a simple, non-invasive modality to detect subtle mechanical changes in myocardium.

T6-2
THE IMPORTANCE OF THE VISUAL AND QUANTITATIVE EVALUATION OF DaTSCAN EXAMINATION IN THE CONFIRMATION OF ADVANCED STAGE PATIENTS WITH PARKINSON'S DISEASE BEFORE DUODOPA TREATMENT

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INTRODUCTION: Duodopa treatment may be effective for patients with advanced stage Parkinson's Disease (PD), in case of good response to Levodopa therapy and the combinations of the available convencional antiparkinson medicaments doesn't provide the expected results. The aim of the present study is to prove the importance of the visual and quantitative evaluation method of 123-I-Ioflupane (DaTSCAN, GE Healthcare) examination in determining the advanced stage of PD and the necessity of the Duodopa procedure.
METHODS: Duodopa treatment ensures a consistent level of Levodopa in the blood considering the current circumstances as well. Examinations were performed for 16 patients diagnosed severe PD based on clinical symptoms they were waiting for Duodopa treatment and in other 24 patients who were diagnosed PD or Parkinson's Syndrome (PSP, MSA). During the visual evaluation a well-established (Benamer HTS, P. J. 2000) visual scale was applied (normal, abnormal grade I, II, III) by two independent experts. During the quantitative evaluation the patientes CT and MRI pictures were registered and MRI mask was used on the SPECT image in the different regions.
RESULTS: There was considerable agreement between the visual scores given by the two observers and the visual score correlated with the clinical stage of PD. In case of patients awaiting Duodopa treatment there was substantial agreement between the two independent observers ($\kappa = 0{,}625$, $p = 0{,}04$). Severe PD was confirmed with a sensitivity of 100% and specificity of 54% by one of the observers, and it was determined with a sensitivity of 100% and specificity of 42% by the other observer. There was a significant difference between the distribution of the visual grade of the two groups of patients, because of two observers provided higher grade (II., III) in patients with Duodopa therapy than the other group. There was also a similar correlation considering the Hoehn and Yahr scale. The mean count of VOI putamen — with lower specific uptake ratio — was compared with the mean count in VOI occipital cortex was significantly lower in case of both evaluating methods in patients with PD before Duodopa therapy than the other group of the patients. Duodopa patients had been diseased for significantly longer period than the others.
CONCLUSION: Both the visual and quantitative methods support the differenciation of the various stages of PD. Visual technique is an appropriate way to confirm the advanced stage of PD, which can be proved by quantitative parameters of the objective method. We expect that DaTSCAN examination will be able to help in predicting the efficiency of Duodopa treatment.

T6-3
EVALUATION OF 18-FDG PET/CT IN DIAGNOSIS OF LARGE VESSEL VASCULITIS

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INTRODUCTION: Large vessel vasculitis (LVV) is a group of granulomatous inflammatory diseases and includes the giant cell arteritis (GCA) and Takayasu arteritis (TA). The increased inflammatory markers (C-reactive protein, erythrocyte sedimentation rate) and the clinical signs are not specific for LVV, and not always congruent with disease activity. The early diagnosis and treatment is essential to avoid the late complications. 18-FDG accumulates in activated inflammatory cells, and has superior sensitivity for the detection of vasculitis in early stage of disease and for evaluating therapeutic response. The PET/CT method provides better anatomical localisation. The aim of this study was to diagnose vasculitis in new cases and to reveal relapses.
METHODS: 24 patients (17 females, 7 males, mean age: 61 years) were involved into the study from 2015 December. The patients were selected from the Department of Rheumatology. The 18-FDG PET/CT was performed to diagnose primary in 19 cases and to evaluate the relapse in 5 cases. We included cases with increased inflammatory markers, non-specific clinical symptoms (weightloss, fever, malaise) and suspicious clinical symptoms: extremity claudication, chest-abdominal pain, visual disturbance, jaw claudication, headache, temporal artery tenderness, swelling, proximal myalgia). 18-FDG PET/CT images were evaluated visually by two nuclear medicine physicians, in consensus, who were blinded to clinical and laboratory data.
RESULTS: 18-FDG PET/CT revealed LVV in 6 (6/19) patients as primary diagnosis. PET/CT proved extensive LVV in one patient who had arteritis temporalis as clinical diagnosis, the 18-FDG uptake was increased in the following arteries: in the thoracic aorta and major branches, in the abdominal aorta, bilateral common iliac, bilateral external iliac and bilateral femoral arteries. We detected relapses in 2 patients who were previous diagnosed as LVV. The changing of clinical features after therapy correlated with the PET/CT diagnosis.
CONCLUSION: 18-FDG PET/CT has important relevance in diagnosis of LVV and is effective in monitoring response to therapy. This hybrid modality is able to identify tissue metabolic changes besides anatomic localisation.

