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Abstracts

POSTER SESSION

P1. MATRIX-PET: A NOVEL PET DETECTOR CONCEPT BASED ON LARGE BLOCKS OF ORGANIC SCINTILLATORS

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Matrix-PET is a novel detector solution for the Positron Emission Tomography. It is one of the two methods which is developed at present at the Jagiellonian University [1]. The detector idea is a subject of a patent application [2]. Novelty of the concept lies in using the large and thick organic scintillators blocks as a detector of gamma guanta instead of crystal scintillators used in current commercial PET scanners. Its uniqueness constitutes the solution of light collection allowing for the conversion to the electric signal of direct light. The idea is demonstrated schematically in Figure 1. This method allows to achieve a time resolution which is not affected by the deformation of light pulses due to reflections at scintillators surfaces. Such PET detector would consist of organic scintillator plates. The plates could be set in many ways so as to cover the whole body of the patient, for example as it is shown in Figure 2. The measurement of time and amplitude of light signals is carried out by photomultipliers matrix arranged around the chamber. The interaction point within the plane of the plate can be reconstructed based on both: (i) the distribution of time of the signals from photomultipliers and (ii) distribution of amplitudes of the recorded signals. Such solution enables also determination of the depth at which the gamma quantum has been absorbed (DOI) on the basis of the distribution of amplitudes of signals from photomultipliers which can be arranged also on front and back sides. This feature allows to use thick plates without worsening of spatial resolution due to "the DOI problem" occurring in the current PET tomographs. Enlargement of the thickness, and high acceptance, enables efficient detection of gamma guanta using organic plastic scintillators, which are characterized by excellent time resolution. This solution would also enable effective usage of the TOF method permitting the determination of the annihilation point along the line-of-response based on the time difference in reaching the different scintillation plates by the gamma guanta. Polymer scintillators allow to obtain the time resolution better than 100 ps compared to 600 ps achievable in a current PET

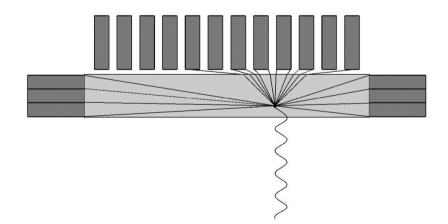


Figure 1. Principle of light collection in the Matrix-PET

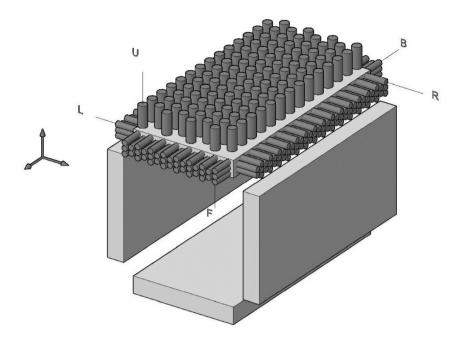


Figure 2. One of the possible arrangement of scintillation plates for the diagnostic chamber of matrix-PET. The location of quantum reaction in a plate plane may be determined with three independent methods based on the (i) amplitude of the signals from the upper layer (U), (ii) from amplitudes of signals from front (F) and back (B), and left (L) and right (R) photomultipliers and (iii) based on time differences of photomultiplier signals from the average weighted with appropriate measurement uncertainties

scanners. Such accuracy of TOF determination may significantly improve the sensitivity (image contrast) which increases inversely proportional with the time resolution and directly proportional to the size of the examined object [3].

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P2. THE ROLE OF 18FDG-PET IN STAGING AND FOLLOW-UP OF ADOLESCENT NON-HODGKIN LYMPHOMA (CASE REPORT)

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Aim: Non-Hodgkin lymphomas in childhood and adolescence are almost exclusively from the group of high- grade lymphomas and according to WHO classification there are four main subgroups: lymphoblastic lymphoma, Burkitt lymphoma, diffuse large B-cell lymphoma and anaplastic large cell lymphoma. Exact staging has critical importance in the stratification into risk groups and treatment decision necessary to achieve optimal response and cure. We present the clinical value of FDG-PET for staging, monitoring therapy response and post-therapeutic surveillance in adolescent patient with NHL.

Methods: Whole-body PET with 18F-FDG was performed according to standard protocol, in our case one patient with zhistologically proven Burkitt lymphoma. Patient-female was 16-year old at the time of confirmation of diagnosis. FDG-PET examinations were performed between March 2006 and Feb. 2011, overall 13 PET scans, with comparison SUVmax ratio in order to monitor therapy response.

Results: The first control FDG-PET after first-line chemotherapy (5 cycles) reported non-response to therapy and changed into more aggressive strategy. Further PET examinations during follow-up revealed two recurrences atypical in breast. After third-line chemotherapy was achieved complete metabolic remission, which continues till now.

Conclusions: Overall survival rate in malignant lymphomas in childhood and adolescence have markedly improved during last years. Several reports have been indicating the usefulness of FDG-PET in pediatric Hodgkin lymphoma, however, that in pediatric Non-Hodgkin lymphoma is not fully investigated. Current international guidelines for response criteria incorporated PET and PET/CT as routine imaging modalities and strongly recommend their use in Hodgkin lymphoma and aggressive subtypes of Non-Hodgkin lymphomas for initial staging and verification of the disease remission. The benefit of PET and PET/CT in early mid-treatment restaging, their impact on long-term disease remission and overall patient survival has to be confirmed by ongoing clinical trials.

P3. ENERGY RESOLUTION AND DETECTION EFFICIENCY OF CSI(TL) CRYSTALS WITH A HIGH CONCENTRATION ACTIVATOR FOR GAMMA RAY TOMOGRAPHY AND POSITRON EMISSION TOMOGRAPHY

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An experimental analysis of energy resolution and detection efficiency is presented for scintillation crystals of thallium-activated cesium iodide (CsI(TI) as a function of the activator (thallium) concentration. The analysis aim is to establish the optimal choice for this kind of crystals coupled to PIN photodiodes of large surface which will be used in performing of detection system for positron emission tomography device. These crystals have a high density, are non hygroscopic and can be manufactured at small dimensions which assure a good spatial resolution. The experimental detection efficiency of (30–65)% and the experimental energy resolution of (2.8–5.9)% at gamma radiation from 22Na, 137Cs and 60Co sources, were measured. The analysis has been conducted using crystals having TI concentration larger than 1000 ppm.

P4. BREAST CANCER PRESENTING AS A 18FDG/PET INCIDENTALOMA IN A PATIENT WITH INTESTINAL GIST

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Inroduction: 18FD/GPET imaging is widely used in clinical oncology. 18FDG/PET imaging is a clear advance in the approach to staging and monitoring breast cancer. Positron imaging offers better accuracy than conventional imaging in the identification of metastatic disease both in the initial staging of breast cancer and in follow-up.

