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ABSTRACTS BOOK

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#### **ORAL SESSION**

#### **E1**

## PRIMARY SYSTEMATIC TREATMENT OF BREAST TUMOUR: LINKS BETWEEN DIAGNOSTIC EXAMINATIONS OBJECTIVE

T. Tökés<sup>1</sup>, K. Iványi<sup>1</sup>, K. Somlai<sup>2</sup>, B. Székely<sup>2,3</sup>, J. Kulka<sup>3</sup>, Gy. Szentmártoni<sup>2</sup>, L. Torgyík<sup>2</sup>, M. Dank<sup>2</sup>, I. Kalina<sup>2</sup>, H. Galgóczy<sup>5</sup>, Zs. Lengyel<sup>6</sup>, T. Györke<sup>4,5</sup>

<sup>1</sup>Semmelweis University, Budapest, Hungary

<sup>2</sup>Department of Diagnostic Radiology and Oncotherapy, Semmelweis University, Budapest, Hungary

<sup>3</sup>2nd Department of Pathology, Semmelweis University, Budapest, Hungary
 <sup>4</sup>Department of Nuclear Medicine, Semmelweis University, Budapest, Hungary

ScanoMed Ltd., Budapest, Hungary

<sup>6</sup>Pozitron-Diagnosztika Ltd., Budapest, Hungary

Background: The role of metabolic imaging is increasing in the measurement of early therapeutic response during cancer patient treatment. Our aim was to measure the effect of primary systemic chemotherapy (PST) on high risk breast cancer patients by using imaging modalities and pathology diagnostics and to find correlation between the applied modalities. The results of FDG-PET-CT examinations, which helped identify the extent of the tumour and the existence of distant metastasis, were available for therapeutic decision, as well as the core biopsy results which showed the tumour's biological behaviour. We compared the metabolic and morphological response, and analysed the relationship of these responses with the proliferation of the tumour, with special emphasis on changes in Ki-67 expression.

Material and methods: We report 22 (21 women and 1 man) of patients treated with PST during 2008–2010. All of them were examined by FDG-PET-CT for staging before chemotherapy and surgery. We excluded patients with distant metastases on pre-operative PET-CT, and those who refused surgery (lack of tissue samples). Standard Uptake Value (SUV) changes were measured on PET scans in the primary tumour and the axillary lymph node region. The calculated  $\Delta \text{SUVs}$  were compared with morphological changes on native CT, as well as with the changes of the expression of Ki-67 proliferation marker measured by specific immune-histochemistry method in the core biopsy and surgical specimens. For analysing the changes we used two-sample T-test and Spearman rank correlation.

**Results:** The reduction of Ki-67 levels proved to be significant (49.41% vs. 16.23%, p = 0.001). A significant decrease was detected in the SUV of primary tumours (12.18 vs. 2.59, p = 0.001), and SUV of the axillary region (11.72 vs. 3.18 p = 0.009). A significant reduction was detected in the size of the primary tumour (30.86 mm vs. 17 mm, p = 0.002), but in the axillary lymph node region the reduction in size proved to be insignificant (18.58 mm vs. 14.58 mm, p = 0.319). Significant correlation was found between Ki-67 and SUV parameters before PST in primary tumours (p < 0.001). There was also a significant correlation between initial Ki-67 values and changes in SUV (p < 0.001), and between Ki-67 changes and in  $\Delta$ SUVs (p < 0.001, correlation coefficient: +0.734).

Conclusions: Metabolic changes correlate well with the regression indicated by the proliferation marker, and with the pathological tumour response, better than the morphological regression, especially in axillary lymph node region. Beside the Ki-67 expression based on core biopsy, the FDG-PET-CT results may play an essential role in the indication of PST. PET-CT seems useful in the assessment of response to treatment, and it can be particularly significant in assessing the early therapeutic response of the tumours.

#### **F2**

## COMPARISON OF FDG PET-CT AND MRI DWIBS TREATMENT FOLLOW UP EXAMINATIONS IN CHILDHOOD LYMPHOMAS

M. Zsbán¹, G. Rudas², L. R. Kozák², Z. Tóth³, G. Kovács⁴, M. Csóka⁴, T. Gvörke³.5

<sup>1</sup>Faculty of Medicine, Semmelweis University, Budapest, Hungary <sup>2</sup>Semmelweis University MR Research Center (MRKK), Budapest, Hungary

<sup>3</sup>Scanomed Ltd., Budapest, Hungary

 $^{42\mathrm{nd}}$  Department of Paediatrics, Semmelweis University, Budapest, Hungary

<sup>5</sup>Department of Nuclear Medicine, Semmelweis University, Budapest, Hungary

**Background:** In the treatment follow up of childhood lymphomas FDG PET-CT is widely used as the most suitable method to assess the tumor viability. The MRI DWIBS (diffusion-weighted whole-body imaging with background body-signal suppression) is a new method without radiation, which is — based on the literature — also reliably determines the viability, but its sensitivity and specificity in childhood lymphomas are unknown yet. The aim of this study is the comparison of the two methods, and determination of the role of DWIBS in childhood lymphomas.

**Material and methods:** In our prospective study we have investigated 7 children with Hodgkin's (HD) and 8 with non-Hodgkin's (NHL) lymphomas. 26 pairs (12 HD and 14 NHL) of comparative PET-CT and MRI DWIBS examinations were performed. The average ages of the patients at the diagnosis were 13 years with HD and 9 years with NHL. Average time between MRI and PET-CT was 4.1 (0–19) days. The imaging results were compared clinical follow up and/or biopsy results. The data processing was based on medical records and on the reports of imaging procedures. In case of uncertain results we reevaluated the MRI and PET-CT images.

**Results:** In HD the results of the 12 MRI and PET-CT examinations correlated well in terms of morphology and viability. In 6/12 cases however, both examination methods showed lymph node regions with FDG-uptake or reduced diffusion without any proven viable tumor. All clinically positive tumors were confirmed by both imaging methods. In the NHL patient group, among the 14 PET-CT and MRI comparative examinations in 3/14 cases the relapse was clinically confirmed, but in 2 cases (which were two relapses of the same patient) MRI gave negative result. In 1/14 interim examinations MRI was positive, while PET-CT negative, but following further additional treatments no viable tumor could be found. In case of 10/14 examinations, although the patients were in remission clinically, in only 4 cases could be supported this by both examinations. From the remaining 6 cases in 4 and 3 cases positivity was found by PET-CT and MRI, respectively.

#### **E3**

### 18F-FDG PET/CT IN THERAPY RESPONSE ASSESSMENT OF BONE-DOMINANT BREAST CANCER

Zs. Hascsi<sup>1</sup>, E. Nagy<sup>2</sup>, N. Fedinecz<sup>1</sup>, J. Varga<sup>2</sup>, J. Tóth<sup>3</sup>, K. Mezei<sup>4</sup>, I. Garai<sup>1</sup>

<sup>1</sup>ScanoMed Nuclear Medicine Centers, Debrecen, Hungary <sup>2</sup>Institute of Nuclear Medicine, University of Debrecen, Debrecen, Hungary <sup>3</sup>Institute of Oncology, University of Debrecen, Debrecen, Hungary <sup>4</sup>Department of Radiooncology, Jósa András Teaching Hospital, Nyíregyháza, Debrecen, Hungary

**Background:** In patients with disseminated breast cancer malignant bone involvement occurs in approximately 70%. Conventional imaging methods, including bone scintigraphy, are highly sensitive for detecting bone me-

tastasis, although they have limited accuracy in assessment of response to therapy. There is no established standard method for monitoring bone metastases. Recent data suggest the promising performance of 18F-FDG PET/CT (PET/CT) for this purpose. Our aim was to retrospectively determine the prognostic value of sequential PET/CT in monitoring systemic therapy of bone-dominant metastatic (BDM) breast cancer.

Material and methods: Retrospective search of our image database identified 23 breast cancer patients with BDM disease, who underwent treatment and had serial PET/CT studies. In this patient group altogether 32 pairs (baseline and follow-up) of PET/CT imaging datasets were reviewed by two experienced specialists. For quantitative analysis the most FDG avid metastasis was defined as target lesion, in accordance with PERCIST criteria. Therapeutic responses were visually classified into four categories: complete and partial metabolic response (CMR, PMR), stable and progressive disease (SMD, PMD). Target lesion SUV and SUL, maximum and peak values were recorded at each time point. Visual response, target SUV/SUL max/peak on baseline, and the absolute and relative change of quantitative parameters were supposed to be predictive for time-to-progression (TTP), which served as a clinical outcome measure. TTP was clinically established by two oncologists independently from PET results (based on other imaging results, tumor markers, and symptomatic findings). The median follow-up time was 230 days.

Results: Forward stepwise Cox regression analysis was used to test for associations between TTP and both dichotomous and continuous variables. Percentage change in SULpeak (p = 0.001), initial SULmax (p = 0.012) and SULpeak (p = 0.030) were most significantly correlated with the outcome. On Kaplan-Meier analysis the survivor curves of four visual and PERCIST response groups were shown to differ. Responders (CMR + PMR) had significantly longer TTP compared to patients with PMD (p = 0.02)

Conclusion: Our retrospective study indicates that PET/CT might have a role in therapy response assessment of BDM breast cancer. Qualitative (visual) evaluation and SUL (rather than SUV) based quantification, as proposed by PERCIST, is feasible to apply when considering a prospective trial to validate these findings.

#### **E4**

#### COMPARING THE DIFFERENTIAL DIAGNOSTIC VALUE OF HIBRID IMAGING TECHNIQUES (SPECT/CT, PET/CT) IN BONE LESIONS

S. Szekeres<sup>1</sup>, Zs. Lengyel<sup>2</sup>, K. Dérczy<sup>3</sup>, Cs. Weninger<sup>3</sup>, E. Schmidt<sup>1</sup>, Zs. Szabó¹, K. Zámbó¹

<sup>1</sup>Department of Nuclear Medicine, University of Pécs, Pécs, Hungary 2Center for Pozitron Diagnostic, Budapest, Hungary

<sup>3</sup>Department of Radiology, University of Pécs, Pécs, Hungary

Background: The purpose of our study is to compare the diagnostic efficacy of 99Tc-MDP bone scintigraphy completed by SPECT/CT and the 18F-FDG PET/CT examinations in evaluation of bone metastases.

Material and methods: Due to the collaboration of two departments we have an opportunity to compare the results of patients who underwent the oncological evaluation program including 99Tc-MDP bone scintigraphy completed by SPECT/CT and the 18F-FDG PET/CT examinations.

Results: We diagnosed with SPECT/CT in 48% of patients some type of benign lesions (degenerative disease, traumatic injury or consequence of operation). In the cases of these patients the results of 18F-FDG PET/CT in the whole bone system concerning the bone metastasis were negative as well. Furthermore bone metastases were found in 22% of patients with the SPECT/CT and PET/CT, too. In the 30% of the patients the results of above mentioned between the two different methods were not concordant. Conclusions: The 99Tc-MDP bone scintigraphy completed by SPECT/CT can particularly improve the detection of the exact etiology of lesions. The diagnostic value of these two different methods have a good correlation. The possible deviation can be caused by using different mechanisms to detect the pathologic lesions: 99Tc-MDP bone scintigraphy reperesents the phosphate metabolism while the 18F-FDG PET detects the glucose metabolism and the increased activation of osteoblasts are not always accompanied by increased glucose matabolism.

#### **F**5

#### IMPORTANCE OF FDG PET-CT IN DIAGNOSIS AND FOLLOW-UP OF PATIENTS WITH BREAST CANCER

H. Galgóczy<sup>1</sup>, A. Németh<sup>2</sup>, Zs. Varga<sup>1</sup>, P. Szabó<sup>1</sup>, L. Jorgov<sup>3</sup>, I. Garai<sup>1</sup>

<sup>1</sup>ScanoMed Kft., Budapest–Debrecen, Hungary

<sup>2</sup>Department of Transplantation and Surgery, Semmelweis University, Budapest, Hungary

<sup>3</sup>Department of Radiology and Oncotherapy, Semmelweis University, Budanest Hungary

Background: Our aim was to define extra information of FDG PET-CT examination comparing to the previous diagnostic images; to evaluate the percentage of confirmation of clinically supposed status and to define it's influence on oncologic treatment of patients.

Material and methods: The medical records of 143 consecutive patients with breast cancer referred from three oncologic centers from October 2008 to September 2009 were retrospectively reviewed. PET-CT imaging was performed with GE Discovery ST scanner according to the usual protocol. 143 patients (142 women, 1 man, mean age 56.9 years) have 155 breast tumors. The hystologic subtypes of the primary tumors were infiltrating ductal carcinoma in 102, infiltrating lobular carcinoma in 18, DCIS alone in 9, other/unknown in 26 cases. Hystologically Grade 2 carcinoma occured in largest proportion. 70 conservative operations and 74 mastectomies were performed. In remainder cases the operation was not performed or type of surgical procedure was not known.

Results: Definite diagnosis was established in 129 cases (84.3%), the extent of disease was increased in 40 (31%), diagnosis was unchanged in 24 cases (18.6%), it was negative in 65 cases (50%). The PET-CT result was equivocal in 24 cases (15.6%) having caused partly inadequate referral, partly difficulty of differentiation between tumor and inflammation. PET-CT examination gave excess information for physicians in 31%. The therapy was altered in 40 cases (26%) based on PET-CT result.

Conclusion: FDG PET-CT examination is useful in management of patients with breast cancer in case of adequate indication.

#### **E6**

#### FDG PET-CT IN MANTLE CELL LYMPHOMA

Z. Tóth¹, V. Tóth¹, A. Fekésházy¹, P. Szabó¹, T. Györke¹, L. Kiss², S. Barna², Á. Illés³, I. Garai²

<sup>1</sup>ScanoMed Ltd., Budapest <sup>2</sup>ScanoMed Ltd., Debrecen

3DEOEC Department of Internal Medicine, Debrecen

Background: We assessed the potential role of PET-CT in the diagnostic workup of mantle cell lymphoma, which type of lymphoproliferative disease unites the unfavourable characteristics of aggressive and indolent lymphomas.

Material and methods:122 PET-CT examinations of 56 patients were retrospectively analysed [11 pre-treatment, 17 interim, 20 restaging, 14 pre-, 23 post-Haemopoietic Stem Cell Transplantation (HSCT) evaluations, and 37 PET-CT examinations due to clinically suspected relapse].

Results: 9/11 staging examinations before initial therapy had revealed pathologic FDG accumulating focuses. Among the interim examinations (17) only 6 patients achieved complete metabolic remission (CMR), in 11 cases FDG-avid lesions were found. Among the 10/20 restaging PET-CT examinations indicating CMR, 4 patients relapsed within 1 year. Among the examinations showing CMR on the pre-transplantation PET-CT (9/14), relapse evolved in 1 case in the first year after transplantation. In 1 of 23 examinations CMR was not achieved after HSCT, from the 21 of 23 cases showing CMR on post-HSCT PET-CT, 2 patients relapsed within 1 year. In 1 of 23 post-transplantation examinations clinical signs of relapse did not develop after positive PET-CT. Clinical relapse suspicion was confirmed by PET-CT in 13 cases, in 5 of 37 cases it was found to be false positive, in the remaining patients relapse did not evolve after negative PET-CT (19/37). Conclusion: FDG PET-CT seems to be an accurate method in the diagnostic workup of mantle cell lymphoma, including pre-treatment staging, interim,

and restaging assessments. Its negative predictive value appears to be acceptable, but remains below the results achieved in Hodgkin- and high grade B cell lymphomas. Regarding the characteristics of the disease its further role may mostly increase in the pre-HSCT prognostic evaluation.

#### **E7**

### 18F-FDG PET/CT IN THE FOLLOW-UP OF BREAST CANCER PATIENTS WITH POSITIVE SLN WITHOUT ALND

Á. Sávolt¹, G. Péley², L. Tóth¹, Z. Mátrai¹, Cs. Polgár³, Zs. Horváth⁴, É. Szabó⁵, K. Borbély⁵

<sup>1</sup>Department of Surgery, Norfolk and Norwich University Hospital, Norwich, United Kingdom

<sup>2</sup>Department of General Surgery, Norfolk and Norwich University Hospital, Norwich, United Kingdom

<sup>3</sup>Department of Radiotherapy, National Institute of Oncology, Budapest, Hungary

<sup>4</sup>Department of Internal Medicine and Oncology, National Institute of Oncology, Budapest, Hungary

<sup>5</sup>Department of Radiology, National Institute of Oncology, Budapest, Hungary

<sup>6</sup>Department PET-CT, National Institute of Oncology, Budapest, Hungary

Background: The Hungarian National Institute of Oncology has just closed a randomized clinical phase III study. The OTOASOR (Optimal Treatment of the Axilla — Surgery or Radiotherapy) trial compared the result of the completion axillary lymph node dissection (ALND) and axillary nodal irradiation (ANI) without ALND in patients with early-stage breast cancer after positive sentinel lymph node biopsy (SLNB). In the investigational arm of the trial patients received 50 Gy ANI postoperatively without ALND. Actually we had information only about the sentinel lymph node (SLN) status, but the further nodal involvement remained unknown. Positron emission tomography combined with computed tomography (PET/CT) has been receiving increasing attention recently for restaging and follow-up of breast cancer. The aims of this study were to evaluate the therapeutic effect of the axillary nodal irradiation and to detect early axillary recurrences or residual diseases.

Material and methods: In year 2009, forty-five T1-2 SLNB positive patients were retrospectively selected from the investigational arm of the OTOASOR trial. All patients underwent surgery (breast-conserving or mastectomy) and SLNB, the SLN(s) were found positive and the patients received 50 Gy ANI instead of completion ALND. Six months after the end of the radiotherapy, patients underwent 18F-FDG PET/CT and mammography combined with breast and axillary ultrasound or breast MRI simultaneously. The findings of PET/CT, mammography and/or breast MRI were compared. Results: Only 5 out of 45 patients had suspicious findings in the axillary tail on mammography combined with breast and axillary ultrasound. In those five patients PET/CT suggested locoregional residual disease in only one patient that was confirmed by core biopsy. In the remaining four cases both the PET/CT and the biopsy showed no evidence of malignity.

**Conclusions:** Our preliminary data suggest that axillary nodal irradiation (ANI) without completion axillary lymph node dissection (ALND) does not increase the risk of recurrence of the sentinel positive patients. Furthermore, the results of our study demonstrate the benefit of 18F-FDG PET/CT in the follow-up of breast cancer patients with positive SLN without ALND.

#### **E8**

#### PROGNOSTIC VALUE OF INTERIM 18FDG-PET/ CT IN PATIENT WITH HODGKIN'S LYMPHOMA, USING DIFFERENT 5-POINT VISUAL SCALE FOR INTERPRETATION

S. Barna¹, N. Fedinecz¹, Zs. Miltényi², F. Magyari², J. Varga³, Á. Illés², I. Garai¹

<sup>1</sup>ScanoMed Ltd., Debrecen, Hungary

<sup>2</sup>Department of Internal Medicine, DE OEC, Debrecen, Hungary

3Department of Nuclear Medicine, DE OEC, Debrecen, Hungary

**Background:** The results of interim 18FDG-PET/CT examinations have great significance in prognosis of HL patients follow-up. Currently definition

of MRU (minimal residual uptake) is not uniform when using 5-point visual scale. The aim of our study is to compare the affect on prognosis of the currently used MRU definition.