T6-4
DIAGNOSTIC VALUE OF Tc99m PERTECHNETATE AND MIBI SCINTIGRAPHY IN CASE OF THYROID NODES

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INTRODUCTION: Our goal was to research our institution's patients' diagnostic value of combined 99m Tc-pertechnetate- and 99m Tc-MIBI scintigraphy in determining the malignant nature of thyroid nodes.
METHODS: Our retrospective investigation included any patient examined with 99m Tc-pertenchnetate- and/or 99m Tc-MIBI scintigraphy from 2009 to 2012 in our institution, a total of 650 (104 male, 546 female; avarage age = 54.55 yrs, SD = 14.38 yrs). We evaluated the number of patients showing increased nodular 99m Tc-MIBI uptake or missing uptake. Patients with normal or higher 99m Tc-pertechnetate nodular uptake were excluded, resulting in a group of 524 (81 male, 443 female; avarage age = 54.22 yrs, SD = 14.77 yrs). We calculated the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy (DA) of 99m Tc-MIBI scintigraphy for malignant thyroid diseases in case of 99m Tc-pertechnetate cold nodules. The malignancy of the evaluated thyroid nodule was confirmed by histological and/or citological diagnosis. The aquired data was processed in light of age groups and gender.
RESULTS: Thyroid surgery and/or FNAB (Fine Needle Aspiration Biopsy) was perfromed in 228 of the cases (28 male and 200 female; avarage age = 52.088 yrs, SD = 11.394 yrs). Out of the 524 patients, 152 had shown increased 99m Tc-MIBI nodular uptake (hot nodule). Out of the 228 cases with pathological diagnosis, 121 cases showed hot nodules on 99m Tc-MIBI scintigraphy. Out of the 20 malignant thyroid tumors, 17 showed high, 3 showed low MIBI uptake. In case of cold pertechnetate nodules 99m Tc-MIBI had a sensitivity of 85.00%, specificity of 50.48%, a PPV of 14.17%, a NPV of 97.22%, and a DA of 53.5%. We found that age and gender did not affect these values except for PPV, in which case the avarage age (M = 54.447 yrs, SD = 13.332 yrs) of false positive patients was significantly higher than for true positive patients (M = 47.529 yrs, SD = 18.648 yrs, $p = 0.022$).
CONCLUSION: Our results confirmed that the main use of 99m Tc-MIBI scinigraphy in case of 99m Tc-pertechnetate cold nodules, is the exclusion of malignancy. A positive MIBI scan can not determine the need for surgical intervention. Although in younger patients the PPV of the examination is the highest, it does not exceed 50%.

T6-5
COMPARISON OF CIGARETTE AND E-CIGARETTE SMOKING TO ALVEOLOCAPILLARY MEMBRANE BY DYNAMIC VENTILATION SCINTIGRAPHY

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INTRODUCTION: Dynamic ventilation scintigraphy (DIT) has proved to be a suitable method for the staging and follow up of the damages of alveolo-capillary membrane (ACM) system of the lungs. The e-cigarette is a new smoking device producing vapor from nicotine solution. Here we present comparative DIT results of e-cigarette users, who returned for one week to traditional cigarette smoking.
METHODS: We included 24 healthy man volunteers (age 20–64) in the study, who regularly used e-cigarette, containing 10 or more mg nicotine/mL concentration fluid. First we acquired a baseline DIT study, calculating the separate clearance half time ($CT_{1/2}$) values of the lungs, and performed respiration tests (FVC, FEV1, PEF, FEV1/FVC) as well as measured CO and COHg concentrations from exhaled air at e-cigarette use. Then we asked the volunteers to return to traditional cigarette smoking for a week's period. After that we repeated the above-mentioned tests, and statistically compared the results, using paired t-test for normally distributed variables, and Wilcoxon's test for the rest.
RESULTS: There was no significant change in the results of PEF and FEV1/FVC respiration tests; FVC and FEV1 slightly decreased ($p < 0.05$), while the exhaled CO and COHg levels were significantly higher at cigarette use ($p < 0.0001$), and increased in every case (CO: from a median value of 2 by 13 ppm; COHg: from a median value of 1.0% by 2.05%). The DIT CTl/2 times were lower at traditional cigarette smoking compared with e-cigarette use in every case ($p < 0.001$, Wilcoxon test): from 66.7 ± 24.3 min decreased by 31.1 ± 16.1 min), to 51.4% (median) of the base value.
CONCLUSION: We first compared at the same persons the direct effect of traditional smoking vs. e-cigarette upon the lung ACM. Our results confirmed the known toxic (especially CO) effect of traditional cigarette smoking causing persistent alveolitis. The normal $CT_{1/2}$ values at e-cigarette use prove that it has no similar effect, there is no sign of alveolitis. So it could be recommended for heavy smokers who are unable to stop smoking, to switch to e-cigarette use, which is more tolerable for the lungs, for the ACM.