Case report: We describe the case of a 65 year old women who presented with GIST. 18FDG/PET was done for the follow up the treatment with Glivec. We revealed a low metabolic rate (SUVmax — 1,9) in upper left quadrant in left breast. The patient underwent mamography, follow core-cut biopsy, that revealed breast carcinoma corresponding to the lesion visualised on FDG/PET. Appearance of breast carcinoma during the routine control of patient with GIST was observed. A relationship between breast carcinoma and GIST has been not vet previously proposed.

Conclusion: This is a rare description of a concomitant breast carcinoma presenting as a FDG/PET incidentaloma alongside GIST. Even discrete findings made in the course of the PET examination have to be examined further.

In the future, further refinements in scanner technology and new radiopharmaceuticals will likely result in better identification of smaller lesions. Dedicated breast PET/CT or PET/Mammography units show promise in improved detection in primary breast cancer, while also providing a method for image guided biopsy.

P5. RELIABLE PRODUCTION OF BEYOND FDG PET ON A DISPOSABLE-BASED FULLY AUTOMATED PLATFORM IN A GMP SITE

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¹IBA Chemin du Cyclotron, 3 Louvain-La-Neuve/BE; ²IBA, 100 Executive Dr., Sterling, VA/US ; ³IBA Pharma, Av.de l'Espérance, 1 Fleurus/BE; ⁴Herlev University Hospital Dep. Clinical Physiology, 54 P1 Herlev/DK; ⁵Aposense Ltd, 5–7 Odem St., Petach-Tikva/IL; ⁶University of Pennsylvania, Dep. of Radiology, Philadelphia PA/USA; ⁷Austin Health, Centre for Nuclear Medicine and PET, Heidelberg/AU

Introduction: PET modality is one the most rapidly growing areas of medical imaging thanks to the availability of innumerous clinical centers with their own biomedical cyclotrons. To be able to cover the growing clinical demands, a flexible, reliable platform (IBA Synthera) was developed for a (c)GMP environment. Well-known conventional chemistry steps were fully automated allowing the synthesis of multiple 18F-tracers beyond FDG.

Materials/Methods: The platform consists of a synthesizer and an HPLC. The synthesizer employs a disposable system (IFP, integrated fluidic processor) where the entire synthesis takes place. The IFPs are named after conventional synthesis steps they are designed to perform: nucleophilic substitution, chromatography, alkylation, distillation, and reformulation. Only one IFP is needed for a single synthesis, but they can be connected in series for multi-step processes.

Results: In this work, several 18F-labeled tracers were synthesized by nucleophilic fluorination: direct fluorination (SN2 and SNAr) and synthon chemistry. The former can be performed in one step (18F-FP-DTBZ1, 18F-fallypride1) or in two steps; fluorination followed by removal of protective groups (18F-FDG, 18F-FMISO1, 18F-FAZA2, 18F-FHBG1, 18F-FAcetate3, 18F-FA853801, 18F-ML-10, florbetaben). Synthons like 18F-FBM (fluorobromomethane), 18F-SFB4 (succinimidylfluorobenzoate) were also synthesized and they may be coupled to adequate precursors via acylation, alkylation or amide formation. For instance, 18F-FCH5 synthesis; 18F-FBM synthon produced in the first step N-alkylates the precursor resulting in 18F-FCH. This example shows the system is able to carry out multi-step processes.

	Yield [d.c.%]		Yield [d.c.%]		Yield [d.c.%]
FLT*	26.5	FCH**	28	ML-10*	66
FMISO**	64	FAZA*	28	SFB**	82.5
Fallypride*	36.2	Florbetaben*	65	FHBG*	9
FBE*	23.7	FP-DTBZ*	6	F-A85380*	34.3

Discussion/Conclusion: In most cases, the crude synthesis product required HPLC purification (*) while for the others cartridge purification (**) was sufficient (Table 1). In every synthesis parameters were optimized with respect to precursor amount, reaction time, temperature and concentration. In most cases synthesis time was < 60 min. even when HPLC purification was included. Good synthesis yields (Table 1), > 95 % radiochemical and chemical purity were obtained and were superior when compared to manual synthesis (yields at least doubled). Less radiation exposure, shorter synthesis time and stable yields are the other advantages versus manual synthesis. By simply adapting the recipe and by using adequate IFP the automated platform was able to consistently produce several tracers in high yields and suitable for human injection.

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P6. APPLICATION OF COMPARTMENTAL MODELS FOR POSITRON EMISSION TOMOGRAPHY (PET)

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The development of Positron Emission Tomography (PET) has been rather dynamic during last few decades. Additionally, the progress has been perceptible simultaneously in several areas like the technical structure changes of device resulting in the development of the sophisticated hybrids like PET-CT or PET-NMR, improvement of software, increase in the amount and type of the radiopharmaceutics. Those modern diagnostic tools have been created and are currently available and more common in diagnostic centres. This kind of imaging allows us to observe not only physiological processes but also biochemical and pharmacological changes [1]. Moreover, PET method is so-called "molecular imaging" characterized by high sensitivity and ability for quantitative measurement [2].

However, more diagnostic information and quantitative physiologic analysis may be obtained if additional software packages are applied. Compartmental models are the basis for tracer kinetic analysis in PET. Those models are mostly used for blood flow, oxygen metabolism, cerebral metabolic rate for glucose or receptor concentration estimations [3, 4].

The number of compartments for the model depends on its application. The common model consists of 3 tissue compartments (or 4 compartments), where there are respectively arterial blood, free ligand in tissue, specific binding and non-specific binding. The transport between compartments is described then by six rate constants, usually linearly related to the concentration changes. But the single tissue compartment model is also applied, eg. for blood flow measurement by 150 labelled water. Similarly two tissue compartment model fits properly for [18F]FDG kinetics description. On the other hand a more complex multicompartment models like that of FDOPA metabolism analysis can be found [2].

Predictably, a series of general assumptions is necessary, some of them are common for all analysis like the instantaneous mixing within the single compartment, and the others depend on the experimental design and the statistical noise [3]. Then under appropriate conditions the system is described by a set of first order linear differential equations.

It was pointed out that compartment models may have some limits of application, eq. when data have high temporal resolution or with highly extracted radiopharmaceuticals. However, it seems — that for a typical temporal resolution of PET exam, the use of a distributed model has no advantage over a compartment model for PET receptor quantification [5].

Many compartment models have been applied so far for quantitative PET data evaluation and they are still under development, what is the most important conclusion — it seems that they are to play an important role in molecular imaging.

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P7. STAGING OF PRIMARY UTERINE CERVICAL NON-HODGKIN'S LYMPHOMA WITH FDG-PET/CT: A CASE REPORT

Dudu Kumptete

Turkey Association of Nuclear Medicine

Approximately one-fourth of the malignant lymphomas arise in extranodal organs. Primary non-Hodgkin's lymphoma (NHL) of the female genital tract (FGT) is extremely rare. We report one case of primary extranodal NHL of the cervix.