Material and methods: Interim 18FDG-PET/CT examination of 82 newly-diagnosed HL patients (male: 40, female: 42, average age: 36 year) were evaluated by London, Hutchings, Gallamini and Barrington criteria. The 18FDG-PET/CT examinations were performed on the same camera according to the standardised protocol. Two experienced specialist analysed the studies. All patients had six courses of ABVB/EBVD and if it was necessary received radiotherapy according to the protocol. The result of interim 18FDG-PET/CT did not affect the later used therapy. The median follow-up period was 24 months (9–47 month). Kaplan-Maier analysis was performed to determine the OS and PFS and Mantel-Cox probe to compare the outcome of the different groups.

**Results:** During the observation period 78% of patient had no progression (64 pts/82 pts) Compare to the PET negative group PET positive group were measured poor prognosis on the basis of all four criteria. The Barrington and Gallamini methods are more robust in estimating prognosis. By Cox regression, stepwise method ["forward stepwise" (likelihood ratio)] Barrington method has been proved the most effective of the 4 criteria (p < 10–4). However compared to PET negative group there wasn't significant difference in survival or PFS in either defined MRU group.

**Conclusion:** On the base of our study with the Barrington and Gallamini criteria PET + patients with worse prognosis can be clearly divided by the result of the interim PET-CT examinations, conversely the MRU category has no prognostic value in clinical aspect with any recommended definition. However more patients and longer follow-up is required to refine data.

#### **E9**

## THE PREDICTIVE VALUE OF FDG-PET/CT IN RESTAGING OF HODGKIN LYMPHOMA — WHAT WE CONSIDER AS A POSITIVE REPORT?

K. Kajáry¹, Zs. Lengyel¹, P. Molnár¹, Sz. Szakáll¹, Gy. Tóth¹, A. Rosta², Zs. Molnár²

<sup>1</sup>Pozitron Diagnostics Ltd., Budapest, Hungary <sup>2</sup>National Institute of Oncology, Budapest, Hungary

Background: The negative predictive value (NPV) of FDG-PET(/CT) at the end of treatment in Hodgkin lymphoma is high. However, the rather low positive predictive value (PPV) is often leads difficulties in the clinical practice. In the last years a method was developed for the assessment of PET results, which is based on both CT and PET criteria. The use of SUVs are generally not appropriate to correctly judge the dignity of the lesions. In this retrospective study the aim of the authors was to define the predictive value of restaging PET/CT with the help of a 5-point scoring system. This system, which was developed for interim PET exams to assessment of therapy-effectiveness, correlate lesion's intesities to mediastinal blood-pool or to liver uptake and takes no notice of CT-criteria.

**Material and methods:** They analysed 90 patients, who have PET/CT after the first line treatment between May 2006 and August 2010. The assignment of patients to "positive" and "negative" groups was performed by two different methods. Method 1: "positive" — the highest FDG uptake is higher than the liver uptake (point 4–5). Method 2: "positive" — the highest FDG uptake is higher than the mediastinal blood-pool uptake (point 3–5).

**Results:** The number of positive patients was 31 with Method 1, 14 out of which came to complete remission (CR) during the follow up. The number of negative patients was 59 out of which 56 came to CR. Based on these data PPV was 56% and NPV was 95%. The number of positive patients was 36 with Method 2 with 17 reaching CR during the follow up. The number of negative patients was 54 with 52 reaching CR. Based on these data PPV was 53% and NPV was 96%. The reason of false positivity mostly was inflammation what was already suggested by the reporting physician in some cases.

**Conclusions:** The authors concluded that PET/CT has high NPV and low PPV when using this 5-point scale. There was no significant difference between the results of the two methods. Reporting physicians can provide substantial help to the therapists by specifically stating of the most probably false positive lesions in the report, based on morfology, localization, clinical data, etc.

#### F10

### INTERIM FDG PET/CT EXAMINATIONS IN ADVANCED STAGE HODGKIN LYMPHOMA

Zs. Molnár¹, B. Deák¹, K. Kajáry², Zs. Lengyel², P. Molnár², A. Rosta¹, T. Schneider¹, E. Szaleczky¹, F. Varga¹, E. Várady¹, K. Borbély¹

<sup>1</sup>National Institute of Oncology, Budapest, Hungary <sup>2</sup>Pozitron Diagnostic Ltd., Budapest, Hungary

**Background:** Hodgkin lymphoma (HL) is a highly curable hematologic malignancy. However, it is difficult to estimate the effectiveness of therapy during treatment. According to the literature FDG-PET/CT is the most suitable method for this purpose. The aim of this retrospective study was to summarise our experience with 18F-FDG PET/CT in interim staging.

**Material and methods:** Twenty five scans were performed in 19 patients between November 2007. and January 2010. Eighteen patients received ABVD combination, 1 patient escalated BEACOPP treatment. Fifty three patients were irradiated at the end of chemotherapy. The number of applied cycles varied between 4 and 8, tailored according to the international prognostic score and the rate of clinical response to treatment. Sixteen examinations were performed after 4–6 cycles, and 9 scans after 1 or 2

**Results:** PET/CT results was evaluated using clinical follow-up data. Fourteen scans were true positive, 4 false negative, 4 true positive and 2 false positive. True negativity and false positivity were established by follow up data, true positivity and false negativity by the progression on repeated imaging (CT or PET/CT). Specificity, sensitivity, positive and negative predictive values were found to be 88%, 56%, 71% and 78%, respectively.

**Conclusion:** However the results are not as precise as in case of restaging, PET/CT may help in treatment personalisation.

#### E11

#### PROGNOSTIC VALUE OF STAGING FDG PET-CT IN PATIENTS WITH MALIGNANT MELANOMA IN CORRELATION WITH CLARKE LEVEL

O. Sántha<sup>1</sup>, J. Varga<sup>2</sup>, J. Olajos<sup>3</sup>, I. Garai<sup>1</sup>

<sup>1</sup>ScanoMed Ltd., Debrecen, Hungary

<sup>2</sup>Department of Nuclear Medicine, DE OEC, Debrecen, Hungary

<sup>3</sup>Jósa András Hospital, Nyíregyháza, Hungary

Background: The aim of this study was to find correlation between early staging PET/CT results, Clark level and progression-free survival (PFS) of patients with primary cutaneous malignant melanoma (CMM) lesions. Material and methods: 99 CMM patients (57 women and 42 men, mean age: 40,73; 18–61 years) who underwent PET/CT within 6 months from diagnosis were enrolled in this retrospective study. Diagnosis was determined by surgical removal and histological confirmation. PET/CT evaluation was concluded positive or negative depending on the presence of lesions related to CMM. Last clinical appearance was considered as positive or negative depending on the findings related to CMM. The median follow-up period was 19 months (8–45 mo).

**Results:** Positive PET/CT was found 39 pts/99 pts (37.3%) to be definitely more frequent in patients with higher Clark level lesion (khi-square test: p=0.0066). Unexpectedly, Kaplan-Meier analysis and Mantel-Cox log rank test found no relations between Clark level and progression-free survival (p>0.1). Our data showed a remarkable difference of the progression-free survival curves of patients with positive and negative PET/CT findings on Kaplan-Meier analysis, and Mantel-Cox log rank test (p<0.005). 46% of the patients with initial positive PET/CT result showed progression during the follow-up. The period of progression-free survival was not significantly different between the PET/CT-positive and negative groups which can be the result of relatively short follow-up.

**Conclusion:** PET positivity shows significant correlation with Clark level rising. Positive PET/CT result within 6 months after surgery indicates significantly higher risk of progression.

#### F12

## IS CONTRAST ENHANCED CT NECESSARY BEYOND FDG-PET/CT FOR PRIMARY STAGING IN HODGKIN LYMPHOMA? — OUR EXPERIENCE

K. Kajáry¹, Zs. Lengyel¹, P. Molnár¹, Sz. Szakáll¹, Gy. Tóth¹, A. Rosta², Zs. Molnár²

<sup>1</sup>Pozitron Diagnostic Ltd., Budapest, Hungary <sup>2</sup>National Institute of Oncology, Budapest, Hungary

**Background:** Several study supported the observation that PET-CT examination with "low dose", non-enhanced CT (PET/CT) is more accurate, than contrast enhanced CT (ceCT) in the staging of Hodgkin disease (HD). The aim of the authors was to compare the accuracy of PET/CT and ceCT for primary staging of HD in their practice, including those cases where ceCT was performed as a supplement to standard PET/CT.

**Material and methods:** The authors retrospectively analysed data obtained from imaging of 29 patients newly diagnosed with HD. In the evaluation of PET/CT images they used a 5-point scoring system which was developed for interim PET examinations. Two methods were used for each regions. In Method 1 the region was positive, if its uptake was higher than the liver uptake (point 4–5). In Method 2 the region was positive, if its uptake was higher than the mediastinal blood-pool activity (point 3–5). Two comparisons were made between the modalities, too: ceCT vs. PET/CT and PET/CT vs. PET/CT+ceCT.

**Results:** Disease was upstaged by PET/CT in 3 patients with Method 1 and in 4 patients with Method 2 as compared to ceCT. They did not find any case of downstaging with PET/CT. There were no change in stage when comparing PET/CT and PET/CT with ceCT.

**Conclusions:** The number of patients was rather low, but the results show that PET/CT is more accurate than ceCT in the primary staging of HD. In addition, the authors established that it is not reasonable to supplement standard PET/CT examinations with ceCT in this indication.

#### E13

### IMPORTANCE OF INCIDENTALLY DISCOVERED FOCAL FDG UPTAKE IN THE LARGE INTESTINE

V. Tóth<sup>1</sup>, P. Szabó<sup>1</sup>, Z. Tóth<sup>1</sup>, T. Löbl<sup>2</sup>, M. Steierlein<sup>3</sup>, I. Garai<sup>1</sup>

<sup>1</sup>ScanoMed Ltd., Budapest, Hungary <sup>2</sup>Péterfy Hospital, Budapest, Hungary <sup>3</sup>Zala County Hospital, Zalaegerszeg, Hungary

**Background:** Incidental focal FDG uptake in the colorectal tract is relatively frequently described (0.6–3%) on PET/CT examinations. According to the relevant literature 13–30% of these findings is caused by malignant tumors. The aim of this study is to evaluate the frequency of malignancy in the background of incidental colorectal focal tracer uptake among our patients.

**Material and methods:** In 2009 3148 patients underwent FDG PET/CT scan in our center, mostly because of any malignant disease. Patients with known colorectal cancer were excluded from our study. The examinations were carried out by GE Discovery ST8 PET/CT camera. Only 18F-FDG was used as radiotracer and protocols compiled according to international guidelines were applied. In every case we drew the the refering doctor's attention to the detected focal colorectal tracer uptake and we suggested further investigation.

**Results:** We detected in 55/3148 (1.7%) patients focal incidental colorectal FDG-accumulation. In 43/55 (78%) patients colonoscopy was performed, on colonoscopy 56 circumscribed morphological lesions were described. In these 43 patients we detected 49 focal FDG-uptake, altogether. 9/49 (18%) FDG-accumulating lesions proved to be malignant (verified histologically). 19/49 (39%) lesions showing focal tracer uptake were described as polyp on colonoscopy, in 11/19 cases correct histology could be performed indicating dysplasia in 9/11 (82%) samples. In the remaining cases of focal FDG-uptake other lesions (inflammation, diverticel, etc. 9/49, 18%) or nothing (12/49, 24%) were visible on endoscopy.

**Conclusions:** In our study the frequency of incidental focal FDG accumulation in large intestine upon PET/CT scan and among them the proportion of malignant and premalignant lesions confirmed by histology is equal to data of the literature. Therefore we emphasize the importance of further investigation of patients with incidental focal colorectal FDG uptake.

#### E14

#### PROGNOSTIC VALUE OF INTERIM FDG PET-CT IN NON-HODGKIN'S LYMPHOMAS TREATED WITH COMBINED CHEMO-IMMUNOTHERAPY

T. Györke<sup>2,4</sup>, A. Lantos<sup>1</sup>, T. Masszi<sup>5</sup>, G. Mikala<sup>5</sup>, A. Sipos<sup>5</sup>, J. Demeter<sup>3</sup>, Zs. Nagy<sup>3</sup>, E. Sári<sup>3</sup>, Á. Illés<sup>6</sup>, L. Gergely<sup>6</sup>, Z. Tóth<sup>4</sup>, I. Garai<sup>4</sup>

<sup>1</sup>Semmelweis University, Budapest, Hungary

<sup>2</sup>Department of Nuclear Medicine, Semmelweis University, Budapest, Hungary

31st Department of Internal Medicine, Semmelweis University, Budapest, Hungary

<sup>4</sup>ScanoMed Ltd., Budapest, Hungary

Department of Haematology and Stem Cell Transplantation, St. István and St. László Hospital of Budapest, Budapest, Hungary

63<sup>rd</sup> Department of Internal Medicine, University of Debrecen, Debrecen, Hungary

**Background:** As the individualised personal therapy of lymphomas is getting more widespread, the prognostic value of early (after 2–4 cycles of therapy) fluorodeoxyglucose (FDG) PET-CT (iPET) scans is growing in interest. Several early researches show, that a positive iPET examination indicates poor prognosis in Hodgkin's lymphoma, as well as in non-Hodgkin's lymphoma. Lately, the predictive value of iPET seems to be less obvious in the immunotherapy treated non-Hodgkin's lymphomas. One of the ways of standardised visual assessment of the iPET scans is rating using the London score (LS) system. In our actual research the prognostic significance of iPET was studied in patients with diffuse large B-cell lymphoma (DLBCL) receiving combined chemo-immunotherapy.

**Material and methods:** 35 patients (age: 23–89 years, 13 male, 22 female) with DLBCL, receiving R-CHOP combined chemo-immunotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone) were included in our research, on whom iPET scan was performed after 2–3 cycles of therapy, and were followed clinically for 114–993 days (median follow-up: 405 days). Based on the PET results alone no change of therapy was introduced. The iPET scans were rated visually by the LS. The correlation between the iPET results and the event free survival (EFS) was examined with Kaplan-Meier analysis, considering scans positive with LS  $\geq$  3 (assessment A) and with LS  $\geq$  4 (assessment B). Our study was performed partially in the frame of an International Atomic Energy Agency Coordinated Research Project.

**Results:** Using assessment A, of the 35 patients 19 were PET+ and 16 were PET-. Of the 19 PET+ patients 7 experienced relapse or progression, and 1 of the 16 PET- patients. The difference of the EFS between PET+ and PET- cases was not significant statistically (p = 0.0682). The positive and negative predictive value of the iPET regarding the EFS was 37 and 94%. With assessment B, 11 scans were PET+, and 24 PET-. In 11 PET+ cases relapse or progression occurred in 7 cases, and in the 24 PET- cases, they occurred once. PET+ cases presented with shorter EFS (median: 386 days) than PET- cases (median was not reached). The difference of the EFS between PET+ and PET- cases was statistically significant (p < 0.001). The positive and negative predictive value of the iPET was 63 and 96%.

**Conclusions:** In combined chemo-immunotherapy treated DLBCL patients iPET has significant predictive value regarding the EFS, when the positivity criterion is any FDG avidity greater than liver activity (LS  $\geq$  4). It is important to use standardised criteria for the visual assessment of iPET

#### F15

#### A SIMPLE SEMIQUANTITATIVE TECHNIQUE BY ANALYSING SOMATOSTATIN RECEPTOR SCINTIGRAPHY TO PREDICT THERAPEUTIC EFFECT OF PEPTIDE-RECEPTOR-RADIO-THERAPY

M. Barra<sup>1</sup>, G. Dabasi<sup>1</sup>, P. Reismann<sup>2</sup>, P. Igaz<sup>2</sup>, K. Rácz<sup>2</sup>

<sup>1</sup>Department of Nuclear Medicine, Semmelweis University, Budapest, Hungary

<sup>2</sup>2<sup>nd</sup> Department of Medicine, Semmelweis University, Budapest, Hungary

**Background:** Peptide-receptor-radiotherapy (PRRT) is an effective palliative treatment options for patients with inoperable progressive neuroendocrine tumours and increased uptake of labelled somatostatin analogues on somatostatin receptor scintigraphy (SRS).

**Material and methods:** At the Department of Nuclear Medicine of University Basel 51 Hungarian patients of the 2<sup>nd</sup> Department of Medicine (Semmelweis University) were treated between 2005–2010 with Y-90-DOTATOC or Lu-177-DOTATATE. We have retrospectively analysed correlation between scintigraphic findings (Octreoscan) and therapeutic effect of PRRT in 40 patients. All 40 patients had multiple hepatic metastases of progressive inoperable neuroendocrine tumours originating from the pancreas or lungs or small bowels. We calculated tumour/background ratios (T/BG) of visible liver metastases on pretherapy SRS images taken at 2 and 24 hours after iv. injection of Octreoscan. Patients were followed after PRRT by standard (radiology and laboratory) examinations. Correlation between T/BG values and therapeutic effect of PRRT was calculated.

**Results:** No complete remission was found. Six months after therapy 23 patients (57%) had partial remisson. T/BG values at 2 hours of these patients were significantly higher than in patients without remission (2.07 + 0.22 vs. 1.84 + 0.13, p < 0.05). No significant difference of T/BG values at 24 hours was found (2.01 + 0.24 vs. 1.95 + 0.11, n.s.). All 20 patients with no progression at the one-year follow-up evaluation had also significantly higher T/BG values at 2 hours than patients with progressive disease.

**Conclusion:** Semiquantitative analysis of T/BG of liver metastases at 2 and 24 hours images of pre-therapy Octreoscan scintigraphy is a simple technique to predict therapeutic effect of PRRT in patients with inoperable neuroendocrine tumours. High T/BG at 2 hours predicts good therapeutic effect.

#### E16

### SIGNIFICANCE OF SPECT/CT IN MIBG EXAMINATIONS OF CHILDREN'S NEUROBLASTOMA

M. Sarkadi¹, E. Schmidt¹, Zs. Szabó¹, S. Szekeres¹, K. Dérczy², Cs. Weninger², K. Zámbó¹

<sup>1</sup>Department of Nuclear Medicine, University of Pécs, Pécs, Hungary <sup>2</sup>Department of Radiology, University of Pécs, Pécs, Hungary

**Background:** Morphological and etiological verification of the increased activity on the early and delayed static and SPECT images with the help of complementary "low dose" SPECT/CT examination.