P1. POSTERS: METHODOLOGY, THERAPY

P1-1
DEVELOPMENT OF SOLID TARGET AND PURIFICATION FOR THE PRODUCTION OF SCANDIUM-44

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INTRODUCTION: Scandium-44 (^{44}Sc) is a promising radionuclide that has favorable half-life ($t_{1/2}$ = 3,97 h) and decay characteristics ($E\beta^{+}_{av}$ = 632 keV) for PET imaging. Currently, natural calcium or enriched calcium carbonate-graphite powder mixture is used as target material to produce ^{44}Sc. Our goal was to develop a solid target and compare two novel separation method to obtain ^{44}Sc in cyclotron from the proton irradiation of natural calcium target.
METHODS: The irradiated calcium target was dissolved in 3 molar hydrochloric acid and purified with syringe filter or ion exchange resin (DGA). Filter purification: 400 μL crude ^{44}Sc solution was mixed with 800 μL 3%-ammonia solution to adjust the pH to > 10. Thereafter the entire solution was passed through 0.22 μm filter to trap ^{44}Sc in colloidal form. To wash out the impurities, 5 mL water was passed through the filter. ^{44}Sc was eluted with 0.1 molar HCl. DGA purification: the crude ^{44}Sc solution was loaded onto the DGA column. To remove the impurities, 3 molar HCl and 1 molar HNO_3 was passed through the column. ^{44}Sc was eluted with 0.1 molar HCl. The labeling efficiency of ^{44}Sc was tested with different concentration of DOTA solution and NODAGA-AMBA peptide.
RESULTS: In case of filter purification 30.9 MBq activity was loaded onto the filter. The trapped activity was 29.5 MBq and 29.3 MBq remained after the washing. Eluted activity was 25.5 MBq in 0.1 M HCl. The labeling test was < 95% by 1 micro molar DOTA solution but the yield was only 17.5% using NODAGA-AMBA peptide. In case of DGA purification 115 MBq activity was loaded onto the filter. The trapped activity was 114 MBq and 109 MBq remained after the washing. Eluted activity was 89.3 MBq in 0.1 M HCl. The labeling efficiency was < 98% by 1 micro molar DOTA solution and the yield was 85% using NODAGA-AMBA peptide.
CONCLUSION: ^{44}Sc was successfully produced and purified for peptide labeling. In our next step, we are planning to use enriched calcium carbonate that is necessary to produce isotopically pure ^{44}Sc and allowing its use for clinical PET imaging.

P1-2
OPTIMIZATION OF C-11 LABELED METHYL-IODIDE PRODUCTION

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INTRODUCTION: 11C labelled tracer molecules are often used in PET examination. In most cases the labeling procedure is methylation with [11C]methyl-iodide reagent. We applied the Tracer Maker synthesis panel developed by Peter Larsen to produce [11C]MeI and [11C] Me-Triflate in order to synthesize [11C] isotope labeled radiotracers. Our objective was to optimize parameters of synthesis panel.
METHODS: We produced [11C]MeI by the gas phase method using the Tracer Maker synthetsizer. [11C]CO2 generated in the target was reacted with H2 at 360 °C in the presence of Ni catalyst. The resulting [11C]CH4 was separated from the waste gases by freezing at –190°C on Hayesep adsorbent. Upon heating the Hayesep the [11C]CH4 was released at –10°C and directed to the recirculating circuit containing an iodine column where methane reacted with the sublimated iodine vapours at 720°C. The formed [11C]MeI was adsorbed on Hayesep again, and released by heating to 200°C.
The operational parameters of the module were systematically varied in order to find those, which are influencing the yield. The pressure drop in the system was minimized using a multi stage leak-check program. We determined the decay corrected radioactivity produced in the cyclotron with 44 μA beam current and 2 minute irradiation time. The activity of the produced [11C]MeI with the same parameters was compared to this value. We varied the time of the regeneration of the adsorbents, the flow rate of the target gas, the temperature of the iodine and the high temperature furnace and the flow rate of the recirculation circuit. in order to study the dependence of the yield on these parameters.
RESULTS: The activity of the [11C]CO2 produced by the cyclotron was 12 GBq in our measurements. The initial yields of the system with default settings were 36 ± 3%. With the increase of temperature of the iodine oven only 2% increase was achieved. We observed no change in yield by increasing the flow rate of the recirculation circuit and the temperature of the high temp. oven. Optimization of the target gas flow, increase of the regeneration time, achieving appropriate starting temperature and minimizing pressure drops of each stages of the process resulted in a 52 ± 2% [11C]MeI yield. The radiochemical purity was more than 98%.
CONCLUSION: Based on our measurements, the critical part of the synthesis process was found to be the adsorption of the [11C]CO2 on the molecular sieve. The other parameters showed only minor effect on the yield.