A 66-year old woman presented with postmenopausal vaginal bleeding. Vaginal examination revealed mass on the cervix. The cervical biopsy demonstrated diffuse large B-cell lymphoma. FDG-PET/CT for staging demonstrated a large cervical mass of 37 x 40 mm with uterine invasion of increased FDG uptake (SUVmax: 24.9) as well as pelvic hypermetabolic (SUVmax: 21.0) conglomerated lymph nodes filling the pelvis.

The most common locations of primary extranodal NHL are gastrointestinal tract and skin. Primary NHL of the FGT is extremely rare (about 1.5%). Because of the rarity of lymphoma of the uterus and cervix, their staging, management and follow-up are not well defined. After the diagnosis, a complete physical examination searching for enlarged peripheral lymph nodes and chest, abdomen and pelvic CT scans along with bone marrow biopsy are required. Whole body imaging with FDG-PET/CT scan after the initial diagnosis can detect metastatic peripheral lymph nodes and bone marrow involvement. Therefore, FDG-PET/CT should be used in the initial work up of patients with cervical cancer for staging and management of surgery, radiotherapy and chemotherapy.

P8. NOVEL 68GA-LABELED LYSINE DERIVATIVES OF OCTREOTIDE IN VITRO AND IN VIVO STUDY

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Introduction: Somatostatin receptors are over-expressed in most neuroendocrine tumors and other neoplasms (thyroid, breast, lung, etc). Radiolabelled somatostatin analogues are valuable tools for in-vivo diagnosis and therapy of neuroendocrine tumours (NET) due to the frequent tumoral overexpression of somatostatin receptors (sst). Clearance of a drug normally occurs through the liver and kidneys and it is an important assumption that only free (i.e. not protein bound) drug is available for clearance. One of the decisive parameters is lipophilicity. This is the key physicochemical factor linking membrane permeability – and hence drug absorption and distribution — with the route of clearance (metabolic or renal). For radiopharmaceuticals the excretion pathways are of crucial importance for early and high tumor/background ratios and thus signal intensity in diagnostic by SPECT or PET and low toxicity for therapy. As pointed out above, the in vitro or the in vivo studies in animals can not always predict the drug "performance" in humans. In this study, we investigated biological behavior of the two somatostatin derivatives labeled with gallium-68 with different lipophilicity

Materials and methods: Derivatives of octreotide were synthesized by solid-phase method. They contain DOTA as a chelating group and lysine at various positions in the molecule. These compounds were tested in vitro by using cultures of mouse melanoma B16 and breast adenocarcinoma MCF 7 cell lines. As a control we used human lung fibroblasts cells (HLF).

In vivo experiments were carried out on melanoma-bearing mice C57BI. All animal experiments were conducted in compliance with the Russian animal protection laws and with the ethical principles and guidelines for scientific animal trials. For in vivo experiments F1 (CBA×C57B1) female mice, 18–20 g body weight with melanoma B 16 were used. Experiments with melanoma-bearing mice were made in 9–10 days after inoculation when tumours had grown to approximately 1.5 cm in greatest diameter.

Results: For effective labeling (> 90%) of peptides was found conditions which were unique for each case. The results of in vitro experiments show that the studied compounds could specifically bind to tumor cells quite well.

The ability of sstr subtypes to undergo agonist-induced internalization is an important characteristic of these receptors for transporting radiolabeled somatostatine analogs into the cell.

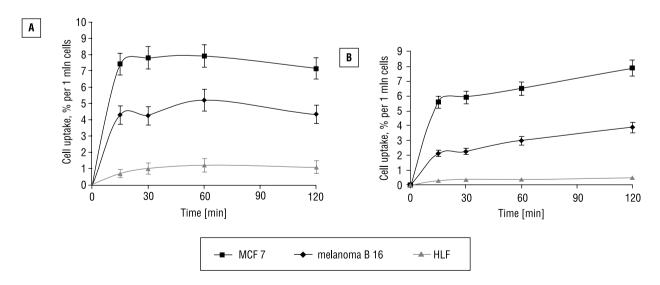


Figure 1. Cell uptake of 68Ga-DOTA-ω-lysine-octreotide (A) and 68Ga-DOTA-α-lysine-octreotide (B)

Our data show that both compounds are rapidly and almost entirely internalized by tumor cells, indicating that their receptor-specific capture. Maximum internalization (about 90%) achieved within 30 minutes after the start of incubation, which suggests the possibility of achieving sufficient to render the level of accumulation.

Biodistribution data are shown in Table 1.

Discussion and conclusion: According to the biodistribution $68Ga-\alpha$ -DOTA-lysine-octreotide some of its obvious advantages such as: more than 2 % ID/g tumor uptake, more than 10.6 muscle/tumor ratio and about 2 tumor/blood ratio after 60 min post injection. As the deficiencies should be noted the slow blood clearance and relatively high accumulation in the liver and kidneys. On the other hand, $68Ga-\omega$ -DOTA-lysine-octreotide also has a number of advantages and disadvantages. The undoubted benefits of this compound include: rapid blood clearance, less accumulation in the liver,

	68Ga- α -DOTA-lysine-octreotide		68Ga-w- DOTA-lysine-octreotide	
Time after injection, min	20	60	20	60
Blood	2.4 ± 1.2	0.5 ± 0.3	1.2 ± 0.3	0.3 ± 0.1
Liver	5.6 ± 3.7	5.3 ± 2.7	1.8 ± 0.2	1.0 ± 0.1
Kidneys	7.2 ± 1.7	5.1 ± 0.8	3.7 ± 1.1	5.3 ± 1.0
Muscle,% / g	0.7 ± 0.2	0.4 ± 0.2	1.3 ± 0.5	0.2 ± 0.1
Tumor, %/g	2.4 ± 0.03	4.0 ± 2.8	2.9 ± 0.7	1.1 ± 0.02

Table 1. Biodistribution of labeled compounds in melanoma B16 bearing mice (% of I.D.)

the value of tumor/blood ratio 4.3 after 60 min post injection, the values of tumor/muscle ratio 4.9 after 60 min post injection. A disadvantage of this compound is to call it is not as strong binding and lower level of tumor accumulation.

Thus, DOTA-lysine octreotide derivates can be studied in future research as tumor seeking agents.

P9. C-11 LABELLED RADIOPHARMACEUTICALS FOR ROUTINE USE

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Introduction: Carbon-11 is ideal radionuclide to apply in positron emission tomography due to its chemical and physical properties. Practically all the biologically active compounds containcarbon, only clever chemistry is required to replace one carbon-12 atom to carbon-11. Its half-life 20.4 minutes long enough to perform even sophisticated syntheses, and to make clinical investigations feasible. The emitted positrons have 0.96 MeV energy what results 0.3 mm mean linear range, allowing good resolution in either human of preclinical PET investigations. In this presentation the production of three C-11 labelled radiopharmaceuticals: methionine, choline and PIB will be discussed.