Material and methods: All of 28 MIBG examinations of 17 children with neuroblastoma were investigated between September 2007 and March 2011. I131-MIBG examinations in 12 cases I123-MIBG examinations in 16 cases were performed. Eleven control studies were made in 7 children, one time in 3 patients and two times in 4 patients. During the examinations of 10 boys (mean age 4 years) and 7 girls (mean age 3.5 years) early and delayed anterior and posterior static and SPECT imaging were performed. In 20 cases complementary SPECT/CT images were made of the skull, the neck, the chest, the abdomen and the extremities.

**Results:** Pathological increased MIBG activity were found in 18 cases in several regions. Multiplex hot spots were seen in 13 cases of them. Metastases were verified in 14 cases on the base of native CT. There were

no morphological changes on the native CT in the localization of the increased activity in 3 cases. In 3 children further contrast agent CT, MRI or US examinations, in 1 child US-guided biopsy were suggested to prove the suspected metastases. In other 3 children the native CT verified the metastases without increased activity beyond the proved MIBG positive metastases with morphological changes.

**Conclusions:** In the 78% of the MIBG positive cases metastases were proved by native CT. Hybrid SPECT/CT provides both the functional information from SPECT and the anatomical information from native "low dose" CT in a co-registerd examination plays a very important role in the etiological diagnosis and staging of the neuroblastoma in childhood and increases the success of the therapy.

#### E17

#### COMPARATIVE DIAGNOSTIC VALUE OF TC-99M AND IN-111 LABELLED SOMATOSTATIN ANALOGUES FOR SOMATOSTATIN RECEPTOR SCINTIGRAPHY. PRELIMINARY RESULTS

Z. Varga<sup>1</sup>, K. Buga<sup>2</sup>, E. Takács<sup>1</sup>, V. Valent<sup>2</sup>, G. Dabasi<sup>1</sup>, I. Szilvási<sup>2</sup>

<sup>1</sup>Department of Nuclear Medicine, Semmelweis University, Budapest, Hungary <sup>2</sup>Department of Nuclear Medicine, Hungary Military Hospital-State Health Centre, Budapest, Hungary

**Background:** Somatostatin receptor scintigraphy (SRS) is a well-established method in evaluating patients with neuroendodine tumours (NET). In-111-pentetreotide (Octreoscan: O) has remained the "gold standard", but some new, Tc-99m-labelled somatostatin analogues are also used. Only few data are available on direct comparison of different radiopharmaceuticals. In our study we compared diagnostic value of O and Tc-99m-EDDA-HYN-IC-octreotide (Tektrotyde: T).

**Material and methods:** We performed T scintigraphy in 63 patients in the last two years. 18 of them had O scintigraphy as well. Both methods were performed according to prodedure guidelines. The first radiopharmaceutical was randomly choosen. The second scintigraphy was performed, if results of the first scintigraphy were equivocal or contradicting to clinical data. SRS was indicated for staging of histologically proven NETs (n = 5), or for postoperative restaging (n = 13). Nine males and nine females were studied, with mean age 57 (41–80) years.

**Results:** Abnormal SRS was found in 12 patients. In 6 postoperative cases no recidive/metastasis were detected. Findings of O and T scintigraphies were concordant in 13 patients. In 5 cases we had discordant results. In 1 patient O was false-negative (in the thorax), and in 1 case T was false negative (in the abdomen). In one patient O found less number of lesions, in another patient T. In one case T was positive in the thoracic and abdominal regions as well, but O was positive in the abdomen only.

**Conclusion:** Based on our study, O and T have similar diagnostic value in evaluating patients with NETs by a patient-by-patient analysis. In our small patient material and various type of NETs T seems to be more sensitive in the thorax, O seems to be better in the abdomen. Further studies are needed to define possible differences of diagnostic value of both radiopharmaceuticals in SRS of tumours with various histological types.

#### E18

## THE IMPORTANCE OF SPECT AND/OR SPECT-CT FUSION IN SENTINEL LYMPH NODE DETECTION WITH PROSTATE CANCER PATIENTS

Z. Galler<sup>1</sup>, I. Balogh<sup>1</sup>, A. Páczelt<sup>2</sup>, J. Varga<sup>2</sup>, F. Salamon<sup>3</sup>, Z. Tóth<sup>4</sup>

<sup>1</sup>Department of Nuclear Medicine, Uzsoki Street Hospital, Budapest, Hungary

Department of Urology, Uzsoki Street Hospital, Budapest, Hungary Department of Pathology, Uzsoki Street Hospital, Budapest, Hungary ScanoMed Ltd., Budapest, Hungary

**Background:** Our aim was studying the usefulness of sentinel lymph node detection with SPECT and/or SPECT-CT fused images in early stage (T1-2, N0, M0) of prostate cancer.

Material and methods: In 85 patients both planar and SPECT images were taken 3 and 21 hours after the transperineal-intraprostatic administration of 100-150 MBq Tc99m-SentiScint. In 20 cases low dose CT has been made as well for better localization of sentinel lymph node (SLN). For SPECT-CT image fusion Mediso-Interview Fusion software was used. During operation Navigator gamma probe was utilized localizing the SLN found by SPECT and/or SPECT-CT examinations. The SLN(s) were examined separately for detailed pathological processing.

**Results:** Except of the 5 lymph nodes in presacral localization detected by SPECT-CT fused images all other SLN were excised. Only in 27 cases were found the SLN in the usual place, obtural triangle (OT), other 32 cases the SLN were excided outside the OT (along with the iliacal arteries, iliacal bifucation - localized by SPECT-CT). In 10 cases SLN-s were detected both inside and outside the OT. In 9/85 cases micrometastasis could be found in SLN by pathological processing.

**Conclusions:** On the bases of our results (1) micrometastasis could be found in very early stage of prostate cancer (9/85) what emphasizes the importance of SLN detection. (2) The localization of SLN outside the OT is a common finding (32/85). In these cases (3) the importance of SPECT-CT fused images is essential for accurate localization of SLN, leading the hand of the surgeon (i.e. tailored surgery).

#### E19

#### PRELIMINARY EXPERIENCES WITH SENTINEL LYMPH NODE SCINTIGRAPHY IN VULVAR CARCINOMA PATIENTS

K. Bús, I. Uracs, C. Wisotzki, T. Derlin, J. Mester, S. Klutmann, M. Clausen

Department of Nuclcear Medicine, University Medical Center, Hamburg–Eppendorf, Germany

Department of Nuclcear Medicine, Semmelweis University, Budapest, Hungary

Background: Reducing radical surgery interventions like evading morbidity by regional block dissection is an important intention for surgeons of today. Since a vulvar carcinoma has an abundant lymphatic circulation it may rapidly create lymph node metastases. Lymph node status is one of the most important prognostic factors in vulvar malignancy, and is of great importance to assort between therapeutic possibilities. Consequently it's substantial to receive a representative sample from the affected region with minimal invasivity. For this purpose was the sentinel node biopsy concept introduced. The method is already broadly used in cases of mammal tumours and malignant melanoma though this technique is only applied in some specialized centres on patients with vulvar carcinoma, therefore the available data is limited

The aim is to demonstrate the method and the early results from the aspect of the nuclear medicine.

**Material and methods:** Scintigraphic analysis in 28 patients with vulvar carcinoma was performed. In cases of midline tumours 4 x 25 MBq Tc-99m-Nanocoll were given peritumourally, the day before the operation. In cases of lateral tumours 2  $\times$  25 MBq Tc-99m-Nanocoll were injected next to the tumour and additional 2  $\times$  25 MBq Tc-99m-Nanocoll were given into the opposite side. Static planar scintigraphies were made from anterior direction and accessory SPECT/CT images were taken. The frontal projections of the sentinel lymph nodes were marked with the help of the acquired static planar images. During the operation the sentinel lymph node biopsies were done with the help of a gamma probe. The removed lymph nodes were pathologically processed and evaluated.

**Results:** We have managed to detect sentinel lymph nodes in every patients (28/28), in both inguinal regions. Surgical detection and removal of sentinel lymph nodes were successful in all cases. Pathological examinations confirmed sentinel lymph node positivity in 8 cases.

**Conclusions:** Sentinel node scintigraphy is a promising, easily performable and available process in vulvar carcinomic cases. Further investigations are necessary to show the reliability of the method, mainly to detect false negative cases and even to refine the diagnostic protocols.

#### E20

### 99MTC-MIBI SPECT/CT IN THE FOLLOW-UP OF NEOADJUVANT CHEMOTHERAPY OF BREAST CANCER

E. Schmidt¹, Y. Al-Farhat², K. Dérczy³, Cs. Weninger³, Zs. Nemerey⁴, J. Czifra⁵, Zs. Szabó¹, S. Szekeres¹, K. Zámbó¹

<sup>1</sup>Department of Nuclear Medicine, University of Pécs, Pécs, Hungary <sup>2</sup>Department of Oncology, Tolna County Hospital, Szekszárd, Hungary <sup>3</sup>Department of Radiology, University of Pécs, Pécs, Hungary <sup>4</sup>Department Radiology, Tolna County Hospital, Szekszárd, Hungary <sup>5</sup>Department Pathology, Tolna County Hospital, Szekszárd, Hungary

Background: The intensity of 99mTc- MIBI accumulation in breast cancer depends on tumor size, on vascularisation and on several important prognostic factors. The aim of our study was to determine the role of 99mTc-MIBI SPECT/CT in the follow-up of neoadjuvant chemotherapy of breast cancer. Material and methodes: 8 breast cancer patients were observed, with the indication of neoadjuvant chemotherapy. Before the beginning of therapy, and after the III. and VI. cycle 99mTc-MIBI scintigraphy were performed. 10 and 60 minutes after the injection of 370 MBq 99mTc-MIBI, planar scans of the chest and axilla, whole body scan and SPECT/CT of the chest were completed. We observed the change of intensity of 99mTc-MIBI accumulation in the breast tumors and axillary lymph nodes, with the quantitative analyses on SPECT/CT slices (VOI, maximum pixel value), compared to the change of tumor and lymph node size and histological finding.

Results: In 7 cases histological findings showed ductal carcinoma. In 5 patients pathological axillary lymph nodes were detected by mammography and US, which were proved by 99mTc-MIBI planar and whole body scans, but chest SPECT/CT showed in all 7 patients pathological lymph node accumulation, in two cases with normal lymph node size. In 1 case the SPECT/CT scan found a pathological mediastinal lymph node and lung metastases, which was an indication for changing the therapy. In 6 cases, the intensity of 99mTc-MIBI accumulation shows a significant reduction already after the III. cycle of therapy. In 1 patient, with mastitis the histology proved an undifferentiated tumor with high malignity. There was no reduction in tumor size and intensity of 99mTc-MIBI accumulation and after mastectomy the histology proved extraosseal osteosarcoma.

**Conclusions:** 99mTc-MIBI SPECT/CT, combining function and morphology, in addition to quantitative analyses is a useful and sensitive method in the follow-up of neoadjuvant chemotherapy of breast cancer. The first examination, before the beginning of therapy can detect unknown metastases, which modifies the therapy.

#### E21

### LIVER VISUALIZATION DURING PREOPERATIVE LYMPHOSCINTIGRAPHY IN BREAST CANCER

Á. Bajner

Department of Nuclear Medicine, Szombathely, Hungary

Background: In a total of 362 breast cancer patients underwent preoperative lymphoscintigrapy at our department between January 2005 and March 2011, we found nonvisualization of axillary sentinel node (SN) in 5 cases. The cause of one failure was supposed technical (partial vascularization of the radiotracer dose during injection), because we detected intense liver activity. In this patient additional tracer injection resulted in SN visualization, histopathologic examination did not reveal metastasis in SN. From October 2010 we introduced an additional liver image as part of standard lymphoscintigraphy protocol.

In this study we investigated the reasons other than technical pitfall, such as pathophysiologic mechanisms, that may be responsible for visualization of liver during preoperative lymphoscintigraphy in breast cancer.

Material and methods: We reviewed the series of 39 unselected, consecutive patients with breast cancer who had additional liver image as part of standard preoperative lymphoscintigraphy procedure. All patients had

a subareolar injection of 60 MBq Tc-99m-albumin colloid (Senti-Scint, particles' size: 100–600 nm), in a volume of 0.5 ml, administered in the index quadrant. Gamma camera images of the axillary region and of liver activity were acquired 18 h after injection. Liver activity was assessed by visual evaluation. We analysed whether axillary SN metastasis was associated with an increased liver visualization rate.

**Results:** Three of 39 patients showed a faint visualization of the liver, all of them had detectable SN in axilla. In the visualized-liver group (n = 3) histology revealed axillary nodal metastasis in 2 patients (67%). In the nonvisualized-liver group (n = 36) the incidence of SN metastasis was only 8% (3 of 36).

Conclusion: There is a significant difference in incidence of axillary nodal metastasis between the visualized and nonvisualized-liver groups in our series, suggesting that pathophysiologic mechanisms associated with nodal involvement might be responsible for systemic radiocolloid uptake. Some studies showed direct lymphaticovenous connection in involved lymph nodes, suggesting an anatomic pathway for radiocolloid to gain access to the systemic circulation. These studies might provide an anatomical explanation for our findings. Our initial results should be confirmed in a larger patient population.

#### **E22**

# SENSITIVITY AND SPECIFICITY OF IN 111 OCTREOTIDE WHOLE-BODY IMAGING IN THE DETECTION OF THORACIC AND ABDOMINAL ABNORMALITIES COMPARED TO SPECT-CT IMAGING

A. Kiss<sup>1</sup>, S. Barna<sup>1</sup>, L. Szabados<sup>1</sup>, J. Varga<sup>2</sup>, I. Garai<sup>1</sup>

<sup>1</sup>ScanoMed Ldt., Debrecen, Hungary

<sup>2</sup>Department of Nuclear Medicine, University of Debrecen, Debrecen, Hungary

**Background:** The In 111 Octreotide scintigraphy is proved to be the most effective diagnostic method in detecting the somatostatine-receptor-positive neuroendocrine tumors.

The aim of our examination is the determination of region-dependent sensitivity and specificity of In 111 Ocreotide scintigraphy during whole-body and SPECT-CT imaging.

Material and methods: We have chosen 81 patients (26 male and 55 female, mean age 39.7  $\pm$  9.5 yrs) to our retrospective examination, all of them were diagnostized with neuroendocrine tumor with histological evidence. Some of the examinations were primary health checks, to determine receptor status and to plan subsequent treatment, on the other hand the examination aimed to detect recidive process. 24 hours after injecting the In-111 Octreotide (Covidien) i.v. we did the examination with the help of an AnyscanSC (MEDISO) dual-head SPECT-CT camera. In every cases whole body imaging then SPECT-CT tomographic imaging were performed. The whole body and SPECT-CT evaluation were performed by two experienced physicians independently from each other, considering positive those focal accumulations having at least the same activity level as the liver. In SPECT-CT examination we considered those accumulations to be a clear positive that belong to pathological morphology. We determined its sensitivity and specificity of whole body study compared to SPECT-CT through statistical processing.

**Results:** There is a significant correlation between the two methods — whole body and SPECT-CT imaging — in the evaluation of the results ( $\chi^2 < 0.05$ ). The result of the whole body study differs significantly from the one of SPECT-CT study in the evaluation of both the thoracic and abdominal regions. During the whole body scan we found the negative predictive value to be over 80% regarding both the thoracic and abdominal regions. False positive results were often experienced during whole body scan.

**Conclusion:** Negative whole body scan excludes the presence of somatostatine receptor-positive tumors with a high probability. While in case of positive results it is recommended to perform an additional SPECT-CT scan to exclude false positive accumulations.

#### F23

#### HOW CAN SPECT-CT FUSIO HELP IN THE DIAGNOSIS OF NEUROENDOCRINE TUMORS?

F. Halasi<sup>1</sup>, Z. Galler<sup>1</sup>, I. Balogh<sup>1</sup>, V. Tóth<sup>2</sup>, Zs. Varga<sup>1</sup>

<sup>1</sup>Department of Nuclear Medicine, Uzsoki Street Hospital, Budapest, Hungary <sup>2</sup>ScanoMed Ltd., Budapest, Hungary

Background: Neuroendocrine tumors (NET) are an uncommon type of neoplasm frequently with late symptoms. The somatostatin receptor scintigraphy (In111-OctreoScan) is a very sensitive but lower specific method for detecting both the primary and the metastatic lesions. Some aspecific accumulation (acute and chronic inflammations, etc.) causes diagnostic problems.

The aim of our study was to analyze the importance of the SPECT-CT fused imaging at the diagnosis of NETs in the daily routine. Is it possible to distinguish the specific and aspecific accumulation with the fusion of SPECT and CT images? Is it able to increase the sensitivity and the specificity (the diagnostic accuracy) of the scintigraphy?

Material and methods: 12 patients with known NET underwent (1) diagnostic CT or MR examination (2) serum Chromogranin-A investigation and (3) In111-OctreoScan examination — whole body and the necessary additional images, SPECT examinations — after 24, 48, 72 hours of the intravenous injection of radiopharmaceutical. All of the patients low dose CT examination was performed as well. The SPECT-CT fused images were reconstructed with MEDISO Interview XP Fusion- software.

Results: In every (12/12) case accumulation sites of In111-OctreoScan were detected. Most (10/12) of the patients had unusual localization and/or uncommon extension of tracer uptake as well. In these cases localizing and identifying the accumulation was difficult by only-SPECT. With the help of the SPECT-CT fused images we were able to identify more preciously the extension, localization of OctreoSan accumulation and the previously described lesions by CT or MR than SPECT alone. We also compared the sensitivity of the serum Chromogranin-A levels with the OctreoScan examinations resulting a lower sensitivity for the Chromogranin-A.

Conclusions: The In111-OctreoScan examination completed with SPECT images plays an important role in the diagnosis of NETs. The sensitivity and the specificity, ie. the diagnostic accuracy of the examination can be improved with SPECT-CT image fusion in the detection of primary and metastatic lesions as well.

#### **E24**

#### PREPARATION AND EVALUATION OF SOMATOSTATIN ANALOG CONTAINING KITS USED FOR IN VIVO **LOCALIZATION AND TARGETED RADIONUCLIDE THERAPY**

G. Jánoki<sup>1</sup>, R. Török<sup>1</sup>, L. Balogh<sup>2</sup>, Z. Pöstény<sup>2</sup>, J. Thuroczy<sup>3</sup>, Gy. A. Jánoki<sup>4</sup>

<sup>1</sup>Radiopharmacy Laboratory Ltd., Budaörs, Hungary

<sup>2</sup>Natl. "FJC" Radiobiology and Radiohygiene Research Institute, Budapest, Hungary

3St. Stephan University, Veterinary Faculty, Budapest, Hungary <sup>4</sup>Medi-Radiopharma Ltd., Érd, Hungary

Background: Radiolabelled somatostatin analogs are important tools for the in vivo localization and targeted radionuclide therapy of somatostatin receptor positive tumours. The aim of this study was to develop instant freeze-dryed kit containing HYNIC-Tyr3-Thr8-octreotide and DOTA-Tyr3-Thr8-octreotide used for labelling with diagnostic (99mTc and 68Ga) and therapeutic (90Y and 177Lu) isotopes.