P1-3
QUALITY CONTROL OF RENOSCINT-MAG3: COMPARISON OF RADIOCHEMICAL QUICK TESTS AND PHARMACOPEIAL RADIO-HPLC METHOD

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INTRODUCTION: A growing demand arises by clinical users for easy-to-handle, rapid tests for quality control of radiopharmaceuticals after labelling. In our experiments we compared easy-to-handle, quick tests to pharmacopeial radiochemical purity method.
METHODS: Renoscint-MAG3 (Medi-Radiopharma) preparations were labelled with ^{99m}Tc isotope in the maximal activity concentration according to the manufacturer's instructions. Thin layer chromatography (TLC) and solid phase extraction (SPE) methods were performed and compared to pharmacopeial radio-HPLC method (PhEur). Ethyl acetate: butanone or water: acetonitrile mobile phase were applied on TLC layers (ITLC-SG or GMCP-SA or Whatman 3 mm). Evaluation of developed layers were done by using miniGita TLC scanner (Raytest). SPE was performed on SepPak C18 cartridge (Waters) with hydrochloric acid, phosphate buffer and ethanol as eluents. The activity of the factions were measured with dose calibrator (Isomed 2010). The reference method was performed using Agilent 1200 HPLC system with Gabi flow through radiodetector (Raytest).
RESULTS: The solid phase extraction showed 0.6 to 1.3% lower radiochemical purity (RCP) results than those of radio-HPLC method. The amount of hydrophilic impurities correlated well as measured by using the two methods (SPE and HPLC). Difference of RCP results came from the amount of lipophilic impurities. The amount of hydrophilic impurities separated on instant thin layers (ITLC-SG, -SA) were similar to those of HPLC reference method. Evaluated the two type of layers the ITLC-SG method gave a more efficient separation and approached better the results of the reference method (difference +0.3–0.9% compared to the HPLC method). Reduced hydrolyzed technetium colloids were not detected on the Whatman 3 mm layer.
CONCLUSION: Improving the efficiency of the elution of ^{99m}Tc-mertiatid (MAG3) fraction might optimize the separation. Using ITLC-SG layer in ethyl acetate: methyl ethyl ketone mobile phase for determination of hydrophilic impurities is more accurate and efficient than using GMCP-SA layer. All the quick tests (TLC and SPE) resulted in radiochemical purity results that meet the requirements of the pharmacopeia and the SmPC. All the investigated quality control quick tests are suitable for rapid quality checking of Renoscint-MAG3 after labelling at clinical site as compared to reference pharmacopeial radio-HPLC method.
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P1-4
EFFECT OF STORAGE IN DISPOSABLE POLYETHYLENE/POLYPROPYLENE SYRINGE ON THE QUALITY OF NANOSCAN RADIOPHARMACEUTICAL

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INTRODUCTION: Effect of storage in disposable polyethylene/polypropylene (PE/PP) syringe was studied on the quality of Nanoscan 500 micrograms radiopharmaceutical in order to support economical clinical radiopharmaceutical usage.
METHODS: Samples (n = 5) were taken from ^{99m}Tc-isotope labelled Nanoscan radiopharmaceutical (Medi-Radiopharma) into disposable PE/PP syringes (B.Braun) and stored for 10 hours at room temperature. The quality control of radiopharmaceutical in syringe was evaluated by using thin-layer chromatography (TLC), particle size distribution (dynamic light scattering, DLS) according to pharmacopeia and SmPC of the manufacturer. Measurements were done in every 2 hours after labelling until 10 hours. TLC method was performed on ITLC-SG layer in methyl-ethyl-ketone and saline 0.9%. Developed TLC layers were evaluated by using miniGita TLC scanner (Raytest), colloidal size distribution by using Zetasizer ZS (Malvern). Syringe retention was also measured with dose calibrator (Isomed 2010). Standard bioassay was executed in Wistar rats administered Nanoscan radiopharmaceutical, which has been stored in disposable syringes. Whole-body mapping was performed by using Nucline gammacamera (Mediso), organ activities were measured with 2480 Wizard2 automated gamma counter (Perkin Elmer).
RESULTS: Chromatography for unbound, free pertechnetate showed no impurity neither in case of samples from ampoules nor samples from syringes at any time points. TLC for non-colloidal, soluble species resulted in no difference between samples from glass vial and PE/PP syringes at any time points, and all the results (0.0–0.4%) met requirements of the pharmacopeia and the SmPC. Mean colloidal size (15.5–16.0 nm) and polydispersity (PdI = 0.33–0.44) measured with DLS method showed no changing tendency in the investigated time interval. No change was observed in syringe retentions (8.3 ± 0.5%) during the storage up to 10 hours. No difference was found in biological distribution of Nanoscan radiopharmaceutical stored in disposable PE/PP syringes compared to the distribution of radiopharmaceutical stored in its glass ampoule when bioassay were performed in rats. There was no result from any of the applied methods which differed between samples stored in its own glass ampoule and in disposable PE/PP syringes in the investigated 10-hour time period.
CONCLUSION: Storage in disposable PE/PP syringes had no influence on the quality of Nanoscan product, consequently radiopharmaceutical stored in PE/PP syringe passed pharmacopeial requirements up to 10 hours.
Support was provided by „Kincstári Monitoring Rendszer" KMR_12-1-2012-0057.