Methods: The C-11 isotope was produced on a GE PETtrace cyclotron with the ¹⁴N(p, α)¹¹C nuclear reaction, using high purity nitrogen gas containing 1% oxygen as target material. The resulting ¹¹CO2 was converted into [¹¹C]methyl iodide in gas phase using a PET trace MelMicroLab module (GEMS, Uppsala. Sweden). This was used for the subsequent radiochemical syntheses performed on in house built synthesis modules.

L-[¹¹C-methyl]methionine was prepared by the methylation of L-homocysteine by [¹¹C]methyl-iodide in the presence of KF/Al₂O₃ catalyst, as was described earlier by Smitz et al. and more recently by Mitterhauser et al..Because during the routine production runs, unexpected impurities was detected (Szikra et al.) a new SPE purification step had to be introduced. The product was absorbed on a cation exchange column, the impurities were washed out, and the pure material was eluted.

[¹¹C]cholinewas produced by the on-column method, first described by Pascali et al., then modified by Sher et. al. In this case the methylation of dimethyl amino ethanol took place on a SepPak column, from where after washing with ethanol and water the [¹¹Cl]choline was eluted by saline solution without any further purification.

For producing [¹¹C]PIB([*N*-Methyl-¹¹C](4'-methylaminophenyl)-6-hydroxybenzothiazole) the methyl iodide was converted into methyl triflate, which reacted with theprecursor in methyl ethyl ketone in sot time at moderate temperature (2 minutes , 80 °C). The product molecule was separated from the reaction mixture on a semipreparative column (Licrospher 100 RP18, 10 μ m (Merck) with 0.1 N ammonium formate pH = 4: acetonitrile eluent.

Quality control methods were developed and implemented for all these radipopharmaceuticals, including HPLC and GC measurements.

Results and discussion: With these syntheses useful amount of radiopharmaceuticals has been produced for either routine or experimental use. In a typical run with irradiation of target at 45 μ A for 20 minutes 6–12 GBq[¹¹C]methionine or [¹¹C]choline was produced. The radiochemical purity of [¹¹C]cholinewas always < 99.9%. In case of [¹¹C]methionine the average radiochemical purity is 98 %, however in several cases it was below the allowed 95%, and also the presence of iodide ions was noticed. Therefore a purification step had to be inserted in the procedure applying a cation exchanger. The evaluation of the effect of purification is under progress. Applying the same conditions 1000 ± 200 MBq of [¹¹C]PIB was obtained with a radiochemical purity > 95% and the specific activity of 120 ± 20 GBq/µmol at the end of synthesis.

In Hungary marketing authorization is required for routine use of any radiopharmaceuticals, what makes the access to these very difficult. The department has obtained marketing authorization for [11C]methionine and currently is applying for [11C]choline. The [11C]PIB would be used only for clinical studies after the IMPD has been approved.

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P10. NEW RADIOPHARMACEUTICALS RESEARCH CENTER (CCR) AT MAGURELE, ROMANIA

D Niculae, I Ursu, L Craciun

Horia Hulubei National Institute for Physics and Nuclear Engineering (IFIN-HH) Department of Radioisotopes and Radiation Metrology, Magurele, Ilfov, Romania

The present status of IFIN-HH CCR (Radiopharmaceuticals Research Centre) project is reviewed and its development perspectives are addressed.

The CCR benefits from a TR19 cyclotron (ACSI, Canada) with 4 external beam lines, dual particle irradiation (protons and deuterons), simultaneously dual target irradiation, variable energy (14–19 MeV for protons) for the production of commonly used PET radioisotopes (F-18, N-13, O-15, C-11, Pd-103, I-124 as well as research isotopes); hot cells, automated synthesis modules, automated dispenser, quality control laboratory and microPET.

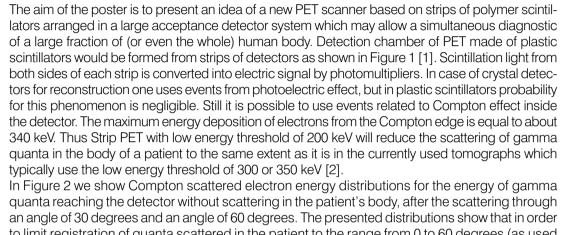
At CCR are envisaged researches in the following areas:

- studies on new molecular targets (small molecules, antibodies, peptides, aptamers) showing specific and preferential uptake to tumor sites and other pathological processes labelled with positron emitters as potential PET radiopharmaceuticals;
- pharmacokinetics and pharmacodynamics of active subsatnces; testing of therapeutic properties and distribution, methabolism, elimination, toxicity studies of drugs using PET imaging;
- functional information and quantitative determination by fusion of images comming from different imaging techniques aiming volume corrections in small lesions, stadialization, global methabolic activity;
- production of Tc-99m through nuclear reaction ¹⁰⁰Mo (p,2n) ^{99m}Tc for diagnosis and research in nuclear medicine;
- targetry developments.

P11. STRIP-PET: CONCEPT OF TOF-PET SCANNER BASED ON POLYMER SCINTILLATOR STRIPS

P Moskal, T Bednarski, A Heczko, M Kajetanowicz, Ł Kapłon, A Kochanowski, G Konopka-Cupiał, G Korcyl, W Krzemień, K Łojek, W Migdał, M Molenda, Sz Niedźwiecki, P Salabura, M Silarski, A Słomski, J Smyrski, Z Rudy, J Zdebik, M Zieliński

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to limit registration of quanta scattered in the patient to the range from 0 to 60 degrees (as used in the currently produced tomographs) one has to use an energy threshold of about 200 keV. To compensate for low density of plastic scintillators several layers of strips could placed around a patient [3] as it shown in Fig.3. The total thickness of cylinders of 5 cm results in efficiency of 20% when requiring signals with energy deposits larger than 200 keV.