Material and methods: During our experiments HYNIC-TATE and DOTA-TATE peptid-chelate conjugate were selected. Experiments gained during technetium kit development were used to develop kit pharmaceutical form. Vials containing 20 microgram of HYNIC-TATE, tricin, EDDA, SnCl2 and mannitol at pH 5.3 were compounded in one step and freeze-dryed (Comp I) Simultaneously a therapeutical kit containing 100 microgram of DOTA-TATE, gentisic acid, sodium acetatet puffer (pH 5.5) and glycin were compailed and freeze-dryed (Comp.II) and filled with nitrogen gase. After formulation experiments the appearence, pH, water content and the amount

of Sn(II) were determined. During labelling experiments in 1 ml volume 2 GBq were used and reconstituted kit content was heated in boiling water for a 20 minutes. For determination of labelling efficiency and stability ITLC and RP-HPLC were used up to 4 hours. For in vitro receptor binding AR4-2J cell line for in vivo distribution healthy Wistar rats were used. The Comp II kit was labelled with 177Lu-chloride and evaluated by all methods listed above. The compiled Comp I and Comp II kits were evaluated by studying the appearance (homogenous pellet) water content (less than 1%) solubility (fast clear solution within 1 minutes) and pH (5.2-5.4). Because of the proper selection of bulking agents and freeze-drying condition used during compounding the kits showed good stability as well.

Results: After radiolabelling the radio-TLC and radio-HPLC evaluations showed high labelling efficiency (more than 95%). During stability evaluation when solution were stored at room temperature up to 4 hours no decomposition were detected. Both compounds showed very fast blood clearance in rats with less than 0.1% of ID remained in blood after 3 hrs of injection. Excretion of radiopeptides occurred via the kidney and urinary system. After 6 hours more than 95% of ID were eliminated through kidneys. The developed kit containing HYNIC-TATE and DOTA-TATE during testing showed high labelling efficiency and stability. The cell binding and biodistribution results (high binding and fast blood and urinary excretion) were as expected. Conclusions: Based on our good preliminary results experiments by using 68Ga and 90Y may start soon. Experiments in dogs and cats bearing spontaneous tumour expressing somatostatin receptors and using SPECT/CT and PET/CT technique may help to evaluate the clinical applicability of our radiolabelled somatostatin analogs for in vivo localization and targeted radionuclide therapy.

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#### **E25**

#### PREPARATION OF 18F-LABELLED SERUM ALBUMIN WITH CHEMOSELECTIVE METHODS

I. Kertész, L. Kárpáti, T. Márián, Gy. Trencsényi, I. Lajtos, L. Galuska Department of Nuclear Medicine, Universitiy of Debrecen, Debrecen, Hungary

Background: The overall aim of the present work is to develop a suitable method for fluorine labelling of serum albumin with the appropriate radioactive concentration for in vivo testing of tumour blood pool in small animal. Material and methods: For the radiolabelling a simple method was selected which includes the preparation of [18F]-4-Fluorobenzaldehyde ([18F]FBA) and successive conjugation with SANH (Succinimidyl 6-hydrazinonicotinamide acetone hydrazone) — serum albumin conjugate via hydrazone formation. Alternatively, a thiol reactive compound (N-[6-(4-[18F]fluorobenzylidene)aminooxyhexyl]maleimide — [18F]FBAM was prepared from [18F] FBA and N-(6-aminooxyhexyl)maleimide. The labelling agent was reacted afterwards with a thiol functionalized serum albumin. The modified protein was synthesized by means of SATA linker (N-Succinimidyl S-Acetylthioacetate). After removal of the protecting group, the resulted free sulfhydryl group and the maleimide moiety of [18F]FBAM easily forms a stabile thioether bond. The 18F-labelled serum albumins were purified with gel filtration. The purities of the compounds and the metabolic stabilities were assessed by HPLC and TLC. For in vivo experiments rats were injected i.v. with 18Flabelled serum albumins. After tracer injection animals were anaesthetized and 10 minutes PET scans were acquired using a small animal PET scanner (MiniPET-II) to visualize the biodistribution of the radiopharmaceuticals. For organ-distribution, different tissues were removed and their activities were measured with a gamma counter. The radioactivity of the samples was used to determine the differential absorption ratio (DAR).

Results: We have successfully radiolabelled the SANH modified serum albumins with [18F]FBA, and SATA modified BSA with [18F]FBAM also. During our labelling experiments [18F]FBAM was found to be an excellent agent for conjugation to thiol groups, even at low concentrations. After the gel filtration the radiochemical purities were over 98% in all cases. In preliminary biodistribution studies we have realised divergent properties of the compounds. 30 min after the administration of hydrazone bond containing albumin

Abstracts

(18F-SANH-BSA and 18F-SANH-HSA) the MiniPET-II images showed that the majority of the radioactivity remained in the blood in contrast to the thiol modified albumin (18F-SATA-BSA), where we found a fast blood clearance and the tracer was filtrated by the liver. It is perhaps due to the intermolecular reaction of the non-covered thiol groups and the formation of colloid. By taking the DAR values 60 min after the tracer injection high uptake was found in the urine (18F-SANH-BSA and 18F-SANH-HSA), liver (18F-SATA-BSA) and blood (18F-SANH-BSA and 18F-SANH-HSA).

**Conclusion:** We have compared two simple methods for the preparation of 18F-labelled serum albumins. All the compounds have good stability *in vitro*, and it is clear that the amount of the applied albumin has an essential role in the biodistribution pattern in vivo. Optimizing the parameters, 18F-SANH-HSA can be a promising candidate for the imaging of tumour blood-pool.

#### **E26**

## PREPARATION OF AND INVESTIGATION ON SENTINEL LYMPH NODE SPECIFIC, DESIGNED RADIOPHARMACEUTICALS

J. Környei, E. Szemenyei, V. Horváth, L. Baranyai Institute of Isotopes Co. Ltd., Budapest, Hungary

**Background:** Localization of colloids used in the clinical routine for sentine lymph node detection is based on their particles size and particle size distribution. On the other hand, a hypothesis is known from the literature that glycoproteine and/or phytate receptors are expressed on the lymph node(s) possessing direct drainage to the tumour. An IAEA project "CRP F 22045" aimed to prepare and investigate designed radiopharmaceuticals binding to these receptors. In this presentation the work of the Hungarian group is shown, regarding Tc-99m-dextran-cysteine-cysteine-mannose (DCCM) and Tc-99m-calcium-phytate (CAFY) colloids.

Material and methods: To prepare DCCM, aminoethanethiol was reacted with allyl-dextran followed by coupling cysteine-cysteine and serine-mannose side chains. The presence of the functional groups was investigated by ESI-MS technique while particle size and particle size distribution was controlled by dynamic light scattering method. Tc-99m labelling was accopmlished via [Tc≡N], technetium nitrido intermedier, obtained when pertechnetate was reduced with stannous chloride in presence of a succinic acid dihydrazide derivative. To prepare CAFY, Calcimusc injection and the commercially available Fyton kit was used by adjusting phytate/calcium molar ratios of 4:1, 3:1, 2:1, 1:1, 1:2, 1:3 and 1:4. In the frame of this project, some preclinical studies on rat SLN model were carried out in Romania and India.

Results: Presence of functional groups in DCCM was proved. As for stochiometry, 25 mmol cysteine-cysteine and 13 mmol serine-mannose groups were coupled to 1 mmol dextrane while 46 amino groups remained free. Size of DCCM particles was found as 7.6  $\pm$  0.6 nm. Yield of Tc-99m nitrido labelling was > 90%. On the other hand, DCCM was stable only for 3 months, the labelling yield decreased to 75-77% when labelling was carried out later. The average particle sizes of CAFY colloids, obtained in presence of phyate excess to calcium were in the range of 100-300 nm. On the other hand, when molar ratio was 1:1 or in the cases of calcium excess to phytate, the particle sizes were larger than 1  $\mu$ m and sedimentation was observed, too. Tc-99m labelling yields were always > 99%, but in the cases of phyate/calcium molar ratio ≥ 1, some non-colloidal Tc-99m-phytate was also formed up to 10-13% of the total activity. Preclinical studies of Tc-99m-DCCM showed a rapid leakage of this colloid due to the very low specific binding (0.8% I.D.). At the same time, three lymph nodes were well visualized in case of Tc-99m-CAFY colloid, prepared at phytate/calcium molar ratio of 2:1, possessing average particle size of 278 nm.

Conclusion: Nitrido labelling of DCCM was successfully accomplished since cysteine-cysteine side chains on the dextran-matrix ensured an easy complexation with technetium. On the other hand, the lack of receptor specific binding of Tc-99m-DCCM can be explained partly by the effect of technetium nitrido core to the molecular geometry, partly by the relative low amounts of serine-mannose side chains (13 mmol/mmol dextran). Localization of Tc-99m-CAFY colloid in sentinel lymph nodes can be due to both receptor binding and the favourable particle size.

#### F27

# HOW TO MAKE SATISFIED ANIMAL OWNERS, REFERRING VETS AND RADIOPHARMACEUTICAL INVESTIGATORS AT THE SAME TIME — SPECT/CT EXAMINATIONS IN DOGS AND CATS

L. Balogh¹, Z. Pöstényi¹, V. Haász¹, A. Polyák¹, K. Zambó², E. Schmidt², M. Sarkadi², G. Janoki³, R. Török³, J. Thuróczy⁴, L. Seres⁵, Gy. Janoki³

<sup>1</sup>NRIRR, Budapest, Hungary

<sup>2</sup>Institute of Nuclear Medicine, University of Pécs, Pécs, Hungary

<sup>3</sup>Radiopharmacy Ltd., Budaörs, Hungary

<sup>4</sup>Veterinary Faculty, Szl University, Budapest, Hungary

5Mediso Ltd., Budapest, Hungary

**Background:** Few years earlier we cleared up that whole body SPECT/CT examinations are safe, non-invasive method in healthy animals and in late stage canine oncological patients too. Based on that preliminaries different whole body SPECT/CT by applying different 99mTc labelled radiopharmaceuticals have been started to carry-out in spontaneously diseased animal patients.

Material and methods: Healthy Beagles and laboratory cats, then client owned dogs and cats altogether over 30 suspected or known oncological cases were referred for SPECT/CT whole body examinations. Applied radiopharmaceuticals included 99mTc-pertechnetate, -MDP, -MIBI, -DMSA(V), -HYNIC TATE. The injected radioactivity differed between 5–12 MBq/bwkgs. Anaesthesia was monitored during the scans and radiotoxicological effects were checked by monitoring the haematological and biochemical blood parameters before then 6 hours, 2 days and 1 week post examination. The goal was to detect primary tumor localizations, extensions and to visualize regional and far metastases (WHO staged diagnosis). On stadium based diagnosis optimum-therapy was offered to owners then follow-up examinations were carried-out in case of accepted offers.

Results: 99mTc-pertechnetate SPECT/CT proved to be extremely useful in diagnosing, staging and follow-up of thyroxin producing thyroid carcinomas and to select the patients for radioiodine therapy. 99mTc-MDP SPECT/CT revealed very important data in localization of primary and metastatic bone tumors, planning surgical procedures and/or bone pain palliation treatments. 99mTc-MIBI wash out examinations work also using the hybrid imaging. 99mTc-DMSA(V) SPECT/CT proved to be informative in a wide variety of soft tissue and bone tumors. Specific receptor affin agents showed higher sensitivity and specificity in SPECT/CT hybrid scans than in the single SPECT modality.

**Conclusion:** Whole body SPECT/CT examinations in many oncological diseases could be the choice of veterinary oncologists also from clinical point of view — and paralelly these examinations provide a very reliable data-pool for biomedical researchers.

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#### **E28**

### POSSIBILITIES OF PRODUCTION AND UTILIZATION OF PET RADIOPHARMACEUTICALS IN HUNGARY

P. Mikecz<sup>1</sup>, Gy. Tóth<sup>2</sup>, Z. Fodor<sup>1</sup>, L. Trón<sup>1</sup>, L. Galuska<sup>1</sup>

<sup>1</sup>Department of Nuclear Medicine, University of Debrecen, Debrecen, Hungary

<sup>2</sup>Positron Diagnostic Ltd., Budapest, Hungary

In the last 5 years the number of PET investigations had raised nearly tenfold in Hungary, this year it is near to 12000. In the procedures [18F]FDG (2-[18F] fluoro-2-deoxy-D-glucose) is used in nearly 100%. The use of C-11 labelled methionine and acetate besides the FDG is negligible. In our country the technical conditions of PET radiopharmaceutical production are excellent. Two laboratories obtained production licence, and marketing authorizations for FDG and the above mentioned C-11 tracers. This makes possible to provide FDG not only for Hungary, but for the neighbouring countries (Romania, Serbia, and Bulgaria) as well. The registered C-11 labelled tracers are used on the spot. The process of registration of C-11 labelled choline has been

started in Debrecen. Beyond the tracers for human use, numerous other positron emitting compounds are regularly produced for research purposes. For example fluoroethyl tyrosine is produced in the Pozitron Diagnosztika Health Centre. In the University of Debrecen a "radiopharmaceutical shelf" was established what contains several radio-chemicals for cell or small animal experiments. To help cancer research production methods were implemented for the proliferation marker — 3'-deoxy-3'-[18F]-fluorothymidine (FLT), for the tracer detecting bone lesions — sodium[18F]fluoride and for the hypoxia marker — 1-(5-fluoro-5-deoxy-a-D-arabinofuranosyl)-2-nitroimidazole (FAZA). The multidrug resistance can be investigated by [11C] verapamil. For neurology and addiction studies the [18F]fallypride and desmethoxy-[18F]fallypride are available. For these molecules besides of the production methods full scale quality control procedures were developed, so for a short notice they could be "taken from the shelf". These tracers could be used even for human applications. As it was emphasized in the recent interdisciplinary meetings, there is a real clinical need for the above mentioned and other radiopharmaceuticals in Hungary. However — because of the current legislation - marketing authorization would be required for each tracer. This is significantly differs form the practice of developed countries. In these the physicians can choose from a wide variety of pharmaceuticals. Although in Europe many companies and research laboratories obtained marketing authorization for FDG, only three further radiopharmaceuticals were registered (NaF, FDOPA and F-choline) by a professional company. Despite this in the PET laboratories one can use a lot of positron emitting diagnostics observing the regulation of local authorities. In order to make possible that the patients in Hungary could benefit from the most sophisticated PET technique, the change of the pharmaceutical legislation in Hungary have to achieved such a way, that the production and local use of PET radiopharmaceuticals in centres having cyclotrons and GMP conform laboratories would be faster licensed and easier to performed. It has to be emphasized, that these tracers have no pharmacological effects due to their very low concentration, they are short lived and from one batch only a few investigations can be performed. In the new legislation the relevant international examples have to be considered. These tracers have to be produced under GMP conditions, and must be used locally. For commercial purposes naturally marketing authorization must be required. If there would be no change in the recent practice, the expansion of the supply of PET radiopharmaceuticals in Hungary would take many years, even it could fail due to the administrative difficulties and financial burden.

#### **E29**

### PET/CT IMAGING IN DOGS AND CATS — TUMOR TARGET SCALE AND UNUSUAL UPTAKE

L. Balogh¹, Z. Pöstényi¹ V. Haász¹, A. Polyák¹, T. Márián², I Garai², L. Galuska², L. Balkay², Gy. Trencsényi², T. Nagy², J. Trencsényi², Gy. Janoki³, G. Janoki³, R. Török³, J. Thuróczy⁴

<sup>1</sup>National Research Institute for Radiobiology and Radiohygiene, Budapest, Hungary

<sup>2</sup>Department of Nuclear Medicine, University of Debrecen, Debrecen, Hungary

Radiopharmacy Ltd., Budaörs 4 Veterinary Faculty, Szt. I. University, Budapest, Hungary

**Background:** Despite that the clinical usefulness of 18FDG PET/CT in human oncology is well understood much less data are available from the veterinary side. Pet owners and referring vet clinician's expectations regarding to specific and sensitive diagnosis accompanied with researcher's needs and 3Rs expectations result a unique chance for co-operation in the field.

Material and methods: Client owned dogs and cats altogether over 60 suspected or known oncological cases were referred for 18FDG PET/CT whole body examinations. The goal was to detect primary tumour localizations, extensions and to visualize regional and far metastases (WHO staged diagnosis). On stadium based diagnosis optimum-therapy was offered to owners then follow-up examinations were carried-out in case of accepted offers.

**Results:** 18FDG PET/CT revealed very sensitive in case of a wide variety soft tissue and bone tumours eg.: osteosarcomas, mast cell tumours, soft tissue sarcomas, melanomas and different epithelial tumours. Some benign, low metabolic rate tumours (adenomas, lipomas, fibromas, intracranial) showed much lower 18FDG-uptake where the method seems to be questionable. Few degenerative-, inflamed- and hypertrophic tissues (arthrosis, lymph adenitis, muscle hypertrophy) revealed intense focal uptake that could be confusing in differential diagnoses.

**Conclusion:** Whole body PET/CT scans could be the choice of veterinary oncological imaging too from clinical point of view – and parallely these examinations provide a very reliable data-pool for biomedical researchers. **Acknowledgements:** Scientific work was supported by several national (OTKA-68376, JEDIONKO, KMOP-1.1.1-08/1-2008-0017, GOP-1.1.1-09/1-2010-0107) and international projects (IAEA-CRPs, EMIL NoE).

#### E30

#### NEW QUALITY CONTROL KIT FOR EVALUATION OF 99MTC LABELLED RADIOPHARMACEUTICALS BEFORE PATIENT INJECTION AT CLINICAL SITE

G. Jánoki<sup>1</sup>, R. Török<sup>1</sup>, L. Balogh<sup>2</sup>, A. Polyák<sup>2</sup>, Gy. Jánoki<sup>3</sup>

<sup>1</sup>Radiopharmacy Laboratory Ltd., Budaörs, Hungary <sup>2</sup>National "FJC" Research Institute for Radiobiology and Radiohygine Budapest, Hungary

<sup>3</sup>Medi-Radiopharma Ltd., Érd, Hungary

**Background:** The drug authorities all over the world require quality control study of radiopharmaceuticals if it is prepared in a multidose form at the clinical/hospital site. Our aim was to develop a quality control kit with appropriate properties to be used at any clinical site for quick determination the quality of 99mTc labelled radiopharmaceuticals coming from any manufacturer. Additionally the sufficient documentation for recording and archiving with detailed user quidance were also considered.

Material and methods: Quality Control kit for measuring parameters that influence the clinical applicability of 99mTc labelled radiopharmaceuticals as radiochemical purity Al(III), Sn(II) and pH were compiled. The requirements were the following: The ITLC methods must be validated or based on verified pharmacopeial methods (PhEur, USP, BPh). The methods have to be fast and efficient and the kit should contain all the necessary tools and materials needed to carry out the selected method.