P1-5
MICROBIOLOGICAL TESTING OF ASEPTIC EXTEMPORANEOS PREPARATION OF GALLIUM-68-PEPTIDE CONJUGATES WITH MEDI-MEDIA-FILL KIT IN NUCLEAR MEDICINE LABORATORIES

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INTRODUCTION: The nuclear medicine laboratory should garantee the sterility and low bacterial endotoxin content of parenteral radiopharmaceuticals according to the current good practice for radiopharmaceuticals production. The microbiological purity can only be assessed after the administration of radioactive material, so exact knowledge of the aseptic preparation and its microbiological monitoring is of key importance. It can predict the microbiological purity of the radiopharmaceuticals prospectively. Our aim was to examine the aseptic preparation of the Ga-68-DOTA-TOC conjugate by previously developed microbiological quality control kit, MEDI-MEDIA-FILL kit.
METHODS: Before starting the preparation the aseptic environment must be ensured by sanitation (cleaning and disinfection). The microbiological contamination was checked by solid microbiological culture media TSA contact plates. During the aseptic preparation the media-fill method was applied, the aseptic process was carried out by a general microbial broth, TSB solution. The Ge-68/Ga-68 generator elution, the radiolabelling, the dilution and the sterile filtration were simulated. At each step samples were taken from TSB solution and incubated at 23 °C and 32 °C for 14 days as prescribed. The working surfaces and the operator were also sampled by contact plates at the end of the preparation, and the test plates were incubated at 23 °C to 32 °C for 5 days.
RESULTS: The sanitation was considered adequate if there was no visible colonies on agar plates (< 1 CFU/sample) after the incubation. The aseptic procedure was appropriate if TSB solution was a clear fluid indicating sterility. Turbidity of TSB solution observed by necked eyes, and the colonies grown on agar plates indicated some microbial contamination because of incorrect aseptic preparation, insufficient sanitation procedure, or inadequate personnel hygiene. The microbiological tests were performed in three independent repeats in accordance with the validation requirements.
CONCLUSION: Application of the media-fill method in nuclear medicine laboratory can ensure the safe preparation of parenteral products, because it can help to estimate the microbiological risks and troubleshoot the hygiene risks. The method can be also applied for the professional staff's regular education, job training and checks required to work well. Documented good results obtained with MEDI-MEDIA-FILL kit and its supply kits in these studies can demonstrate the proper operation of the laboratory for the authorities, and the existance of safety standards in healthcare.
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P1-6
XOFIGO THERAPY NEEDS INTERDICIPLINARY COOPERATION

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INTRODUCTION: 223Radium dichloride (Xofigo) is an effective therapeutic tool for patients with symptomatic multiple bone metastasis of castration-resistant prostate cancer (mCRPC) without soft-tissue metastasis. Several clinical trials are going on to define optimal pretreatment clinical criteria for the most effective („personalized") use of Xofigo in the dynamically changing therapeutic stage.
PATIENTS: Various clinical data of our first 21 patients with mCRPC were analysed before, during and after Xofigo treatment. 7 patients had previous chemotherapy (docetaxel).
Treatment had to be finished after one to three injections in 4 patients because severe granulo- and/or thrombocytopenia. In 3 patients Xofigo therapy was temporarily suspended due to reversible cytopenia (but continued 6–8 weeks later). Xofigo treatment was finished in two patients (due to newly developed brain metastasis and relapsed peptic ulcer respectively) and in other two patients with suspected radical nerve compression. These two patients presented severe ischialgia and neurological symptoms. Both patients had the same symptoms in their history long years before. We indicated MRI examination, and in both cases radical nerve compression was found. 13 patients had the full course of Xofigo treatment. The average number of injections was 4.53 per patient. The median follow-up period was 4.54 ± 3 months. No death occurred during the treatment and the follow-up.
METHODS: Bone pain was monitored by a subjective scoring system. Hemoglobin, absolute number of granulocytes and thrombocytes were measured not in every four, but in every second week during the Xofigo treatment The serum level of prostate-specific antigen (PSA) and alkaline phosphatase (SAP) were measured before and in every eight weeks during and after the treatment. In all 13 patients with full cycle of treatment bone scintigraphy was performed before and 6–8 weeks after the last injection of Xofigo.
RESULTS: Xofigo-induced critical cytopenia occurred more frequently in patients with previous chemotherapy. In 18 out of 21 patients (and in all 13 with full course) bone pain has significantly decreased. Serum PSA level was slightly increased during the treatment periode with exception of 2 patients. SAP level tended to be decreasing continuously, however, it started to rise again in the follow-up period. Bone scintigraphy demonstrated diminishing of abnormally increased focal osteoblastic activity.
CONCLUSIONS: Our first experience with Xofigo treatment underlines the importance of detailed knowledge of the history of patients before the planned Xofigo therapy. Close interdisciplinary cooperation is important not only with the uro-oncologists. In patients with previous low back pain and neurological symptoms in the history, neurological examination and MRI have to be performed. Previous chemotherapy seems to be increase the risk of interrupting Xofigo treatment. In patients with well-tolerated Xofigo treatment a second course of Xofigo might be indicated to increase the quality of life and possibly overall survival.