Novelty of the concept lies in employing predominantly the timing of signals instead of their amplitudes. The solution proposed will allow for the determination of position and time of the reaction of the gamma quanta based on the time measurement. The hit position versus the center of the scintillator (Δ I) is determined based on time difference measured on both sides of the scintillation strip. The time at which gamma quantum hits the module can be determined

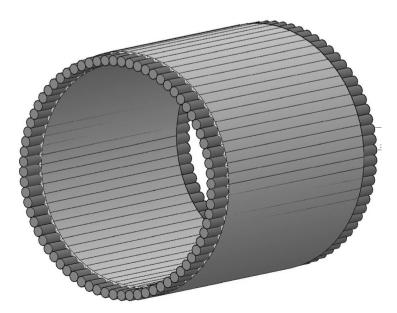


Figure 1. Detector arrangement in plastic scintillator PET. Patient would lie inside the barrel, along scintillator strips

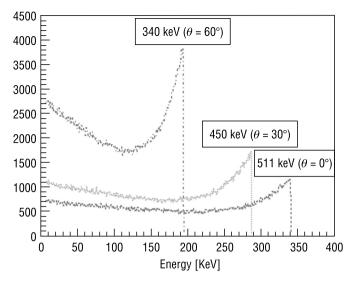


Figure 2. Energy distribution of electrons scattered in the Compton effect by gamma quanta with an energy shown in the plot. The distributions were made without taking into accout the energy resolution, which for the strip detector readout on both sides isabout 18% (compared to LSO blocks which energy resolution is about 12%[4])

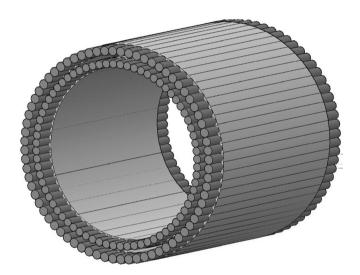


Figure 3. Two layer version of scintillation barrel

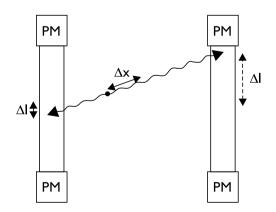


Figure 4. Schematic illustration of a new PET concept — Strip PET

as an arithmetic mean of times measured on both sides of the module. Position (Δx) along the line of response is determined from time difference between two modules [4].

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P12. THE DIAGNOSTIC ROLE OF ¹⁸F-FDG PET/CT IN PATIENTS WITH NEUROENDOCRINE TUMORS

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Introduction: ¹⁸F-Fluoro-deoxy-glucose positron emission tomography — computed tomography (FDG PET/CT) is important hybrid imaging modality in evaluation and monitoring of oncology patients. Neuroendocrine tumors (NETs) are neoplasms that arise from various neuroendocrine cells. Nuclear medicine techniques are known to play important role in diagnosis and therapy of NETs. Although, glucose metabolism is usually low in these tumors, more aggressive and high grade NETs can have elevated glucose metabolism, where FDG PET/CT may provide significant information. The aim of this retrospective study was to evaluate the usefulness of FDG PET/CT in diagnosis and management of patients with NETs, such as gastroenteropancreatic and pulmonary NETs, paraganglioma and medullary thyroid carcinoma (MTC).

Patients and methods: Sixteen patients (8 male and 8 female, mean age 47.3 ± 12.20 years) underwent FDG PET/CT examination at Center of Nuclear Medicine, Clinical Center of Serbia in Belgrade. Patients were diagnosed with NET (n = 6), paraganglioma (n = 6) and MTC (n = 4). PET/CT scanning was performed for staging or restaging. All patients were submitted to a routine whole-body imaging (from the base of the skull to the mid-thigh) on hybrid PET/CT scanner Siemens Biograph True 64, 90 minutes after intravenous injection of FDG. Images were evaluated by two nuclear medicine physicians and one radiologist, and were analyzed both qualitatively and semi-quantitatively by measurement of standard uptake value (SUV). Results of FDG PET/CT were reviewed retrospectively and compared to follow-up clinical data, including results of multi-slice computed tomography (MSCT), ultrasound and magnetic resonance imaging (MRI), or biochemical marker values and findings of other nuclear medicine techniques (¹¹¹In-pentreotide, ¹³¹I-MIBG, ^{99m}Tc(V)-DMSA scintigraphy). When available, histopathology results were used to confirm diagnosis. The minimal follow-up period was three months.

Results: FDG PET/CT scan suggested presence of metabolically active disease in eight patients. During clinical follow-up, in four of these patients stabile or progressive disease was observed, confirmed by new lesions seen on conventional imaging methods or high biochemical marker values. In one patient, with metastatic mixed lung adenocarcinoma/small cell NET, focus of high FDG metabolic activity was seen on the neck, suggesting active disease in lymph nodes. This patient underwent biopsy and disease progression was confirmed by histopathology, with dominant anaplastic component. In one patient with MTC and positive PET scan, histopathology of the cervical lymph nodes overruled the existence of disease. Two patients, who were suspected to have active disease on PET showed no signs of illness during follow-up and were considered disease free. Thus, PET/CT findings in these three patients were considered to be false positive. In eight patients no foci of metabolically active disease were described on PET/CT. One patient with MTC had enlargement of cervical lymph nodes during follow-up and was submitted to biopsy. Histopathology results showed the presence of MTC in two excised lymph nodes, suggesting that FDG PET/CT finding was false negative. Other patients with negative PET scan remained disease free during follow-up. Overall, positive predictive value of PET/CT was 62.5%, while negative predictive value was 87.5%.

Conclusion: Our results suggest that FDG PET/CT can have significant role in management of patients with neuroendocrine tumors. The negative predictive value of FDG PET/CT was high in our study, suggesting good prognostic value of negative scan and that the real benefit of this hybrid imaging method can be in excluding the presence of disease.

P13. SYNTHESIS, RADIOCHEMICAL AND IN VITRO AND IN VIVO EVALUATION OF HER2/NEU-DERIVED PEPTIDE AS A POTENTIAL BREAST CANCER IMAGING AGENT

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Objectives: The overexpression of HER2/neu on several human cancers including breast and ovarian cancer and the low expression of this tumor-associated antigen on normal tissues makes it an attractive molecular target for the diagnosis and therapy of cancer. To develop tumor antigen-based peptide for breast cancer imaging, we prepared and characterized a HER2/neu-derived peptide containing the following sequence: Acetyl-Gly¹-Gly²-Cys³-Asp⁴-Lys⁵-Nle⁶-Phe⁷-Gly⁸-Ser⁹-Leu¹⁰-Ala¹¹-Phe¹²-Leu¹³-CONH₂.

Methods: The peptide was prepared by solid-phase synthesis technique according to Fmoc/HBTU methodology and radiolabeled with Tc-99m by stannous/tartrate exchange labeling method. *In vitro* tumor cell-binding and cellular internalization studies were performed on SKBR3 and MDA-MB-231 breast cancer cell lines and *in vivo* biodistribution was determined in healthy mice and nude mice induced with MDA-MB-231 xenografts.

Results: The structure and purity of the tumor-associated antigen peptide was confirmed by mass spectrometry and HPLC. Radio-HPLC analysis showed that the peptide labeled efficiently with Tc-99m (> 95%) and formed one radioactive compound. Tc-99m-HER2/neu displayed high resistant to cysteine transchelation and high metabolic stability in human plasma in vitro. The radiopeptide exhibited high affinity binding to SKBR3 and MDA-MB-231 cells with the K_d values of 9.55 \pm 2.74 nM and 4.40 \pm 1.08 nM, respectively. The radioactivity internalized into SKBR3 and MDA-MB-231 cells was 35 \pm 3.8% and 38 \pm 4.57%, respectively. In vivo biodistribution in normal mice is characterized by rapid clearance from the blood and excretion by both the renal and hepatobiliary routes. The uptake in the major organs (lungs, liver, stomach, kidneys, etc.) was low (< 6% ID/g) both at 1 and 4 h p.i. The radiopeptide showed moderate tumor uptake (2.58 \pm 0.62% ID/g) as early as 1 h p.i., which reduced to 1.48 \pm 0.51% ID/g at 4 h p.i. in nucle mice bearing breast tumor xenografts. The uptake in the tumor was always higher than the radioactivity in the blood and muscle.