Results: The master chromatograms selected and provided will give a proper guidence for determination of radiochemical impurities (e.g.: 99mTcO4, 99mTc-Sn colloid). The newly developed Medi-Check kit can be applied for the following radiopharmaceuticals: MDP, HDP, DTPA, PYP, DMSA, BRIDA, HSA, MAA, HSA colloid (all size), MAG3, HM-PAO, MIBI, Tetrafosmin and Na99mTcO4. With the additional tests in the kit one can measure the limit value of Al(III) (10  $\mu$ g/ml) and the stannus content semi-quantitatively (10-500 µg/ml). Based on our experience by using the Medi Check QC kit it is possible to determine the radiochemical purity of radiopharmaceuticals within 10 minutes. The prepared documentation and User guide will allow to determin the radiochemical purity of different radiopharmaceuticals simultaneously. The documentation prepared can be easily integrated into the quality management documentation of an accreditated nuclear medicine laboratory and complie with the requirements (documentation, traceability, archiving etc...) of the drug authorities

**Conclusion:** The newly compilled quality controll kit can be upgraded modulary. Based on the experience gained during application of new MediCheck QC kit showed that it can be a quick efficient and very useful tool in the daily routine work in any nuclear medicine laboratory. The potential long lasting application of this kit fits into the planned or already existing quality assurance/accreditaion program of any licensed nuclear medicine laboratory.

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#### F31

#### **MYOCARDIAL SUV OF C-11-ACETATE IN NORMAL HEART**

M. Moravszki<sup>1</sup>, A. Radácsi<sup>2</sup>, D. Kiss<sup>2</sup>, Gy. Tóth<sup>3</sup>, Zs. Lengyel<sup>3</sup>, I. Szilvási<sup>1</sup>

<sup>1</sup>Department of Nuclear Medicine, Military Hospital — State Health Centre, Budapest, Hungary

<sup>2</sup>Department of Nuclear Medicine, Semmelweis University, Budapest, Hungary

<sup>3</sup>Pozitron Ltd., Budapest, Hungary

Background: C-11-acetate (C-A) PET has been used for imaging of prostate and some other types of cancer and for non-invasive evaluation of myocardial oxidative metabolism. Analysis of uptake and washout of C-A by using kinetic models informs on myocardial blood flow and oxygen consumption. Dynamic A-C PET/CT is useful in cardiology but the technique is complicated. Static parameters of various dynamic processes are used for functional evaluation in nuclear medicine. In our study we measured myocardial SUV of C-A on a static image taken at 20 minutes after injection in patients without cardiac disease.

Material and methods: Myocardial uptake of C-A was evaluated in patients with prostate cancer referred to PET/CT. 20 consecutive patients without known cardiac disease, cardiac medication or diabetes (mean age: 63.5 ± 11.4 years) were enrolled in the study. After physical rest and 6 hours fasting 3.7–9.25 MBq/kg of C-A were injected. C-A was produced using our cyclotron and synthesis procedure approved by national authorities. Standard whole-body PET/CT (Siemens Biograph TruePoint HD, low dose non-enhanced CT) was performed from the skullbase to mid-thigh (6–7 bed positions with 3 minutes data acquisition). Imaging of the thorax started at 19–22 minutes after injection. After reconstruction (OSEM with 8 subsets/4 iterations) short and long axis slices of the heart were displayed. SUVmean values of C-A in manually selected myocardial, pulmonary, hepatic regions were calculated with Osirix 3.7.1. free DICOM viewer. Right ventricle, anterior, inferior, septal, and lateral walls of the left ventricle were separately analyzed with ROIs drawn on the midventricular slices.

**Results:** The heart was well visualized in all patients. Activity distribution was homogenous in each patient. No significant differences were found between SUVmean of the anterior, inferior, lateral and septal wall (3.42  $\pm$  0.25, 3.69  $\pm$  0.24, 3.52  $\pm$  0.22, 3.97  $\pm$  0.28). Good correlations were found between the SUVmean of the different walls (r = 0.74–0.86). SUVmean of the right ventricle (2.09  $\pm$  0.32) was significantly lower than that of the left ventricular regions (p < 0.01 for all) with no correlation to them. The liver had a mean SUVmean of 5.47  $\pm$  0.89.

Conclusion: Myocardial SUV of C-A at 20 minutes after injection is an easy to get parameter. We have established normal values of the left and right ventricle. They seem to be statistically reliable. Clinical usefulness of these parameters need further studies in patients with various cardiac diseases. Based on our preliminary results, we have started dynamic C-A examinations to measure absolute myocardial perfusion (mL/min/g) by using dipyridamole, 5 minutes data acquisition, PMOD Cardiac Modeling data processing.

#### E32

#### COMPARISON OF THE ACCURACY OF CORONARY CT ANGIOGRAPHY (CTA) AND MYOCARDIAL PERFUSION SCINTIGRAPHY (MPS) IN THE DIAGNOSTICS OF CORONARY ARTERY DISEASE

Zs. Szabo¹, T. Molnar², E. Varadi³, A. Konyi⁴, E. Schmidt¹, S. Szekeres¹, K. Zambo¹

<sup>1</sup>Department of Nuclear Medicine, University of Pecs, Pecs, Hungary <sup>2</sup>Department of Anesthesiolgy and Intensive Care, University of Pecs, Pecs, Hungary

<sup>3</sup>Department of Radiology, University of Pecs, Pecs, Hungary <sup>4</sup>Heart Center, University of Pecs, Pecs, Hungary

**Background:** A comprehensive assessment of CAD should include both information on coronary artery anatomy and functional information about the haemodynamic relevance of coronary artery lesions in order to avoid

redundant revascularization procedures. Combination of CTA and myocardial perfusion imaging is non-invasive, and its diagnostic accuracy of flow-limiting coronary stenosis is as good as the "gold standard" quantitative coronary angiography (QCA). We aimed to compare the accuracy of the three different diagnostic tool in our cohort.

**Material and methods:** Consecutive patients with known or suspected CAD were retrospectively enrolled and referred to our institution for MPS and CTA between january 2009 and december 2010. Statistics:  $\chi^2$  test (SPSS 12.0 software).

Results: In 53 patients (mean age 56.1 ± 10.7 years, male: 20) referred for coronary angiography (CTA) and MPI (using single-photon emission-computed tomography) were performed and the findings were analyzed retrospectively. One MPS és 3 CTA findings were rejected due to artefacts. MPS Results: negative 10, transient 26, permanent 23, resting hypoperfusion 5 cases. CTA: negative 10, non-significant stenosis (NSS) 42, significant stenosis (SS) 9. Transient ischemia revealed by MPS correlates significantly with NSS detected by CTA (p = 0.003). There is no significant correlation between permanent hypoperfusion revealed by MPS and SS detected by CTA (p = 0.09). When transient or permanent perfusion abnormalities were compared (total number = 34) to findings of CTA, a significant correlation was found in both NSS and SS groups (p = 0.01,  $\,$ p = 0.03, respectively). When transient+permanent perfusion defects were compared (total number = 12) to CTA, they significantly correlated only with NSS (p = 0.04). Additionally, QCA was performed in 8 patients. The QCA was negative in 3 patients, despite both MPS and CTA have been detected transient ischemia and NSS previously in one case.

**Conclusion:** The clinical value of anatomical and functional information provided by MPS and CTA are very simiral and the combination of them even seems as accurate as the quantitative coronary angiography in evaluation of coronary pathology in our relative small cohort.

#### E33

## DIAGNOSTIC VALUE OF EARLY GATED MYOCARDIAL PERFUSION SPECT WITH ERGOMETRIC STRESS IN DETECTING MYOCARDIAL STUNNING.

M. Tóth¹, K. Buga¹, M. Moravszki¹, I. Szilvási¹

<sup>1</sup>Department of Nuclear Medicine, Military Hospital, Budapest, Hungary

**Background:** ECG-gated myocardial perfusion SPECT (GSPECT) gives simultaneous information on myocardial perfusion and global/regional left-ventricular (LV) function. Ergometric stress can provoke myocardial stunning.

We studied the usefulness of early GSPECT (15-G: 15-minutes after excercise) compared to the standard GSPECT (60-G: 60-minutes after exercise) in detecting exercise-induced reversible LV dysfunction in patients with ischemic heart disease (IHD).

**Material and methods:** 37 patients (mean age  $58 \pm 9$  year) with angiographic evidence of IHD were enrolled in the study. 21 had decreased (50%) LV ejection fraction (EF) at rest by echocardiography (US). We performed 15-G, 60-G and resting GSPECT. Standard two-days Tc-99m aquisition protocol was used (dual-head camera,  $180^\circ$  circular rotation, 8 frame/cycle gating). LV-EF of the three studies were compared using quantitative (QPS/QGS) program. Functional parameters were related to perfusion data.

**Results:** From 16 patients with normal LV-EF by US EF decreased in 5 patients by 60-G and in 7 patients by 15-G. In all of them decrease was more pronounced by 15-G (in 3 patients more than 5%). Mean decrease of EF value by 15-G was 2.4%, statistically non-signifikant. From 21 patients with low LV-EF by US EF decreased in 14 by 60-G and in 16 by 15-G. Decrease was more pronounced by 15-G in 12 patients. Mean decrease of EF value was 4.9% by 60-G (p < 0.05) and 6.0% by 15-G (p < 0.01).

**Conclusions:** 15-G is useful in detecting exercise-provoked LV-dysfunction. Transient decreasing of LV-EF is more frequently found by 15-G than by 60-G. Early gated myocardial perfusion SPECT is indicated routinely because it can detect myocardial stunning in patients with low and with normal resting EF as well.

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#### F34

#### RELATIONSHIP BETWEEN REVERSIBILITY SCORE ON CORRESPONDING LEFT VENTRICULAR SEGMENTS AND FRACTIONAL FLOW RESERVE IN CORONARY ARTERY DISEASE

B. Kracskó¹, I. Garai¹, P. Lugosi³, B. Tar³, Zs. Nagy³, G. Vajda², Zs. Köszegi².³

<sup>1</sup>ScanoMed Ltd., Debrecen, Hungary

<sup>2</sup>Department of Cardiology, University of Debrecen, Debrecen, Hungary

<sup>3</sup>Jósa András Hospital Ltd., Nyíregyháza, Hungary

**Background:** Currently the indication of percutaneous coronary intervention is based on the fractional flow reserve (FFR) in the intermediate coronary stenosis. It is a simple, reliable and reproducible method, but it does not take into consideration the lokalisation of stenosis. The aim of this study was to find correlation between the severity of perfusion abnormality detected by scintigraphy and the FFR value as well as the localization of a particular coronary lesion.

**Material and methods:** 28 patients (male: 22, female: 6, age 62  $\pm$  7.62) were enrolled our retrospective analysis. The supplied left ventricular segments on the standard 17-segment polar map were rendered to each coronary branch. FFR measurements on 36 vessels (20 LAD, 6 LCx, 10 RCA) were compared with the myocardium perfusion SPECT studies performed before the invasive procedure. The lesions belonged to 6.47  $\pm$  2.47 myocardial segments (range: 1–12). We introduced a new ischemic index by combining the FFR with the number of the corresponding myocardial segments (left ventricular ischemic index: LVIi). This index was correlated with the regional myocardial perfusion defects identified on the scintigramms. Perfusion reversibility score of 2 or above was considered as indicative of active ischemia (regional Difference Score: rDSc).

Results: 13 lesion proved to be significant based on intracoronary pressure measurements (FFR < 0.75), which ones supplied 92 left ventricular segments. 50 segments showed reversibility out of the 92 segments (rDSc:76) The remaining non-significant 23 FFR values (> 0.75) corresponded to 138 LV segments (rDSc: 21). Close linear relationship was found between the LVIi and the rDSc (p < 0.001). Also a linear relationship (p < 0.001) could describe the connection between the FFR and the rDSc among the cases with lesion-associated myocardial territory of similar extensions (7-8 segments). Analyzing all the FFR values independently of the localization of the lesions, they also correlated significantly to the rDSc but the relation was less tight. LVIi predicted active ischemia (> 2 rDSc)on myocardial scintigraphy with 77.8% sensitivity and 94.4% specificity when the cut off value was set to 0.96. FFR alone predicted the ischemia on the scintigraphy with 72% sensitivity and 94% specificity at the best 0.8 cut off value. The area under the Receiver Operating Characteristic (ROC) curve was significantly higher for LVIi than FFR(0.92 vs. 0.78; p = 0.03).

**Conclusion:** The isotope data indicate that LVIi > 0.96 associates clinically relevant stenotic lesion. In our opinion, the FFR value not alone, but together with the corresponding left ventricular segments should be taken into consideration for the correct clinical decision making.

#### E35

## THE IMPORTANCE OF MYOCARDIAL PERFUSION SCINTIGRAPHY AND MULTISLICE CORONARY CT IMAGE FUSION IN SEVERE CORONARY CALCIFICATION

I. Balogh<sup>1</sup>, G. Kerecsen<sup>2</sup>, E. Marosi<sup>2</sup>

<sup>1</sup>Department of Nuclear Medicine, Uzsoki Street Hospital, Budapest, Hungary

<sup>2</sup>Pozitron-Diagnosztika Health Centre, Budapest, Hungary

**Background:** Even in the era of "state of the art" Multislice Coronary CT (MSCT) — 64 slices dual source — in the cases of serious coronary calcification the severity of coronary artery stenosis could be questionable. We investigated the diagnostic importance of MSCT and myocardial perfusion scintigraphy (MPS) fused imaging on this field — is there any ischaemia on MPS, if there is how severe is it and in the cases of questionable multivessel disease where is the culprit laesion?

**Material and methods:** In 23 cases with severe coronary calcification (Agatson Score between 410–3959!) where the results of MSCT was questionable as a second examination stress MPS was performed. The number of coronary artery stenosis (CAS) in 16/23 cases was 1 coronary artery, in 5/23 cases 2 CAS and in 2/23 cases 3 CAS. The subsequent stress-rest MPS were performed using ECG gated SPECT with Tc99m tetrofosmin. MPS results were evaluated with Interview XP, Emory ToolBox and Cedars-Sinai QPS-QGS software, scoring the perfusion, wall motion, wall thickening abnormalities in 4 grade score system. For image fusion PMOD 2,75, MIP-3D display and/or GE CardIQ software was used.

Results: The fused imaging showed significant ischaemia in 6/23 cases and the ischaemia was mild (score 1) or moderate (score 2). In 4/6 positive MPS cases the ischaemia was detected only on one coronary artery supply territories and in 2/6 MPS positive cases in two coronary arteries supply territories. We could found more severe ischaemia in the localization of culprit ("dominant") lesion. In every case the functional stress and rest parameters (ejection fraction, wall motion, and wall thickening) were normal. Conclusion: In many cases of severe coronary calcification on MSCT the significance of coronary artery stenosis remains questionable. The physiological significance of coronary stenosis on MPS and on the MSCT-MPS fused images can help to the correct diagnosis. On the basis of our preliminary results (1) ischaemia (on MPS) in the cases with severe coronary calcification (on MSCT) could be detected only in a few number of cases (6/23) and (2) the ischaemia proved to be mild to moderate. (3) The localization of culprit laesion could be established as well.

#### E36

#### DIAGNOSTIC VALUE OF QUANTITATIVE ANALYSIS OF MYOCARDIAL PERFUSION SPECT IN DETECTING REVERSIBLE PERFUSION DEFECTS

E. Takács¹, Zs. Varga¹, M. Barra¹, A. Radácsi¹, M. Janecskó³, P. Sármán², I. Szilvási¹

<sup>1</sup>Department of Nuclear Medicine, Kútvölgyi Hospital, Semmelweis University, Budapest, Hungary

University, Budapest, Hungary <sup>23rd</sup> Department of Internal Medicine and Cardiology, Semmelweis University, Budapest, Hungary

University, Budapest, Hungary <sup>3</sup>Department of Anaesthesiology, Kútvölgyi Hospital, Semmelweis University, Budapest, Hungary

**Background:** to determine the positive predictive value (PPV) of myocardial perfusion scintigraphy (MPS) using quantitative parameters compared with coronaria angiography (CAG) findings as gold standard and to analize false positive cases.

Material and methods: During a one-year periode 253 patients with known or suspected coronary artery disease (CAD) had perfusion defect on Tc99m-tetrofosmin stress-rest MPS in our department. A quantitative software (Cedars-Sinai QPS/QGS, score values) was used to evaluate perfusion defects. Severity and extent of stress perfusion defects were quantitated by summed stress score (SSS), and reversibility by summed difference score (SDS) using a normal data base. Tissue attenuation correction was not applied. 86 of these 253 patients were investigated by invasive CAG within 1 month after MPS. 52 patients had significant coronary artery stenosis. PPV of reversible perfusion defects was determined in this group retrospectively.

**Results:** In patients without significant coronary stenosis on CAG (n = 34, false positive MPS) SSS was significantly less, than in patients with significant stenosis (n = 52, true positive MPS),  $9.5 \pm 5.02$  vs.  $14.0 \pm 9.12$ . The difference is statistically significant (p = 0.03). There was no significant difference between SDS values of the two groups ( $5.0 \pm 3.98$  vs.  $6.0 \pm 2.89$ , p = 0.82). But if MPS was considered to be positive only with SDS equal or above 4, number of false positive results decreased from 34 to 12, and PPV increased from 62% to 86%. Majority of false positive perfusion defects (64.3%) were localized on the inferior wall, half of them had SDS value below 4.

**Conclusions:** According to our results, use of a higher cut-off value for significant perfusion defect is recommended to reduce the number of false positives cases, especially in case of inferior location. Evaluation of SSS value can help to avoid false positive MPS results.

#### E37

## ROLE OF MYOCARDIAL PERFUSION SCINTIGRAPHY IN THE AGE OF CORONARY CT ANGIOGRAPHY. OUR PRELIMINARY RESULTS

M. Moravszki<sup>1</sup>, K. Buga<sup>1</sup>, M. Tóth<sup>1</sup>, G. Kerecsen<sup>2</sup>, I. Préda<sup>2</sup>, R. G. Kiss<sup>2</sup>, I. Szilvási<sup>1</sup>

<sup>1</sup>Department of Nuclear Medicine, Military Hospital — State Health Center, Budapest, Hungary

<sup>2</sup>Department of Nuclear Medicine, Military Hospital — State Health Center, Budapest, Hungary

**Background:** Role of myocardial perfusion scintigraphy (MPS) should be re-evaluated in the age of coronary CT-angiography (CCTA). In our study we have analysed results of MPS and CCTA in eighteen patients with ischaemic heart disease (IHD) to define diagnostic value of MPS.

Material and methods: 18 patients had CCTA and MPS within two months. CCTA was performed using Siemens dual-source CT (in Pozitron Ltd). Stress MPS was performed with one-day Tc-99m-tetrofosmin (400 + 900 MBq) protocol using a dual-head SPECT (GE Infinia, Xeleris). Mean age of patients: 59.5 (39–72) years. 10 patients had clinical suspicion of IHD. 8 patients after PCI were examined because new clinical symptoms. In 12 patients CCTA was the first examination and MPS was indicated to evaluate clinical significance of abnormal CTA. In 6 patients CCTA was indicated because positive findings (ischaemia) of MPS.