P1-7
RADIOIODINE THERAPY FOR TREATMENT OF BENIGN THYROID DISEASES — A 14 YEAR RETROSPECTIVE ANALYSIS

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INTRODUCTION: Over the past seven decades radioiodine has been a choice of treatment for thyroid diseases. However, dose estimation for optimal therapeutic outcome remains challenging. In our study we analyzed data from patients treated with radioiodine for benign hyperthyreoidism between 2002 and 2015 at the Department for Nuclear Diagnostics and Therapy, Borsod County University Hospital. The purpose of our study was to review effectiveness of radioiodine therapies applied at our department and draw consequencies for future therapeutic protocols.
METHODS: Altogether 160 patients (20 men and 140 women, age 54.4 ± 25) undergoing radioiodine treatment in our department between 2002 and 2015 were evaluated. Indications for therapy were Graves-Basedow (86%), Plummer's disease (5%) and autonomic adenoma (9%). Inclusion and exclusion criteria were determined according to national and EANM guidelines. The primary aim of therapy was to terminate hyperthyreoidism. We used iodine uptake studies and Marinelli formula to estimate optimal dose for radioiodine therapy, the applied dose varied between 70 and 150 Gy (average: 81) in Graves disease and between 100 and 300 Gy (average: 134) in cases of toxic adenoma. Searching our clinical database and following patients we scanned treatment success at 1 year and development of hypothyreoidism during the follow-up period. We evaluated correlations between uptake studies, administered doses and therapeutic outcome.
RESULTS: We could trace patients for ca. 2–5 years after treatment and analyzed thyroid status, additional treatments and clinical outcome. At the 1 year follow-up visit, hypothyreosis has been already diagnosed in 23%, and 35% of patients were euthyroid. One year after treatment hyperthyreosis persisted in about 30% of patients which was significantly reduced (to 5%) during the follow up period (2–5 years). Retreatment was needed in 15 cases (9%).
CONCLUSION: Radioiodine therapy is an effective alternative treatment for benign hyperthyreoidism, with a 95% cure rate in our department. Additional laboratory data and uptake studies as well as patient history may be useful to choose the accurate dose for radioiodine therapy.

P2. POSTERS: „IN VIVO" IMAGING

P2-1
EFFECT OF CHOLESTEROL RICH DIET ON TUMOR GROWING

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INTRODUCTION: In developed countries, the most common cause of death are cardiovascular disease and cancer. In our opinion the high cholesterol level increases the risk of cancer. Our research goal was to create dyslipidemic tumor bearing rat model which is suitable for investigating malignant tumors and hypercholesterinemia quickly and safely at the same time.
METHODS: Adult Fischer-344 and Long-Evans rats were used for the experiments. Rats were divided into control groups and Ne/De or My1/De tumor bearing groups. During the experiments two different diets were used. 1: Standard diet, 2: Cholesterol rich diet. In one part of the test, beginning of the diet was equal to the time of tumor transplantation. In the other part of the test, the diet started two weeks earlier to the time of tumor transplantation. Two weeks after transplantation whole body ^{18}F-FDG-PET/MRI scans were performed and tumor existence, size and ^{18}F-FDG enhancement were determined. After the imaging rats were sacrificed, healthy kidneys and tumor bearing kidneys were removed and weighted. Blood samples were taken and lipid profile was determined from the serum.
RESULTS: Using cholesterol rich diet the total cholesterol level increased eight times, the LDL level increased thirty times, the HDL level increased four times the triglycerides level increased eight times. Weight of left kidney (3.36 ± 1.05 g) showed significant difference from right kidney (1.07 ± 0.25 g) in My1/De tumor bearing rats fed with standard diet. Tumor bearing left kidney showed no difference (3.19 ± 0.62) in My1/De tumor bearing rats fed with cholesterol rich diet when beginning of the diet was equal to the time of tumor transplantation. Tumor bearing left kidney significantly increased (6.73 ± 0.69) in My1/De tumor bearing rats fed with cholesterol rich diet when beginning of the diet was two weeks earlier to the time of tumor transplantation. Weight of the right kidney did not differ ($p = 0.1$) using standard or cholesterol rich diet.
CONCLUSION: We have created a dyslipidemic tumor bearing rat model which model can be used for test of huge number of chemo preventive molecule quickly and efficiently in preclinical condition.