Conclusions: This initial study towards the development of a peptide-based tumor imaging agent indicated that the HER2/neu-derived peptide possess certain favorable *in vitro* and in *vivo* properties and deserve further evaluation in order to determine the real potential of this new and attractive class of peptides for tumor imaging.

P14. FIRST EXPERIENCE OF PET-CT APPLICATION IN UKRAINE

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Introduction: First Ukrainian PET-CT started to function in Kyiv City Center of Nuclear Medicine in September 2011. ¹⁸FDG was used for diagnostics purposes. That pharmaceutical was synthesized in PET unit cyclotron.

Materials and methods: 230 patients with different oncology pathologies were investigated: **Discussion:** Proved diagnosis — 138, new lesions (which was not detected by other methods) — 58, restaging — 55. Besides, PET-CT was used in 5 patients for radiotherapy planning. **Conclusions:** We used PET-CT diagnostic in according to experience of our European colleagues. Our own experience proved high sensitivity of the method in oncology practice. In the nearest future after synthesizing new pharmaceuticals 11C we are going to broaden PET-CT diagnostic for other medical fields as well as for oncology practice.

Lung cancer	32
Breast cancer	53
Ovarian cancer	6
Uterine cancer	7
Vaginal cancer	3
Fallopian tube cancer	1
Cervical cancer	2
Soft tissue cancer	6
Unknown primary	9
Prostate cancer	3
Thyroid cancer	3
Pancreatic cancer	7
Colorectal cancer	18
Stomach cancer	3
Esophegeal cancer	1
Bone cancer(sarcoma)	1
Lymphoma (non-Hodgkin s Hodgkin)	45
Melanoma	11
Head and Neck cancer	3
Urinary tract cancer	13
Tumor of the mediastinum	3

P15. A ONE-STEP AUTOMATED RADIOSYNTHESIS OF ¹⁸F-FECNT FROM MESYLATE PRECURSOR

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Introduction: Dopamine transporter (DAT) is critical to the regulation of dopamine neurotransmission and is decreased by Parkinson's disease. The fluorine-18 labelled ligand 2-beta-carbomethoxy-3-beta-(4-chlorophenyl)-8-(2-fluoroethyl)-nortropane (FECNT) has promising properties and appears to be an excellent DAT imaging agent in human PET study. This radiopharmaceutical can be widely used in the diagnostics of the Parkinson's and other neurological diseases. However, it hasn't been used for routine clinical trials because of a very low radiochemical synthetic yield. A semi-automated synthesis of [¹⁸F]FECNT based on the two-steps has been developed with 16% decay corrected yield [1]. We hypothesize that N-[¹⁸F]fluoroalkylnortropane analogs could be synthesized at hight yield by direct ¹⁸F-fluorination from N-mesylate precursors. This compound and non-radioactive FECNT as a standard for identification of [¹⁸F]FECNT by HPLC chromatography were synthesized in accordance with requirements for Investigational Medicinal Product (IMP) and a one-step automated synthesis of [¹⁸F]FECNT was developed.

Methods: Synthetic approach adopted to synthesis of FECNT standard and precursor was based upon the published procedures [2, 3] with some modifications. The essential feature of this route was the reaction of Grignard reagent with the critical intermediate anhydroecognine methyl ester, which was obtained from cocaine hydrochloride by hydrolysis in hydrochloric acid and estrification with methanol. 3- β -substituted tropane derivative obtained in Grignard reaction was subjected to demethylation [4]. Non-radioactive FECNT was prepared by direct N-(2- fluoroethyl) alkylation of analytically pure 3- β -substituted nortropane precursor. The alkylating agent, 2-fluoroethyl brosylate, was prepared from 2-fluoroethanol and 4-bromobenzenesulfonoyl chloride. The crude product was purified by recrystallization. Mesylate (MsOECNT) precursor was synthesized from 3- β -substituted nortropane precursor in two steps by N-hydroxyethylation with 2-bromoethanol and subsequent mesylation of the obtained alcohol with appropriate anhydride and purified by preparative HPLC.

Automated synthesis of [¹⁸F]FECNT was carried out using ¹⁸F-multifunction synthesizer (Syn-Chrom, Raytest). The [¹⁸F]fluoride was produced with 11MeV negative–ion cyclotron by the ¹⁸O(p,n)¹⁸F reaction, trapped on QMA cartridge and eluted by solution containing: Kryptofix (K₂₂₂) in CH₃CN and 0.1 M K₂CO₃. The obtained complex K[¹⁸F]FK_{2.2.2} was heated with mesylate precursor in CH₃CN at 80°C for 15 min. The crude product [¹⁸F]FECNT was purified by preparative HPLC and C18 SepPak extraction. Analytical HPLC with UV and radiometric detection was used to assess the radiochemical purity and [¹⁸F]fluorination yield.

Results: In the present study we investigated and optimized synthetic route of non-radioactive FECNT and developed an automated radiosynthesis of [¹⁸F]FECNT. Overall production yield was 74% for FECNT standard and 81% for MsOECNT synthesis and a purity of these products was over 99% measured by the analytical HPLC (UV, 220 nm). The ¹H NMR and MS analysis confirmed the structure of both compounds. Crude product [¹⁸F]FECNT was prepared with [¹⁸F]fluorination yield of > 70%. After purification, the final product was obtained with a radiochemical purity of > 99%. The radiochemical yield calculated from the beginning of the synthesis was 58% with decay correction. The duration of the total synthesis procedure was 80-90 min.

Conclusions: The reported one-step radiosynthesis, purification and dose formulation of final product will provide a facile and reliable method for the production of high purity [¹⁸F]FECNT suitable for human use. In the future radiosynthesis of [¹⁸F]FECNT from tosylate precursor will be investigated.