**Results:** Seven patients had significant coronary stenosis on CCTA. 5 of them had ischemia on MPS. One of these patients with false-negative results had balanced three-vessels disease. Five patients had non-significant coronary artery stenosis, but 4 of them demonstrated ischaemia. Four patients had no stenosis (2 of them had previous PCI), and MPS was normal in all. One patient had coronary "bridging" with positive MPS. One patient had LAD anomaly, but normal perfusion.

**Conclusions:** Based on our preliminary results in small number of patients, MPS is indicated in patients with equivocal CCTA findings (non-significant stenosis, coronary anomalies), and ishaemia detected by MPS should be followed by CCTA (if invasive coronarography is not indicated).

#### E38

#### PERFORMANCE TEST OF THE MINIPET-II SCANNER FOR SEVERAL COINCIDENCE TIME AND ENERGY WINDOW USING THE NEMA NU-4 STANDARD

I. Lajtos<sup>1</sup>, S. A. Kis<sup>1</sup>, M. Emri<sup>1</sup>, G. Opposits<sup>1</sup>, D. Szikra<sup>1</sup>, G. Hegyesi<sup>2</sup>, L. Balkay<sup>1</sup>

<sup>1</sup>Institute of Nuclear Medicine, University of Debrecen, Debrecen, Hungary

Institute of Nuclear Research of the Hungarian Academy of Sciences, Debrecen, Hungary

Background: The small animal PET scanner (MiniPET-II) performance parameters were evaluated with the National Electrical Manufacturers Association (NEMA) NU-4 standards. Although the measured and calculated parameters characterize well the actual PET scanner, they may depend on the basic settings of the PET system. Some settings cannot be altered at all (number of crystals, axial field of view), while others (energy window, coincidence time window, reconstruction algorithm etc.) can be changed both before the data acquisition and/or during the data processing. In this study we investigated how the calculated NEMA parameters depend on the used coincidence time window (t), and the low threshold settings of energy window (Elt).

**Material and methods:** The MiniPET-II small animal scanner includes 12 detector modules in one ring with LYSO scintillator crystal blocks and position sensitive PMTs. Each crystal block consists of 35 x 35 crystal pins of  $1.27 \times 1.27 \times 12$  mm size and the detector signals are processed

by FPGA based digital signal processing boards. Data collection and image reconstruction were performed by using the M3I (MultiModal Medical Imaging) software framework developed in our institute. All measurements and data evaluation were based on the NEMA standard protocol at three different t (2, 3 and 4 ns) and Elt (250 keV, 350 keV, 450 keV) values. The following parameters were determined: spatial resolution, sensitivity, noise equivalent count rate (NEC), uniformity, recovery coefficients (RC), spillover ratio (SOR).

**Results:** The spatial resolution varied between 1.3 to 2.1 mm at 5 and 25 mm radial distances, independently from the "time window" and Elt. However the NEC values depended on both the t and Elt. At t=2, 3 and 4 ns using the rat phantom the NEC peaks were 13.1 kcps/38 MBq, 14.2 kcps/36 MBq and 14.5 kcps/37 MBq, respectively. The system sensitivity in the centre of FOV increased with the t by the following values: 0.55%, 0.6% and 0.61%. The sensitivity was changed by 20% by Elt. Using the NEMA NU-4 image-quality phantom RC, the SOR and uniformity were also calculated. As it was expected the RC and the uniformity were not dependent on the t and Elt. The SOR parameter changed 20% (water) and 10% (air) in case of the t, and 15–20% when altering Elt.

**Conclusion:** It can be concluded that the calculated performance parameters could depend on the basic settings of the PET system. It means that the t and Elt need to be optimized for a given small animal PET scanner.

#### E39

## SEEKING A SIMPLIFIED FORMULA FOR DESCRIBING THE POSITION-DEPENDENT RESOLUTION OF GAMMA CAMERAS

J. Varga

Institute of Nuclear Medicine, University of Debrecen, Debrecen, Hungary

**Background:** Data characterizing the resolution of gamma cameras are necessary for restoration filters as well as resolution recovery reconstruction algorithms, which can effectively enhance the signal-to-noise ratio and improve the visibility of details in planar and SPECT images. Resolution depends both on the object-detector distance and the scattering medium. We searched for a simple formula to describe the dependence of the modulation transfer function MTF(f) of a gamma camera on the source position and the thickness of body tissue.

Material and methods: We acquired images of line sources with two different gamma energies using a general purpose gamma camera (DHV, Mediso): Tc-99m with a low energy, high resolution collimator (used for the majority of patient studies), and I-131 with a high energy collimator. Target-detector distance varied between 5 and 31 cm, with 0 to 26 cm layer of water as tissue equivalent scattering medium, giving 15 combinations altogether. First we fitted the MTF(f) measured in air by a function of the form exp[-(f^2P)/S], then included the effect of scattering in the model. The goodness of fit was characterized by the residual sum of squared differences

**Results:** We found a close correlation between the source-detector distance d and the parameters of the exponential function in air; e.g. for Tc-99m:  $P=0.00898\times d+0.81,\,S=1.173\times \exp(-0.0865\times d)$  In the presence of scatter we compared several functions, starting from a single exponential term as above, and testing various combinations (weighted sums and products) of such terms. When using a single exp term, we found that in a first approach parameter S depends on the distance only, while the effect of scattering medium appears in the value of P. 5 or 6 constants are sufficient to describe the MTF.

**Conclusion:** The modulation transfer function characterizing the system resolution of gamma cameras can be well approximated by an analytical function with a few parameters. A separate set of constants applies for each camera-collimator-radionuclide combination.

#### F40

## FAST GPU BASED ITERATIVE IMAGE RECONSTRUCTION ALGORITHM FOR PARALLEL PROJECTION MYOCARDIAL PERFUSION SPECT STUDY

Á. Szlávecz1, B. Kári2, G. Hesz1, T. Bükki3, O. Pártos2, B. Benyó1

<sup>1</sup>Department of Control Engineering and Information, Budapest University of Technology and Economics, Budapest, Hungary

<sup>2</sup>Department of Radiology and Oncotherapy, Semmelweis University, Budapest, Hungary

3Mediso Ltd., Budapest, Hungary

Background: Parallel projection based Single Photon Emission Computed Tomography (SPECT) is widely used method in isotope diagnostics for cardiac studies. Many phenomenon's, like photon absorption, scatter, as well as the distance dependent spatial resolution (DDSR) — as a consequence of the parallel projection — produce distortion in SPECT imaging, which may result false diagnostic value. Further imaging imperfection may be expected, if the activity distribution of the imaged object is not in the center of the field of view and 180 degree acquisition technique is applied. Our research activity mainly aimed to create image reconstruction algorithm to be optimized on novel technology based GPU (Graphic Process Unit) including inherent compensation of above mentioned most of the image distortion effects, where is possible to expect significant image quality improvement as a consequence.

Material and methods: The applied image reconstruction algorithm is based on expected maximization iterative algorithm (Ordered Subset Expected Maximization, i.e. OSEM). The imaging model of parallel projection as well as the non-homogeneous photon absorption effect has been included in the forward projection step. The non-uniform photon attenuation map is determined by coregisterted and resampled CT imaging. Dedicated calibration procedure has been worked out in order to describe the point spread function of DDSR SPECT imaging. High performance computing method has been developed due to the intensive computation demand algorithm. The implementation has been carried out by novel nVidia based GPU's being much faster than the conventional multi-core CPU's (Central Process Unit). AnyScan® SC (multi-modality SPECT/CT) and CardioDESK dual head dedicated SPECT system (Mediso Ltd.) were considered for both simulation studies and real measurements (physical phantom and patient studies).

Results and Conclusions: The novel GPU based reconstruction algorithm resulted significant improvement in the spatial resolution. The reconstructed images showed clear-cut better spatial activity distribution. Considering the speed of the implemented reconstruction method is suitable for daily clinical application too (running time is less than 10min. in case of  $128 \times 128 \times 128$  volume discretization with nVidia 480GTX GPU). Nevertheless, during the verification procedures of algorithm has been discovered equivocal hypo-perfusion segment around the apical region of the heart. The effect could be observed systematically on mathematical and physical phantoms as well as on patient studies too. The phenomenon may originate from the partial volume effect (PVE), which is under consideration already. Further image quality improvement can be expected by the scatter correction application around the surrounded volume of the myocardium.

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#### E41

### SCATTER AND ATTENUATION CORRECTION IN MONTE CARLO BASED ML-EM PET RECONSTRUCTION

A. Wirth<sup>1</sup>, Á. Cserkaszky<sup>2</sup>, D. Légrády<sup>2</sup>, B. Kári<sup>1</sup>, B. Domonkos<sup>3</sup>

<sup>1</sup>Department of Radiology and Oncotherapy, Semmelweis University, Budapest, Hungary

<sup>2</sup>Institute of Nuclear Techniques, Budapest University of Technology and Economics, Budapest, Hungary

3Mediso Ltd., Budapest, Hungary

**Background:** In positron emission tomography the processes during the  $\gamma$ -photons lifetime have an essential effect on the reconstructed image quality. Our goal is to develop a reconstruction algorithm, which makes it possible

to take into account the most important events from the isotope decay till the end of the detection, hence providing an inherently artefact-free image. **Material and methods:** The Maximum Likelihood Expectation Maximization (ML-EM) scheme — a member of the iterative reconstruction family — may include a physical model of arbitrary precision. The most realistic results can be achieved with the Monte Carlo (MC) simulation method. The simulation consists of the positron propagation and the -photon transport inside the body and the detector crystals. The material distribution map coming from the CT modality of a PET-CT device serves as the basis of the transport code. In order to stay inside the acceptable reconstruction time-frame, the algorithm has been implemented on the graphics processor (GPU) platform. GATE simulations of mathematical phantoms along with physical phantom and small animal acquisitions on the Mediso NanoPET/CT were used for image quality analysis and validation.

**Results:** The scatter and absorption correction capabilities of the reconstruction algorithm were systematically assessed. In case of realistic matter density values there were no significant scatter and attenuation artefacts in the small animal PET geometry. When the density was artificially increased, a gradual appearance of image deficiencies was observed. By simulating the scatter and absorption processes on-the-fly during the reconstruction process the intensity of the artefacts has been successfully decreased. The graphical processors proved to be an ideal platform for the Monte Carlo simulations: more than two order of magnitude faster runs could be achieved than on CPU.

**Conclusion:** The results achieved so far point toward the possibility of the clinical and pre-clinical usage of the reconstruction method in the future. The scatter and attenuation corrections will be a key feature in human PET applications.

#### E42

## TOWARDS THE CLINICAL APPLICATION OF BRONCHOSCOPY SUPPORTED BY VIRTUAL PLANNING: FIRST RESULTS

M. Koselák¹, T. Spisák¹, G. Opposits¹, S. A. Kis¹, L. Pohubi¹, L. Galuska¹, Zs. Hascsi², P. Szabó³, M. Emri¹

<sup>1</sup>Department of Nuclear Medicine, Medical and Health Science Center, University of Debrecen, Debrecen, Hungary

<sup>2</sup>ScanoMed Ltd., Debrecen, Hungary

<sup>3</sup>Pulmonology, Josa Andras Teaching Hospital, Nyíregyháza, Hungary

Background: The virtual bronchoscopy supported by PET/CT studies and performed before the operation allows to plan the intervention and thus increases the efficiency of the therapy. Since such method is not available at the University of Debrecen, we have aimed the development of a complex software system to support the bronchoscopic operations by virtual tools. Material and methods: The MultiModal Medical Imaging software system developed in-house was used for the work. In the phase of the image procession, PET/CT and diagnostic CT scans of the patients are used. At first the low-dose CT and the diagnostic CT images are registered taking care of the quality, since the alignment should be optimal near the bronchi. The registered images, the 3D metabolic information of the PET and the vascular density information of the CT image are used for input data to aid the virtual navigation and the accurate localization of the transbronchial needle aspiration biopsy. The registration, the surface models and the input data of the navigation are prepared in the Department of Nuclear Medicine. The date of the scans and the state of the image sets are traceable by the partners on the R&D web site of the department (www.minipetct.hu). The completed PET/CT and diagnostic CT images prepared for the virtual bronchoscopy, the registered surface models and the functional data for the navigation are also downloadable from the website. The bronchoscopic operation is performed in the Department of Pulmonology of Jozsa Andras Teaching Hospital.

**Results:** An easy-to-use software system that supports the planning of bronchoscopic procedures has been developed. Besides, to support the project including the monitoring of states of image data, a web interface has also been designed. During the development, PET/CT studies of five patients (including the diagnostic CT data in three cases) were used to validate the software and build up the interactive interface of the virtual bronchoscopy.

Abstracts

**Conclusions:** The complex software system developed to support virtual bronchoscopy, enables to examine how the operation planning affects the quality of the diagnosis and the therapy, thus, a long-term clinical program can be launched. The experiences of the development can be useful in following tenders and projects.

#### E43

Oral session

### ANATOMICAL LOCALIZATION SOFTWARE FOR INDIVIDUAL AND POPULATION ANALYSIS OF PET DATA

T. Spisák¹, G. Opposits¹, A. Jakab², M. Koselák¹, S. A. Kis¹, L. Trón¹, E. Berényi², M. Emri¹

<sup>1</sup>Department of Nuclear Medicine, Medical and Health Science Center, University of Debrecen, Debrecen, Hungary

<sup>2</sup>Department of Biomedical Laboratory and Imaging Science Medical and Health Science Center, University of Debrecen, Debrecen, Hungary

**Background:** The anatomical localization of the physiological processes and pathological disorders of the brain investigated by cranial PET studies can be performed effectively using digital brain atlases. Although the number of the available brain atlases shows a significant increase, the support of this technique by information systems is still poorly accomplished. The purpose of our work was to develop a uniforming method and a database model handling various deterministic brain atlases, and based on it, an interactive software assisted by brain atlas databases for the promotion of the multi-modal medical imaging projects proceeded in our institute.

Material and methods: After the comparative analysis of 6 different anatomical, deterministic, web-accessible brain atlases a particular atlas definition was constructed, which enables the uniform handling of various atlases. As part of this system we have developed components and database models for maintaining the label maps and the region systems contained by the atlases. By implementing the deployed uniforming model, a framework was constructed, providing tools for the integration, maintenance and utilization of atlases in various tasks. A graphical user interface application, called BrainLOC, has also been developed to perform localization and region analysis tasks. The software is built upon the MultiModal Medical Imaging software development system.

Results: According to our purpose, a model and framework for uniforming the examined atlases has been developed. Based on these, the BrainLOC application (www.minipetct.com) was deployed. The software became one of the most important tools of several institutional projects, and among others it permits of the atlas-assisted anatomical localization and region analysis of PET data aligned into atlas-space. BrainLOC is published under student and academic licenses for educational and research purposes.

**Conclusion:** Using BrainLOC, the database of 6 different brain atlases can be used simultaneously for localization and region analysis tasks emerging by cranial PET studies. Applying the appropriate atlas or an arbitrary collection of regions from different atlases provides the opportunity for the quantitative anatomical analysis of functional images. In the future our uniforming method and database model is planned to be extended towards integrating so-called probabilistic atlases.

#### E44

### GRAPH THEORETICAL MODELING OF BRAIN CONNECTIVITY USING PERFUSION PET DATA

M. Emri, S. A. Kis, M. Koselák, G. Opposits, P. Mikecz, T. Spisák, L. Trón Department of Nuclear Medicine, University of Debrecen, Debrecen,

Background: In the recent years, a large number of studies have investigated the complexity of structural and functional brain connectivities by graph theoretical analysis. This approach allows to characterize the nature of the human brain networks modeled by regional interactions of structural, functional, diffusion weighted magnetic resonance imaging (T1, fMRI, DWI), quantitative electroencephalography (EEG), magnetoencephalography (MEG) measurements, low resolution electromagnetic tomography

(LORETA) and PET tracer distribution, as well. The Institute of Nuclear Medicine takes efforts to develop PET ligands enabling the investigation of neurodegenerative diseases. In these projects we intend to apply graph theoretical network analysis besides the commonly used image processing methods. For this reason, we aimed to develop a complex image processing system which allows to examine the properties of brain networks derived by EEG, MRI- and PET data.

Material and methods: For the software development the MultiModal Medical Imaging system has been applied. Since complex PET image database, containing healthy and pathological data of volunteers, is available only in our previous projects based on the GE 4096 scanner, 15O-Butanol perfusion scans were used for tests. Perfusion scans of eight healthy subjects and eleven schizophrenic patients investigated by auditory odd-ball paradigm were used to create functional brain networks. SPM5 software was used to eliminate the global effects from the spatial standardized (MNI152) and Gaussian filtered (16 mm isotropic kernel) PET-data. Using these adjusted perfusion values, the nodes of the functional network were delineated by the regions of the LPBA40 probability brain atlas. The strength of the regional connections were modeled by the population level correlations and partial correlations. Graph theoretical analysis was applied to characterize the network properties of the investigated populations. During the development and the analysis, a number of graph parameters (edge density, global efficiency, characteristic path length, clustering coefficient, small-worldness etc.) were computed and a 2D- and 3D atlas driven graph visualization application was developed, as well.

**Results:** According to our goals, a complex graph theory based network analysis and visualization software has been worked out to investigate brain connections using MRI, EEG and PET data. For tests the networks created from brain activation data of healthy subjects (8) and schizophrenic patients (11) were used. We showed that the edge density and the clustering coefficient of brain networks decreased, while the length of the characteristic path increased. The networks of the control group showed small-world property, while this parameter was negligible in the case of diseased subjects. Although, the low number of measurements has not allowed to make robust statistical population-level inferences about the network differences but our results correspond to literature of the discipline.

Conclusion: Our software is an efficient tool to build, visualize and analyze brain connectivity investigated by MRI, EEG and PET studies. Due to the low number of measurements and the short axial field of view of GE 4096 scanner which has not allowed to create whole-brain related networks, the results are suitable only for tests. However, our experiences showed that the development of multimodal (PET/MRI/EEG) networks based on dynamic PET scans and advanced correlation techniques, belongs to the advanced topics of brain connectivity research.

#### E45

## INTERDISCIPLINARY ON-LINE ACCESSIBLE EDUCATIONAL MATERIAL FOR DEVELOPING AND APPLYING EXPERTS OF IMAGING PROCEDURES

B. Kári<sup>1,3</sup>, K. Karlinger<sup>1</sup>, D. Légrády<sup>2</sup>, T. Györke<sup>3</sup>, Cs. Pesznyák<sup>2</sup>, Sz. Czifrus<sup>2</sup>, V. Bérczi<sup>1</sup>

<sup>1</sup>Department of Radiology and Oncotherapy, Semmelweis University, Budapest, Hungary

<sup>2</sup>Institute of Nuclear Techniques, Budapest University of Technology and Economics, Budapest, Hungary

<sup>3</sup>Department of Nuclear medicine, Semmelweis University, Budapest, Hungary

**Background:** Imaging diagnostic is one of the most intensively developing interdisciplinary scientific field, which is essential in the full spectrum of healthcare. The interdisciplinary knowledge and its continuous refreshment is absolute necessary for both experts training and specialists who are already working on this field (both engineering/physicists and medical, biologist's sides). Consequently, a modular on-line educational technique with its essential curriculum has been created, in order to do continuous refreshment as well as to adapt quickly to the current requirements and to support the tele-education by high level way on both theoretical and practical fields.