P2-3
IN VIVO IMAGING OF ISCHEMIA-REPERFUSION USING PET RADIOTRACERS

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INTRODUCTION: Angiogenesis is the process of new blood vessel formation. One can be observed physiologically in wound healing and embryogenesis but it has discovered in several human pathological disorders such as tumors, coronary artery disease or retinopathia diabetica. The asparagine-glycine-arginine (NGR) peptide sequence known as a possible biomarker of angiogenesis. Previous studies have shown that the NGR peptides are specifically bind to APN/CD13 molecules expressed by tumors. Ga-68 labeled NGR peptides allowed the preclinical PET conducted non-invasive detection of neo-angiogenic processes.
METHODS: The peptides were synthetized by solid phase peptide synthesis. The NGR derivate was conjugated with NOTA macrocyclic chelator. The complete ligand was purified by RP-HPLC and then was lyophilized. The product was characterized by MS. The labeling optimization experiments were accomplished with Ga-68 at room temperature and at 95 °C. Left eye of rats (Fischer-344) (n = 5) were ligated surgically using a cannula guided loop. Ischemia can be induced by tightening the noose (90 min.) furthermore it can be terminated by loosening it. The upper mentioned surgical procedure suitable to develop lesions that occur during reperfusion. One day after ischemia-reperfusion (I/R) induction labeled radioligand (15 MBq in 150 μl saline) was injected intravenously (lateral tail vein) to surgical and non-surgical control (n = 2) groups. After the appropriate incubation time (90 min) the radiopharmaceutical distribution was determined in vivo using PET (MiniPET-II small animal PET scanner) and CT (Micro-CT).
RESULTS: NGR derivate conjugation with NOTA chelator was prepared successfully. 68Ga-NOTA-c(NGR) was produced with high specific activity (5.13–5.92 GBq/μmol) and with excellent radiochemical purity (95% <), at all cases. The quantitate labeling range was determined. It was over 10 μmol/dm^3. The octanol-PBS partition coefficient (LogP) of the radiolabeled compound was successfully defined.
In the left bulbus of the surgical group significantly ($p \leq 0.05$) higher tracer uptake was observed (SUV mean) compared to the control (internal control) and non-surgical control group. Western blot analysis confirmed the presence of neo-angiogenic markers (APN/CD13).
CONCLUSION: The above outlined application ideal for study in vivo I/R mediated receptor expression in rat eye model. Thus, creates an opportunity to develop modern diagnostic methods in various pathological processes.

P2-3
FDG UPTAKE CHARACTERISTICS OF MALIGNANT PULMONARY TUMORS EXPERIENCES OF KAPOSVÁR

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INTRODUCTION: Malignant lung cancer is one of first established and nowadays still the most common FDG PET/CT indication. We evaluated the FDG uptake intensity of different histological type pulmonary cancers and analysed the semiquantitative SUV based discrimination opportunities using PET/CT imaging data of PET Medicopus Nonprofit Ltd.
METHODS: PET/CT examinations of 215 patients (149 men, 66 women) acquired in our institute between September 2014 and 2016 were retrospective evaluated. All patients underwent stage assessment oncological whole body scan, due to verified malignant lung cancer (104 adenocarcinoma, 96 squamous cell carcinoma, 7 large cell carcinoma, 3 adenosquamous carcinoma, 2 carcinoid tumor, and 1 lepidic carcinoma, 1 small cell lung cancer and 1 angiosarcoma) larger than 2 cm in diameter. Lean body mass normalized SUVmax values of corresponding pulmonary lesions were calculated using spheric VOI measurement provided by Syngo.via application. The semiquantitative tracer uptake values of pulmonary foci were correlated to available histological data.
RESULTS: The pulmonary lesions showed variable FDG uptake, tumors with high intensity tracer accumulation and only faint uptake were also found [SUV(lbm)max ranged from 1.2 to 29.7]. The lowest uptake was detected for an adenocarcinoma lesion while a squamous cell tumor visualized with the most intensive FDG accumulation. The statistical analysis of the two subgroups containing sufficient number of lesions revealed significantly higher intensity FDG accumulation for squamous cell cancers than for adenocarcinomas (t-test, $p < 0.00005$), however a considerable overlap between the two groups were also found.
CONCLUSION: In concordance with the international literature data significant difference was found in the FDG accumulation intensity of squamous cell lung cancers and adenocarcinoma types using our own lung cancer patient population, however due to the considerable overlap, semiquantitative SUV(lbm)max parameter was unable to provide individual histological prediction.