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P16. RADIOLABELING AND *IN VITRO* EVALUATION OF SHORT PEPTIDES THAT HAS A POTENTIAL AS ANGIOGENESIS IMAGING RADIOTRACERS

Mohammed Al-Qahtani, Yousif Al-Malki

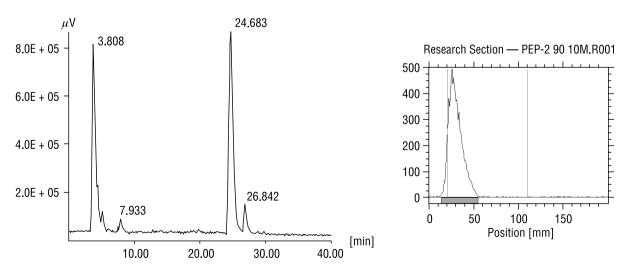
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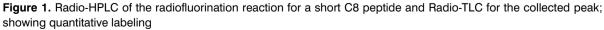
Introduction: The growth of new blood vessels (angiogenesis) sustains tumor spread and growth or metastasizes by supplying oxygen and nutrients. Angiogenesis has been identified as a target site for therapeutic intervention because of its important role in tumor growth, metastasis, and inflammatory diseases. Angiogenesis is regulated by both activator and inhibitor molecules. Angiogenesis is an equally important component of certain normal physiological processes such as embryogenesis, wound healing, and the female reproductive cycle. The basement membrane (BM) is a delicate cell-associated sheet-like extracellular matrix and covers the basal aspect of all epithelia and endothelia. It surrounds muscle, fat, and peripheral nerve cells.

Molecular markers for angiogenesis such as vascular endothelia growth factor receptors (VEG-FRs) and the integrins (e.g. $\alpha v\beta 3$) have become the logical targets for investigation. The integrins are expressed and upregulated during angiogenesis. The receptors are known to bind peptides containing the arginine, glycine, and aspartic (RGD) amino acids sequence. This small peptide has been investigated extensively. Additionally the radiolabeled (F-18, Tc-99m, In-111, and Cu-64) analogs are being investigated as tracers for noninvasive measurement of angiogenesis. These agents have shown promise in both animals and human patients. Therefore there is need to develop imaging methods that would measure the actual process at the molecular level. Additionally several VEGFR-2 antagonists have been identified based on the quinolyoxy-phenyl and quinazolin-4-yl pharmacophore.

In this study monomeric C8 peptide and a number of its derivatives, labeled with ^{123/125/131} I and in some cases ¹⁸F and then evaluated using human umbilical vein endothelial cells (HUVEC) cell line for in vitro.

Methods: All needed reagents and solvents were purchased and used with no further purifications unless its necessary. Reaction progress was monitored using both Radio-TLC and HPLC. The eluent was monitored with a variable-wavelength detector and a flow-through sodium iodide scintillation Nal(TI) radioactivity detector. Radioactivity determined with a dose calibrator. The targeted peptide was radioiodinated applying the direct electrophilic method using either chloramine-T or lodogen as an oxidant reagent. For fluorination the 2,5-dioxoazolidinyl-4-fluorobenzoate (SFB) was used as labeling agent in a direct conjugation process.







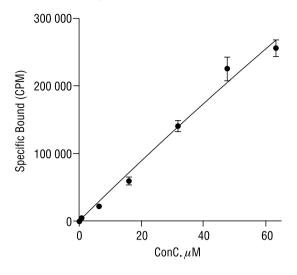


Figure 2. Examples of the Saturation binding studies

Results: The radiosynthesis and characterization results as well as initial biological evaluation will be presented.

Conclusions: The preliminary results indicates that short peptides of the C8 derivatives that been tested are promising imaging tracers of the angiogenesis biological process. **Research support:** This work was supported by King Abdualaziz City for Science & Techno-

logy (AT-29-15).

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P17. CENTRE FOR BIOLOGICAL AND CHEMICAL SCIENCES NEW POSSIBILITIES IN PRECLINICAL RESEARCH USING PET, SPECT AND CT TECHNIQUES

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The Positron Emission Tomography (PET) is a method of nuclear medicine allowing non-invasive diagnostics of many diseases of internal organs. Oncology is one of the fields of clinical medicine where application of PET expands rapidly. The PET allows early and accurate tumor detection as well as enables direct monitoring of progress in the oncological treatment. There is also a growing interest in application of PET method, combined with SPECT and CT techniques, in the research related to the metabolism of practical drugs, e.g. those used in treatment of diseases of the nervous and cardiological systems. Simultaneously to clinical applications, PET technology for small animal imaging (animalPET), is one of the quickest developing diagnostic methods used in preclinical investigations of new radiopharmaceutics and in studies of the metabolism of drugs.

In 2009 The University of Warsaw has signed a contract with the Ministry of Science and Higher Education (Poland) to build a new research centre. The joint project of the Faculties of Biology and Chemistry of the University, called the Centre for Biological and Chemical Sciences (CENT III), will be located at the Ochota Campus on the ground floor of the Radiochemistry Department. CENT III will perform the function of a modern technology centre, conducting research and development activities connected with the areas of modern technology within the scope of the faculties. These areas are strategic from the point of view of national development and include biotechnology. biomedical technologies, environment protection, chemical sciences and new materials applied in medicine and various branches of industry. One of the most important R&D areas of the new Centre will be investigation of biologically active chemicals on small animals, including genetically engineered animals. Two laboratories of The Faculty of Chemistry of The University of Warsaw: the Laboratory of Electrochemical Power Sources and Laboratory of Biomolecules established a team with the purpose of setting up the first animalPET scanner in Poland. A new Laboratory of Molecular Imaging will be equipped with a variety of modern scientific tools required in PET experiments, including a high resolution multimodality imaging system using PET, SPECT and CT techniques, automatic synthesis units for nucleophilic and electrophilic substitution, hot cells, a quality control system, equipment necessary for synthesizing isotope labeled compounds and full anaesthesia system used in small animals research. The laboratory will be opened by the middle of 2012.

The Laboratory of Molecular Imaging will provide a modern research space for scientists of the Ochota Campus interested in investigation of biologically active chemicals on small animals. We hope that our knowledge and unique equipment will help emerging novel ideas and will allow accomplishment of many scientific goals. Convenient location of the laboratory, which will be close to many R&D institutions, e.g. the Nencki Institute of Experimental Biology (Polish Academy of Sciences), the Mossakowski Medical Research Centre (Polish Academy of Sciences), the Warsaw Medical University, and the Heavy Ion Laboratory of the Warsaw University, will allow us to establish strategic cooperation and will create flexible facility for preclinical investigation of new drugs.

In April, 2012 the University of Warsaw and Carestream Health, Inc., will sign a Letter of Intent to establish mutual cooperation for the development of molecular imaging techniques. The parties declare to create at the University of Warsaw, at the Centre for Biological and Chemical Sciences, a Center of Excellence & a Reference Site for Carestream Molecular Imaging and their Albira and Multispectral digital imaging instruments. The cooperation will include:

- Opening the regional Centre of Excellence focused on the development of molecular imaging techniques as modern tools in preclinical research, especially: Positron Emission Tomography (PET), Single Photon Emission Computed Tomography (SPECT), Luminescence and Fluorescence techniques.
- Improvement of the scientific qualifications of the personnel of the Centre of Excellence at the University of Warsaw.