**Material and methods:** Complexity of the imaging field and the demands of the specialists on both medical and engineering/natural science sides have been deeply considered from the daily problems to the highest level scientific questions. Consortium has been created by leading SE, Dept. of Diagnostic Radiology and Oncotherapy (DDRO) with the collaboration of BME, Institute of Nuclear Technique (INT) in order to develop the educational technique and material. Financial background of the project is guaranteed by the TÁMOP 4.1.2-08/A/KMR-2009 (NFÜ) grant from the beginning of 2010, when the project has started. The curriculum is covered by the following main subjects:

- 1. Physical, technical and informatical background (INT, DDRO);
- 2. Medical-biological application fields (DDRO);
- 3. Image based practical method and material (DDRO, INT).

The theoretical chapters can be accessed by the Web based wikipedia user interface. The engineering/physical chapters will be created by Hungarian and English languages, while the medical chapters on gradual level on Hungarian, English and German languages. The post-gradual and continuous medical education (CME) curriculum exists only on Hungarian language. The (3) practical subject contains anonymous, continuously expandable real pre-selected image database (mathematical/physical/anatomical phantom set and human examinations). The image database can be evaluated independently of the geographical location with the available rights. Harmony of the theoretical and practical knowledge have serious role, because the main goal are the recognition, interpretation and discovering of the artifacts and noises originating from the digital imaging and image processing — at the "digital age". Considering the above point of views is possible to understand, same information, knowledge and experiences are needed for the applying/researcher-developer experts. In order to get the useful practical skill, an image database system has been developed by tele-communication technique accessibility.

Conclusions: An integrated interdisciplinary knowledge base with tele-education support structure has been evolved by the development of the educational technique with the curriculum for the professionals on the fields of imaging procedures for research, development and application purposes (radiology, nuclear imaging, radiation therapy, ... etc.) on gradual, post-gradual, MSc., PhD. and CME levels. The created educational method and material is suitable for long term perspective for any medical imaging experts (SPECT/CT, PET/CT, PET/MR, SPECT/PET/CT, ...) who are using both directly and indirectly the curriculum (medical physicist, bio-engineers, medical electronics experts, radiologists, ... etc.). The evolved structure is the fundament of imaging procedure project already in the frame of medical physicist education (MSc.) at the BME Faculty of Natural Science (TTK)/ the education has started at September of 2010/.

#### E46

### EXAMINATION OF VISUAL PERCEPTION VARIABILITY IN DETECTING LOW CONTRAST AREAS

L. Balkay, I. Lajtos, G. Opposits

Institute of Nuclear Medicine, University of Debrecen, Debrecen, Hungary

Background: In case of nuclear medicine — and in a wider sense in case medical imaging — it is a frequently asked question that under what conditions will an object (with contrast of Ct and area of A) visible in the final picture. Taking into account the mapping and imaging characteristics of the given device it is theoretically possible to estimate the expected Ck image-contrast resulting from the given CT contrast and to estimate the type and size of background's in the environment of the area. The decision if a given low contrast area is visible or not depends however on the analyst as well. In other words, detectability is not simply physical characteristic (for example the spatial resolution) of the imaging device, but also the result of the cooperation between the device and the analyst. Since the last decade the Rose-criterion, which says that an area is detectable if Ck\*s\*A > 4-59, can also be found in study books as a detectability rule of thumb. The Rose-criterion was born in the 1950s using to the TV imaging and from the examination of small (1-2 pixels) areas. Our aim was a quantitative analysis of the detectability in case of images in nuclear medicine, while examining the detectability of the different contrast areas at distinct human observers with different perception ability.

Material and methods: We developed a computer simulation program with which it is possible to randomly produce areas with differing activity (contrast) at the same time given a certain background distribution. We randomly set the following data when producing the images: the background activity, the number, size and contrast of the given lesion. We added Poisson noise to the images during the calculations. After each simulation the person who used the program had to indicate what he or she considered as suspected area. The program continuously stored the successful selections with all the actual data of the simulation. We also examined with the program how it influenced the detectability if the image contained postfiltering or if the palette used for the display was color or grey. Each person who took part in the research ran 500–1000 simulations. We evaluated and processed the stored simulation results

**Results:** We found the Rose-criterion true only in case of small "A" areas. If the pixel number is larger another relationship seems to be acceptable. The type of the color palette, which we used for the simulation tests did not influence the detectability, however further image processing may alter the threshold value significantly. A skillful picture analyst can detect low contrast areas with larger probability however there is only small difference between professionals and not qualified people.

**Conclusions:** It is not possible to describe the detectability of low contrast lesions only with the technical parameters of the imaging device. The detectability can only be characterized with a probability because of the different visual perceptions ability of the evaluating persons. The different visual perceptions can be analyzed with properly built simulation programs.

#### E47

### HOW EFFECTIVE IS THE RADIOIODINE THERAPY IN TREATING THE GRAVES-BASEDOW DISEASE?

K. Kállai<sup>1</sup>, J. Varga<sup>1</sup>, E. Nagy<sup>2</sup>

<sup>1</sup>Department of Nuclear Medicine, Debrecen, Hungary <sup>2</sup>1<sup>st</sup> Department of Internal Medicine, Debrecen, Hungary

**Background:** Hyperthyroidism is becoming more and more common these days. One of its treatment is the radioiodine therapy, which has been practiced in Debrecen for more than 50 years now. Our aim was, to examine the success rate among the Graves-Basedow patients whom we treated, and to try to identify factors that should be taken into account in order to improve the outcome.

**Material and methods:** We reviewed the follow-up data 1, 6, 12 and 24 months after the radioiodine therapy of 27 Graves-Basedow patients with nodule and 92 without nodule, treated between 2007 and 2009. To determine the status of the thyroid we took into account the TSH, free T4 and T3 levels, and the necessity of further treatment. Cases with and without nodules were evaluated separately. We examined the connection between the estimated thyroid dose (54–252 Gy) and the developed thyroid status with Kruskal-Wallis test, and examined the connection between the initial anti-TPO level, presence of nodules, and the speed and rate of the development of hyperthyroidism using the chi-square test.

**Results:** The number of the patients followed after 1, 6, 12 and 24 months were — 116, 103, 86 and 49 respectively. The majority of the patients (66% without nodule, 69% with nodule) still had hyperthyroidism after one month, but these numbers gradually decreased later, and after 12 months — 67% and 47% of the patients were already hypothyroid, respectively. The difference between the outcome of the patients with or without nodule became significant after 12 months ( $\chi^2$ , P = 0.014). The developed thyroid status did not show a significant connection with either the (just slightly varying) thyroid dose used (Kruskal-Wallis test), or the increased starting level of anti-TPO ( $\chi^2$ ).

**Conclusion:** The planned absorbed doses of 70 Gy for Graves-Basedow disease without and 100 Gy with cold nodules present successfully terminated hyperthyroidism in the majority of the patients. Moreover, hypothyroidism developed in a significant number of cases. Based on our results an increase in the planned doses, as some recommendations suggest, does not seem justified. We did not find the anti-TPO level capable of predicting the outcome.

#### F48

### SAFETY REGULATIONS FOR OPERATING PROCEDURES WITH UNSEALED RADIONUCLIDES

L. Ballay<sup>1</sup>, T. Séra<sup>2</sup>

<sup>1</sup>National Research Institute for Radiobiology and Radiohygiene, Budapest, Hungary

<sup>2</sup>Department of Nuclear medicine, University of Szeged, Szeged, Hungary

The Hungarian radiation protection regulatory system is quite complete at the level of act, ministerial and governmental orders, standards, but at the lower level namely the set of operational guidance, safety regulation, is deficient. The basic safety standards for the application of ionizing radiations are found in the Decree No. 16/2000 (VI. 8.) EüM of the Minister of Health, while the recently revised MSZ 62-7 standard contains the information on how to design radiation safety of radioisotope laboratories, at the same time there is no guidance on what is considered as good practice working with radioactive materials. In the seventies and eighties the effectively used radioisotope and X-ray safety guides described good practice but these had became invalidated, and not considering some paragraphs of the Decree No.16/2000. (VI.8.) there are no safety guides which would have replaced these. The aim of the presentation is to raise attention, to the safety regulations for operating procedures with unsealed radionuclides and to review its aims, scope of applicability and delineate its general contents. The main goal of the safety guide is to become "The guide of good practice for working with unsealed radioactive sources", intended to be used by those who work at radioisotope laboratories, primarily at nuclear medicine departments. The first version of the document was developed with the support of the HAEA (Hungarian Atomic Energy Authority) (OAH ÁNI/ABA 01/09).

The presented version was updated in collaboration with HSNM (Hungarian Society of Nuclear Medicine).

#### E49

### RADIATION PROTECTION OF PERSONNEL WORKING IN A NUCLEAR MEDICINE DEPARTMENT

É. Szücs<sup>1</sup>, I. Garai<sup>1</sup>, O. Sántha<sup>1</sup>, J. Varga<sup>2</sup>

<sup>1</sup>ScanoMed Ltd., Debrecen, Hungary

<sup>2</sup>University of Debrecen, Institute of Nuclear Medicine, Debrecen, Hungary

**Background:** The aim of this study was to identify the factors having a significant influence on the measured radiation doses, including the scope of activity and individual style of work, by processing the personal dosimetry data of an institute with extensive "in vivo" nuclear medicine profile. We compared the data of film and digital dosimeters in cases of radionuclides with different gamma energies, and tested the effect of using automatic FDG infusion system on the staff dose.

Material and methods: The exposure of personnel was measured by film dosimeters evaluated by the National Personal Dosimetry Service, and Thermo Scientific EPD Mk2+ digital personal dosimeters read out locally. Exposure data measured by film dosimeters were collected over a 10 years' period in three divisions, including gamma camera imaging and PET. 27 persons were enrolled in this study. Inactive periods and end of employment were noted. A total of 950 film dosimetry and 75 digital dosimetry data were analyzed. We classified film dosimetry data into 9 categories by the scope of activity. Digital dosimeters were utilized by PET/CT personnel (13 people) and in gamma camera hot lab (1 person). Since film data refer to 2 months' periods, digital dosimetry data were summarized for 2 month intervals as well. The normality of the distribution of data groups was checked by Shapiro-Wilk test. Because of the lack of normality, non-parametric tests were used to compare the groups: Mann-Whitney for two groups, and Kruskal-Wallis test for several groups. Since the differences between film and digital readings showed Gaussian distribution, Student's paired t-test was used for their comparison. The significance of various factors was tested using the general linear model. Results: 85% of the doses were under 0.6 mSv/2 months. No significant difference was found between data obtained by film and digital dosimetry. However, there was a significant difference between the doses of personnel having different scopes of activity (Kruskal-Wallis test: p < 0.0001). The highest doses were measured in the PET/CT department and the hot lab. Using the automatic infusion system significantly reduced the doses: digital dosimetry data showed an average reduction of the effective doses by 0.16  $\mu$ Sv/h (2 sample t-test, p = 0.008). Exposures of people doing the same job showed high variances.

**Conclusion:** Our results suggest that the rotation of the staff between working places is justified to equalize radiation exposure. The individual variances of exposure point out the importance of regular theoretical and practical education, and the skilled usage of radiation protection devices available.

#### E50

### AUTOMATED MONITORING OF THE MINIPET-II SMALL ANIMAL PET SCANNER OPERATION PARAMETERS

I. Lajtos<sup>1</sup>, S. A. Kis<sup>1</sup>, G. Opposits<sup>1</sup>, L. Balkay<sup>1</sup>, J. Imrek<sup>2</sup>, L. Trón<sup>1</sup>, M. Emri<sup>1</sup>

<sup>1</sup>Institute of Nuclear Medicine, University of Debrecen, Debrecen, Hungary <sup>2</sup>Institute of Nuclear Research of the Hungarian Academy of Sciences, Debrecen, Hungary

**Background:** The MiniPET-II small animal PET scanner was proved to be a useful tool in many biological projects, which require high level of availability. Thus the system requires systematic hardware and software monitoring, rapid identification and replacement of defective components. Furthermore we perform methodological developments, thus the MiniPET-II software system changes constantly. Our aim was to work out an effective automated monitoring system on daily basis to check the operating parameters and to send messages (SMS and e-mail) in case of failure.

Material and methods: The development of system was performed by using MultiModal Medical Imaging software framework developed in our institute. The monitoring software performs automated control of the detectors, the data acquisition and network infrastructure, and the image reconstruction and archiving pipelines. The evaluated system parameters are stored in a technical database available for technical material on www.minipetct.hu. In case of error the software sends message to the authorized personnel of the scanner via SMS and e-mail. The backup storage devices and automated  $\,$ error reporting system allow for quick troubleshooting and high availability. Results: We developed an automated monitoring system supported by a database, which is able to determine the technical status of the MiniPET-II, thus increasing system reliability. The software monitors the operation of the detector (signal processing electronics, FPGA code), the data acquisition system, network communications (network switch elements, data collection server, data acquisition program, disk capacity, archiving system), the reconstruction pipeline (server restoration, reconstruction software, image quality) and the operating environments (temperature of labs and servers. humidity rate and air pressure of the lab), as well.

**Conclusion:** The designed infrastructure and the developed monitoring system decreased the measurement failures of MiniPET-II scanner during clinical research projects and provided high availability (higher then 95%).

#### E51

## SEMIQUANTIFICATION OF MYOCARDIAL PERFUSION AND ECG-GATED SCINTIGRAMS USING TWO SOFTWARE PACKAGES.

A. Radácsi<sup>1</sup>, Z. Olbrich<sup>1</sup>, I. Balogh<sup>1</sup>, K. Bor<sup>1</sup>, A. Rónaszéki<sup>2</sup>

<sup>1</sup>Euromedic Diagnostics Hungary Ltd., Budapest, Hungary <sup>2</sup>Department of Cardiology Péterfy Sándor Hospital, Budapest, Hungary

**Background:** The aim of this study was to compare the diagnostic value of ischemia, wall thickening and wall motion of the Corridor4DM (4DM) and Cedars-Sinai (QPS,QGS) software packages for semiquantification of myocardial perfusion (MPS) and EKG-gated (MGS) scintigrams.

**Material and methods:** we studied 123 (52 males with a mean age of 62.9 years, 71 females with a mean age of 61.4 years) consecutive patients who underwent two-day stress/rest (99m)Tc-tetrofosmin MPS and MGS studies. All patients had pharmacological stess-test with Dipyridamole. The reference classification for MPS and MGS studies regarding presence or absence

of ischemia and normal or decreased wall thickening and motion were obtained from two physicians (with more than 25-, 10 years experience in nuclear cardiology). Semiquantitative processing was done using 4DM, QPS, QGS software packages. A 17-segment analysis was performed. Ischemia was defined as a summed stress score > 5, plus a summed difference score > 2, normals as a summed stress score < 5. Decreased wall motion or thickening was defined as a summed score > 5.

**Results:** In 30/123 cases had myocardial ischemia according to the two physicians, and 24 and 26 patients fullfilled the criteria for 4DM and QPS. In 6/93 cases and in 9/93 cases were false positive ischemia for 4DM and QPS. In 8/123 cases had decreased wall thickening, and 16/123 had decreased wall motion and the criteria were fullfilled all of them for 4DM and QGS. In 28/105 cases and in 6/105 cases were false positive decreased wall thickening for 4DM and QGS. In 17/107 cases and in 4/107 cases were false positive decreased wall motion for 4DM and QGS. The differences in false positive rate between 4DM and QGS were statistically significant (p < 0.001). **Conclusion:** 4DM and QPS showed negligable difference for ischemia. QGS showed considerable significantly higher specificity for decreased wall motion and thickening.

#### E52

### POST-STRESS SDMA, BUT NOT ADMA IS ELEVATED IN PATIENTS WITH TRANSIENT MYOCARDIAL ISCHAEMIA

T. Molnár<sup>1</sup>, Zs. Szabó<sup>2</sup>, E. Plózer<sup>3</sup>, É. Bartha<sup>3</sup>, B. Biri<sup>4</sup>, L. Nagy<sup>4</sup>, S. Kéki<sup>4</sup>, E. Schmidt<sup>2</sup>, S. Szekeres<sup>2</sup>, K. Zámbó<sup>2</sup>

<sup>1</sup>Department of Anaestesiology and Intesive Therapy, University of Pécs, Pécs, Hungary

<sup>2</sup> Department of Nuclear Medicine, University of Pécs, Pécs, Hungary ³|st Department of Internal Medicine, University of Pécs, Pécs, Hungary

**Background:** Asymmetric and symmetric dimethylarginines (ADMA and SDMA, respectively) are protein breakdown products. ADMA inhibits directly eNOS, whereas SDMA competes with the NO precursor arginine for uptake into the cells. We aimed to analyse both biomarkers in patients with coronary artery disease (CAD) referred for stress/rest myocardium perfusion scintigraphy (MPS).

**Material and methods:** All patients with suspected CAD were undergone a two-day dipyridamole (DP) stress/rest protocol. Venous blood was taken before (as baseline) and after DP stress for biomarkers (L-arginine, ADMA, SDMA). Beside, hemodynamic parameters and respiratory rate were obtained during DP stress. Statistical analysis: chi-square test and independent sample test were used and data were presented as either mean  $\pm$  SD or mean and 95% confidence interval.

**Results:** In patients with CAD, baseline ADMA and SDMA were significantly higher when compared to healthy subjects. Post-stress SDMA, but not ADMA was significantly higher (mean: 0.57, 95% CI: 0.49–0.64 vs. 0.40, 0.33–0.49, p=0.007) in patients with transient myocardial perfusion abnormality revealed by myocardial perfusion scintigraphy. However, neither ADMA nor the L-arginine/ADMA and L-arginine/SDMA ratios were significantly different before and after DP stress.

**Conclusions:** Serum SDMA could distinguish patients with similar symptoms and risk factors nevertheless differential response to dipyridamole stress, thus with different stage of coronary atherosclerosis. In addition, sustained elevation of serum SDMA in combination with an abnormal moycardial perfusion scan should be also considered beside traditional risk factors in patients undergoing elective cardiac evaluation.

#### E53

### DETECTION OF PULMONARY EMBOLISM WITH PERFUSION SPECT/CT

A. Radácsi, Z. Olbrich, K. Gyimesi, K. Bor

Euromedic Diagnostics Hungary Ltd., Budapest, Hungary

**Background:** The aim of our study was to present our experience of the detection of pulmonary embolism with perfusion SPECT/CT.