P2-4
PLACE AND ROLE OF SPECT-CT IN BONESCAN PRACTICE

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INTRODUCTION: The use of SPECT-CT hybrid imaging modality in bone scintigraphy is nowadays routine. The aim of our review is to determine the location and role of this imaging procedure in the bone scintigraphy test, and to investigate the effect of the nuclear medicine hybrid test modality on SPECT-CT for the further load of imaging partners and patients.
METHODS: Our routine use of SPECT-CT equipment began in June 2013. From the nearly 70000 bone scintigraphy studies performed since 1993, the time interval between 2013 and 2016 was analyzed (18589 patients). We investigated the professional distribution of the initial diagnoses of patients referred to bone scintigraphy during this period, the proportion of SPECT-CT studies compared to all bone scintigraphy studies. We have determined the routine decision-making test process protocol we propose to analyze its justification steps. By analyzing the material of the year 2013, we have determined how the application of the SPECT-CT method affects our suggestion in the Nuclear Diagnostic Review for the co-imaging modalities and the patient's further burden.
RESULTS: As expected, we received an extremely high oncology diagnosis (64%). By developing a test protocol for bone scintigraphy, a routinely applicable decision-making element is available for everyday practice. In this process, the role of SPECT-CT is especially prominent in differential diagnosis. The use of SPECT-CT (12% of all bone scintigraphy) resulted in a significant increase in the final diagnosis of the patient, reducing by more than 50% the co-imaging modalities and the additional adverse load of the patient, the cost of care, shortening the pathways of the patient.
CONCLUSIONS: Based on our results, the increase in the number of SPECT-CTs in the protocol is desirable to increase the differential diagnostic accuracy of benign-malignant bone lesions to further reduce the number of additional imaging procedures and the patient's burden.

P2-5
CLINICAL RELEVANCE OF TC-99m HDP SPECT/CT IN THE DIAGNOSIS OF SPONDYLOARTHROPATHIES

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INTRODUCTION: Spondyloarthropathies (SpA) belong to the group of inflammatory arthritis which comprises the ankylosing spondylitis, reactive arthritis, psoriatic arthritis/spondylitis, and arthritis/spondylitis associated with inflammatory bowel diseases. The early diagnosis is extremely important for starting appropriate therapy in time. Our aim is to examine the clinical significance of ^{99m}Tc-HDP SPECT/CT in diagnosis of early and chronic axial SpA.
METHODS: Eight patients (5 females, 3 males, mean age: 42.7 years) were involved into the study from 2016 July. The patients were selected from the Department of Rheumatology according to the clinical features. Firstly, we performed examination of the sacroiliac joint with MRI in the following sequences: T1- weighted STIR for the bone marrow oedema (BME) and T2-weighted sequence for the fat metaplasia (FM). The HDP SPECT/CT was used within one week to examine the sacroiliac joint and spine. Thereafter, the MRI images were fused with SPECT/CT images (Mediso, Interview Fusion). On the MRI images the BME (active lesion) and FM (chronic lesion), on the CT scans the sclerotic lesions (Scl, chronic lesion) were drawn manually as volume of interest (VOI). Uninvolved cortical areas were drawn on the different modality slices as reference region (ref). Then, we determined the isotope (^{99m}Tc-labelled HDP) uptake of the different lesions and areas (mean counts/VOI): VOIBME/VOIref, VOIFM/VOIref, VOIScl/VOIref.
RESULTS: Two active sacroileitis and two chronic sacroileitis without active lesions were diagnosed. On the other 4 patient's sacroiliac joints images (MRI, scintigraphy, CT scans) there were not any pathological lesions. Sixteen lesions of 8 patients were localised on the fused MRI-SPECT/CT images: 3 BME, 7 FM and 6 Scl lesions. The isotope uptake of BME was the highest ($VOI_{BME}/VOI_{ref.}$ 2.33). The radiopharmacon uptake of sclerotic lesions was moderate ($VOI_{Scl}/VOI_{ref.}$ 1.56). The isotope uptake of FM lesions was not different from the HDP uptake of reference regions ($VOI_{FM}/VOI_{ref.}$ 0.97).
CONCLUSION: MRI is established modality in diagnosis of axial SpA. According to the initial results, the different MRI lesions have different isotope uptake, which suggests, that the HDP-SPECT/CT can distinguish the early and chronic stage of axial SpA.