- Organizing scientific conferences, trainings and demonstrations.
- Promotion of new Carestream equipment used for preclinical research.
 Cooperation in scientific projects focused on investigation of new biologically active compounds.

Acknowledgements

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P18. PET/CT WITH 11C-ACETATE VERSUS 18F-FDG IN PATIENTS WITH RECURRENCE BIOCHEMISTRY OF PROSTATIC CARCINOMA

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Introduction: The prostate canceris the leading cause of mortality in the groupof malignancies in men in Mexico, considered a public health problem in this population group. The heterogeneous spectrum of this neoplasm shows a marked increase in mortality, the foregoing marks a change in epidemiological trends in our country in recent years. Patients treated with curative intent have biochemical relapse probability of 15% to 40% at 5 years and about 70% in 10 years, a fact which leads to the importance of imaging techniques that provide timely information on the evaluation of this neoplasm in subclínical stages. There is currently no diagnostic test to detect early and effective recurrence of this disease, even before the evidence of biochemical progression at low levels of Prostate Specific Antigen (PSA) from > 0.2 ng/ml, so we feel the need to study the potential of Positron Emission Tomography and Computed Tomography with the use of specific radiotracers, such as11C-acetate in patients with suspected recurrence of prostatic adenocarcinoma, the radiotracer internationally promises an exceptional advantage in early detection of recurrence with value slow compared to other conventional imaging methods and even PET /CT with18F-FDG.

The 11C-Acetate benefits offered are: Null urinary excretion, thus better visualization of the prostate bed, evaluation of alternative pathways to glycolysis, where its direct incorporation into the Krebs cycle, allows us to study the metabolism of fatty acids direct translation in the synthesis of membrane lipid, very important in prostate tumors whose growth substrate for glucose is not primarily.

Objective: To establish the usefulness and validity of PET /CT with 11C-Acetate as specificradiotracer in the assessment of patients with biochemical recurrence of prostate adenocarcinoma versus 18F-FDG.

Materials and methods: This prospective study was conducted analytical unit in PET/CT cyclotron of the Faculty of Medicine UNAM in the period May 2011 to January 2012. A total of 31 patients diagnosed with prostate cancer, only those with defined biochemical recurrence of PSAvalues > to 0.2 ng/ml and no evidence of other imaging methods for localization of residual tumor.

The acquisition of the PET/CT studies were performed first with 18F-FDG and 1 to 2 days of 11C-acetate. All studies were performed on the computer PET/CT BiographTruePoint64 Siemens Medical Systems, with the protocol of ourdepartment. The image analysis was performed by two radiologists and two nuclear medicine specialists with extensive experience.

Results: A total of 31 male patients with mean age of 67, PSA levels ranged from 0.32 ng/ml to 214 ng/ml, with an average of 18.9 ng/ml. 25 studies were identified positive (83.3%) with 11C-Acetate 6 witha negative diagnosis (16.7%), whereas 18F-FDG identified 10 studies positive for malignancy (33.3%) and 21 negative (66.7%). Statistical analysis revealed a sensitivity of PET/CT with11C-acetate of 88% with a specificity of 100% with a confidence level of 95%, PPV was 100% and NPV of 66.67%, 18F-FDG both the sensitivity observed was 45.4% with a specificity of 100%, calculated PPV are 100% and NPV of 42.86% in the assessment of recurrence. We calculated the correlation of evidence with respect to histopathological study was obtained kappa coefficient for PET/CT with 11C-Acetate 0.73 (95% CI: 0.46–1.00), while for 18 F-FDG was 0.32 (CI: 95% from 0.10 to 0.54). Was performed to measure the consistency of the test according to the criteria of Landisand Koch, revealing a substantial strength of agreement for11C-Acetate and 18F-FDG median.

Lesions detected by both methods clearly show the advantage of 11C-acetate in the detection of local and distant disease.

Conclusions: PET/CT with 11C-Acetate conclusively shows greater sensitivity in detecting prostate cancer recurrence, with a high degree of validity in comparison with 18F-FDG, supported by substantial agreement when compared with the results of histopathology, being statistically significant. As is helpful in monitoring patients with suspected relapse, leading to the imperative of its spread torelated specialists as an excellent diagnostic tool for early diagnosis of this disease.

P19. PET/CT IN MALIGNANT MELANOMA

CA Stan

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Purpose: To assess the diagnostic performance of positron emission tomography/computed tomography (PET/CT) using 18F-fluorodeoxyglucose (FDG) for N- and M-staging of cutaneous melanoma.

Materials and methods: This is a retrospective study who underwent FDG-PET/CT for staging of cutaneous melanoma at the last 50 patients (untill present). Whole-body FDG-PET/CT was performed of about 60- 90 minutes postinjection of about 370 MBq FDG. Diagnostic accuracy for N- and M-staging was determined for CT alone, PET alone, and PET/CT.

Results: PET/CT detected significantly more visceral and nonvisceral metastases than PET alone and CT alone. PET/CT imaging thus provided significantly more accurate interpretations regarding overall N- and M-staging than PET alone and CT alone. Accuracy of PET/CT was significantly higher than that of PET and CT for M-staging and significantly higher than that of CT for N-Staging. **Conclusions:** The diagnostic performance of FDG-PET/CT for N- and M-staging of melanoma patients suggests its use for whole-body tumor staging, especially for detection or exclusion of distant metastases.

P20. BONE MARROW INVOLVEMENT IN SARCOIDOSIS PATIENT DIAGNOSED BY 18FDG/ PET — CASE REPORT

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Background: Sarcoidosis is a chronic inflammatory disease of unknown cause characterized histologically by granulomas in affected tissues, that usually presents with mediastinal and hilar lymphadenopathy and with variable involvement of the lungs. Other organs may be involved, including the skin, kidneys, liver, salivary glands, and bone marrow. The reported incidence of skeletal involvement with sarcoidosis ranges from 3% to as much as 36%. Medical treatment often involves corticosteroid therapy or methotrexate, but in some cases spontaneous regression occurs. The degree of inflammatory activity and systemic distribution of the disease helps in determining appropriate treatment. In most cases, the diagnosis requires confirmation with biopsy.

Case presentation: We report a story of a young woman with an advanced breast cancer, who underwent a 18FDG/PET scan to detect the site of relapse. In three subsequent studies we monitor the response of cancer therapy and also the response to corticosteroid therapy of sarcoidosis. In the first study we find the typically uptake known as a "lambda" pattern that relates to bilateral hilar involvement. In the second study we saw the good response to corticosteroid treatment, but progression of breast cancer. In the last PET scan of this patient we reveal bone marrow involvement of sarcoidosis, that was later confirmed by aspiration biopsy.

Conclusion: In this report, we highlight the role of 18FDG/PET to assess bone marrow involvement and to monitor efficiency of corticosteroid treatment in sarcoidosis patients.