**Material and methods:** Consecutive patients (N=81) suspected of pulmonary embolism from July 2010 to March 2011 were send to perfusion pulmonary scintigraphy in our hospital. PIOPED criterions were taken into account at the evaluation.

**Results:** In 58/81 cases, it was clearly low or high probability of pulmonary embolism, so naitve low-dose CT was not necessary. Based on SPECT/CT, in 6/23 cases it was a high probability -, and in 13/23 cases it was a low probability of pulmonary embolism. Only in 4/23 cases we found as medium probability of pulmonary embolism we suggested Dual-Energy CT.

**Conclusions:** Perfusion SPECT/CT was not sufficient to detect pulmonary embolism only in 4/81 cases. Taking into account the lower radiation exposure, whether perfusion SPECT/CT.

#### E54

## ASSESSMENT OF BRAIN ACTIVITY CHANGES IN LONG-TERM SPINAL CORD STIMULATION BY SPECT/CT AND MRI FUSED TECHNIQUE

K. Zámbó¹, G. Perlaki², G. Orsi², S. Komoly², T. Dóczi³, J. Janszky², N. Kovács², I. Balás³, M. Aradi³, Zs. Szabó¹, E. Schmidt¹

<sup>1</sup>Department of Nuclear Medicine, University of Pécs, Pécs, Hungary <sup>2</sup>Department of Neurology, University of Pécs, Pécs, Hungary <sup>3</sup>Department of Neurosurgery, University of Pécs, Pécs, Hungary

**Background:** The neurophysiologic mechanisms of action underlying spinal cord stimulation (SCS) and especially the long-term adaptive changes initiated by SCS remain obscure.

Material and methods: CT fused single photon emission computed tomography (SPECT/CT) with 99mTc-HM-PAO brain perfusion study was applied to clarify these changes. Nine patients (4 men and 5 women) with a SCS for chronic neuropathic pain (FBSS in 4 patients; CRPS in 5 patients) underwent SPECT/CT scanning after switching off the SCS for at least 1 day and after turning on the stimulation for at least 3 days. Relative changes in regional cerebral blood flow (rCBF) related to stimulation compared with non-stimulation were assessed using statistical methods.

**Results:** Significant rCBF increases were observed during SCS in the right inferior parietal lobulus, the right lateral occipital cortex, the right thalamus, bilaterally in cuneal cortex, the frontal pole, primary motor and somatosensory cortices. Relative decreases in rCBF were noticed in the right inferior temporal gyrus, bilaterally in anterior cingulate gyrus and cerebellum.

**Conclusion:** SCS modulated rCBF in brain areas known to be associated with nociception, pain or emotional assessment of pain.

#### E55

## THE ROLE OF ATTENUATION CORRECTION IN THE QUANTITATIVE EVALUATION OF DOPAMINE TRANSPORTER SPECT IMAGING

Zs. Besenyi<sup>1</sup>, N. Orosi<sup>2</sup>, T. Séra<sup>2</sup>, L. Pávics<sup>2</sup>

<sup>1</sup>Euromedic Hungary Ltd., Szeged, Hungary <sup>2</sup>SZTE Department of Nuclear Medicine, University of Szeged, Szeged, Hungary

Background: The aim of this study is to evaluate the effect of attenuation correction on the quantitative assessment of dopamin transporter brain SPECT. Material and methods: The results of 24 123-FP-beta-CIT SPECT studies were analysed. DAT SPECT-s of 12 healthy volunteers (4 males, 8 females, aged 25–51 years) and 12 depressed patients (1 male, 11 females, aged 20–56 years) were involved in the study. The injected doses were 185 MBq. The acquisition parameters included the step-and-shoot mode over 50 min, with 120 projection angles over 360° in a 128 × 128 matrix. 3D reconstruction was performed using a filtered backprojection (by means of the manufacturer's software), with a Butterworth filter (order 10, cut-off 0.61 cm-1). The SPECT images were reoriented in 3D and were further analysed with and without an automatic uniform Chang attenuation correction (cut-off 0.12 cm-1). On the transversal, reconstructed SPECT slices at the level of the basal ganglia, regions of interest were fixed (larger than 2 × FWHM of

the SPECT resolution) manually in the striatum bilaterally, and the occipital cortex was used as a reference for the non-specific binding site. The binding potential was estimated by the specific to non-specific activity ratio (S/NS, striatum/ occipital region). Each elliptical ROI was visually optimised to that of the actual structure in order to decrease partial volume effects. In the second group we repeated our ROI analysis for each subject without attenuation correction. In the next phase of our study on the reconstructed images, 3D VOI were fixed semi-automatically as well. The quantitative evaluation (S/NS determination) was performed on the corrected and uncorrected images in the same way. First, the images were spatially normalised in the Talariach space with SPM using a template. Then 3D masks were generated by WFU Pickatlas, and were used as a VOI, and Mathlab script calculated the average photon impact.

**Results:** From our ROI analysis in the first group (with correction), the S/NS ratio was 2.78 (1.63–4.26). In the second group (without correction), the S/NS ratio was 2.05 (1.46–3.2). Overall, the correlation between the two groups was significant, but the values displayed an individually large variation of p=0.02. However, after the 3D VOI analysis, these differences seemed less marked.

**Conclusion:** According to our data, the attenuation correction does indeed have an influence on the quantitative SPECT results of DAT scans. Hence it should be taken into account during the interpretation of DAT SPECT investigations.

#### E56

#### IMAGING EXPERIENCES IN NEURO-ONCOLOGY BASED ON 99 METHIONINE PET/CT, 91 MRI AND 50 FDG PET/CT FINDINGS

E. Nagy<sup>1</sup>, L. Novák<sup>2</sup>, J. Varga<sup>1</sup>, B. Szücs<sup>3</sup>, G. Fekete<sup>2</sup>, L. Galuska<sup>1</sup>

<sup>1</sup>Institute of Nuclear Medicine, University of Debrecen, Debrecen, Hungary <sup>2</sup>Department of Neurosurgery, University of Debrecen, Debrecen, Hungary <sup>3</sup>ScanoMed Ltd., Debrecen, Hungary

**Background:** More than a decade 11C-methionine (MET) PET is one of the diagnostic tools of brain tumors complementary to structural imaging methods. Although diagnostic performance of MET PET is well discussed, the

clinical impact of this technique on expected management of patients is not fully investigated. The aim of our retrospective study was to compare the diagnostic value of MET, FDG PET/CT (MET, FDG) and MRI in the detection of intracranial lesions. In addition, we evaluated the clinical impact of MET PET/CT on patient management.

Material and methods: MET, FDG and MRI findings were collected from PET/CT and Medsol data bases between 1 February 2007 and 20 January 2011 (average time interval from MET PET, 11 and 34 days). The diagnosis was confirmed either by histology or clinical follow-up applying additional follow-up imaging examinations (average follow-up time, 322 days). ROC-analyses were performed to assess the diagnostic efficacy of MET PET/CT and MRI. Neurosurgeons estimated the clinical impact of MET PET/CT using questionnaire.

Results: Altogether 115 MET, 58 FDG PET/CT and 101 MRI were assessed in 111 patients, 16 cases were excluded because of inconclusive clinical data. Therefore we analyzed 99 MET, 91 MRI and 50 FDG findings of 95 patients. 78 MET PET/CT scans of 74 patients with brain neoplasms were performed comprising 32 primary and 32 recurrent/rezidual neuroglial lesions as well as 14 other non neuroglial tumors. Sensitivity, specificity. positive and negative predictive values as well as accuracy of MET were 94%, 91%, 97%, 80% and 93%, whereas these values of MRI were 93%, 86%, 95%, 79% and 91% and that of FDG were 88%, 83%, 97%, 50% and 88%, respectively. The areas under the curve of MET and MRI were 0,916 and 0,922, respectively. Histological subgroup analyses revealed that the sensitivity of MET and MRI in gliomas including oligodendroglial component (oligodendrogliomas, oligoastrocytomas) was 95% and 86%, respectively, whereas in astrocytomas MET and MRI had 94% vs. 75% sensitivity. In grade II gliomas, the sensitivity of MET and MRI was 94% vs. 75%, respectively. Retrospectively, the clinical impact of MET PET/CT was estimated in 82 cases. Altogether the therapeutic management was changed after 62 examinations (76%), which implied the following options: treatment to watching, watching to treatment or change in treatment methods.

**Conclusion:** In conclusion, we can state that the diagnostic performance of both MET PET/CT and MRI are high in the detection of intracranial lesions. The diagnostic efficacy of MET is superior to MRI in cases of recurrent/residual and low grade tumors due to its typically increased amino acid transport and metabolism. Our study indicate that MET PET/CT might have major impact on patient management.



#### POSTER SESSION

#### **P1**

#### EFFICACY OF RADIOGUIDED SENTINEL LYMPH NODE **BIOPSY IN BREAST CANCER PATIENTS AFTER NEOADJUVANT THERAPY**

M. Lázár<sup>1</sup>, J. Pieler<sup>2</sup>, Zs. Simonka<sup>2</sup>, A. Paszt<sup>2</sup>, K. Ormándi<sup>1</sup>, Gy. Kelemen<sup>3</sup>, A. Vörös<sup>4</sup>, T. Séra<sup>1</sup>, Gy. Lázár<sup>2</sup>, Zs. Kahán<sup>3</sup>, A. Palkó<sup>5</sup>, B. Iványi<sup>4</sup>, L. Pávics<sup>6</sup>

<sup>1</sup>Euromedic Diagnostics Hungary Ltd., Szeged, Hungary <sup>2</sup>Department of Surgery, University of Szeged, Szeged, Hungary 3Department of Oncology, University of Szeged, Szeged, Hungary \*Department of Pathology, University of Szeged, Szeged, Hungary
Department of Radiology, University of Szeged, Szeged, Hungary <sup>6</sup>Department of Nuclear Medicine, University of Szeged, Szeged,

Background: The role of sentinel lymph node biopsy after neoadjuvant therapy is not fully justified, but according to some authors, it can be used in this patient group almost as efficiently as in patients with no such treatment. Our workgroup applied radiogiuded method for the localization of the former or residual tumour and/or for sentinel lymph node biopsy, but it did not show the usual effectiveness in terms of sentinel node detection, therefore we aimed to compare the efficacy of our method in this two (neoadjuvant treated and non-treated) patient groups.

Material and methods: We enrolled 23 patients treated with neoadjuvant therapy (20 chemotherapy, 3 hormone therapy) and 1114 patients without such treatment in the study. The radiopharmaceutical (99mTc-Senti-Scint, 150 MBq, 0,4 ml) was administered by ultrasound or rarely by X-ray guidance or by palpation intra- or peritumourally, or (in 9 cases) to the ring marker placed into the tumour before the initialization of neoadjuvant therapy. We performed gamma camera acquisition and sentinel node mapping (including skin marking) at least 3 hours after administration. The next day, during the operation sentinel lymph nodes were detected by intraoperative gamma probe and by blue staining.

Results: In the neoadjuvant treated group sentinel node had been detected by gamma camera in 26% (6/23) of patients, during the operation we could remove sentinel lymph node in 30% (7/23) by gamma probe detection and in further 9% (2/23) of patients by blue staining. In the non-treated group these ratios were 82% (912/1114), 87% (965/1114) and further 7% (76/1114) consequently. We could remove sentinel lymph node by gamma probe detection in all 3 patients treated with only neoadjuvant hormone therapy, and in 2 of them gamma camera acquisition was successful as well.

Conclusions: According to our results, radioguided sentinel lymph node biopsy after neoadjuvant chemotherapy is much less effective compared to the non-treated group, but in patients undergoing only neoadjuvant hormone treatment the efficacy of the technique seems to be not affected.

#### **P2**

#### LONG TERM VALIDATION OF SENTINEL NODE **TECHNIQUE IN MALIGNANT MELANOMA** MORE THAN FIVE-YEARS FOLLOW-UP

M. Papós $^{13}$ , J. Oláh², M. Lázár $^{13}$ , J. Varga², E. Varga², G. Mohos², E. Kis², I. Korom², T. Séra $^{13}$ , L. Kemény², L. Pávics $^{1}$ 

<sup>1</sup>Department of Nuclear Medicine, University of Szeged, Szeged,

<sup>2</sup> Department of Dermatology, University of Szeged, Szeged, Hungary ³Euromedic Diagnostics Ltd. Szeged, Hungary

Background: Radioguided sentinel lymph node (SN) biopsy in patients with malignant melanoma (MM) by now is a well accepted method however the validation of the method has to be proven on the basis of long-term follow-up. The aim of this study was to analyse the follow-up data of SN negative patients concerning to the later lymph node involvement.

Material and methods: Between September, 1999 and March, 2005 SN localisation was performed preoperatively by gamma-camera technique using 99mTc-nanocolloid (Senti-Scint), and intraoperatively with gamma-probe in 337 MM patients. In all cases the Breslow thickness of MM was more than 1 mm, or less than 1 mm, but grade Clark IV, or ulcerated or regressed, and clinically the lymph node stage was N0. The validity of the sentinel node biopsy was analyzed on the basis of the follow up of the lymph node status of the SN negative patients. The follow-up period was longer than 5 vears (61-127 months)

Results: SN was identified in 313 patients in one region and in 24 cases in more then one region. In 135 cases (40%) SN was MM positive, and in 202 patients (60%) MM free. More than 5-yers clinical follow up was performed in 152 SN negative cases. In this group the MM associated mortality was 10% (15/152). The survival rate with active disease in SN negative cases was 5% (8/152) and the other patients were clinically tumour free (85%, 129/152). During the clinical follow-up lymph node metastasis was detected in 5% (8/151, lymphatic status of one patient is actually unknown), therefore these cases were classified as false-negative concerning the SN biopsy.

Conclusion: The low false negative rate confirms the validity of SN biopsy technique.

#### **P3**

#### THE IMPORTANCE OF BONE SCINTIGRAPHY IN PATIENTS WITH MANDIBLE DISORDERS

Zs. Fejes<sup>1,2</sup>, M. Lázár<sup>1,2</sup>, L. Pávics<sup>1,2</sup>, E. Máté<sup>3</sup>, A. Végh<sup>4</sup>, J. Piffkó<sup>5</sup>

<sup>1</sup>Euromedic Diagnostics Hungary Ltd., Szeged, Hungary

<sup>2</sup>Department of Nuclear Medicine, Faculty of Medicine,

University of Szeged, Szeged, Hungary Faculty of Science and Informatics, University of Szeged, Szeged,

<sup>4</sup>Pal Heim Children's Hospital, Budapest, Hungary

<sup>5</sup>Department of Oral and Maxillofacial Surgery, Faculty of Medicine, University of Szeged, Szeged, Hungary

Background: In patients with mandible malformations it is important to estimate the degree of maturation and the accurate mapping of the metabolism of the mandible in order to choose appropriate therapy. To decide about these questions are burdened not only by the asymmetric growth of the mandible, but one should also take into account the patients' earlier dental interventions (e.g. orthodontia, tooth extraction etc.); that is it is vital to get an accurate knowledge of dental history. Our goal was to study the possible use of bone scintigraphy with 99mTc-HDP in patients with mandible growth disorders.

Material and methods: In three patients with mandible disorders (male, age: 17-21) bone scintigraphy (99mTc-HDP) was performed with SPECT and targeted planar images (AP, RLAT, LLAT). The relative activity of each region was determined from count/pixel of the ROI. Standard transversal slices of the SPECT scans were used for quantitative ROI analysis. The percentage was calculated using the following formula: (counts/pixel in interested region)/(counts/pixel in left ROI + counts/pixel in right ROI) X 100. The SPECT scan was considered abnormal if the difference of activity between the two ROIs was grater than 10%. Standard software (GE Infinia) and a special code (Ortopan) that were developed before for analysing the data of SPECT, were used to analyse the ROI.

Results: the tracer uptake of the mandible was diffusely, slightly higher than usual in all three patients, which was caused the not to completed growth of mandible and the ongoing orthodontia. The difference between the two sides of corpus mandibulae was 10% in one patient and in one case it was slightly higher than 10%, which was also associated with increased blood pool activity. We did not find differences between the condyles of

Conclusion: We can conclude that the quantitative analysis is important to get additional information.

**Abstracts** 

#### **P5**

### COMPARISON OF UNSPECIFIC BONE SCINTIGRAPHY FINDINGS AND THEIR RADIOGRAMS OR CT IMAGES

F Bat

Department of Nuclear Medicine, Kenézy Hospital, Debrecen, Hungary

**Background:** The aim of this study is to compare unspecific bone scintigraphy findings with their radiograms or CT images, as well as to process the outcomes, and to draw the conclusion.

**Material and methods:** This study was performed on 128 patients, 83 women and 45 men with a mean age of 63 years, who presented unspecific bone scintigraphy findings. All of them are oncological patients. We did the bone cintigraphy as screening, then I suggest selective conventional radiography to specify the etiology of the unspecific findings. I compare the radiological images with scintigrams.

**Results:** Significant part of unspecific findings are localised on the vertebral column (ca. 70%), and mostly the cause of these is degenerative disease (ca. 80%). Their smaller part are localised ont he ribs (ca. 20%), and mostly the cause of these is fracture (ca. 90%).

**Conclusion:** Common use of bone scintigraphy and radiological methods is increases the diagnostic accuracy. The study is shows the importance of the SPECT-CT in present-day nuclear medicine.

#### **P8**

## OPTIMIZATION OF THE IMAGE QUALITY OF MINIPET-II SCANNER BY AUTOMATED VERIFICATION PROCEDURE

S.A. Kis, G. Opposits, I. Lajtos, P. Mikecz, L. Balkay, L. Trón, M. Emri

Department of Nuclear Medicine, University of Debrecen, Debrecen, Hungary

**Background:** Our goal was to develop an automated image processing system with which the impact of new image reconstruction software components on image quality can be studied. Furthermore, we expect the system to be capable to monitor the imaging performance parameters of the MiniPET-II scanner, on a daily bases.

Material and methods: The developed verification software automatically processes the list mode MiniPET-II data acquired with NEMA NU-4 image quality phantom. The measurements are performed with the activity rate and time duration defined in the NEMA standard. On the one hand, reconstruction is carried out by the algorithms used in the everyday practice, the image quality parameters are determined through the methods of the NEMA NU-4 standard, and the quality parameters of each acquisition are stored in a database to provide a tool for the continuous monitoring of the MiniPET-II instrument. On the other hand the software is modular, therefore the reconstruction with new software components and the comparison of their performance to the standard methods can also be performed automatically on a given acquisition. The software is integrated into the MultiModal Medical Imaging (M3I) framework.

Results: As the result of the development we have developed a multipurpose image quality verification system. Using the software, we can check the temporal alternation of imaging ability of the MiniPET-II instrument, failures of the scanner can be detected. Furthermore, the impact of new reconstruction software components on the image performance parameters can be studied in an automated way. Thus, the efficiency of development, testing and verification of new algorithms is definitely improved.

**Conclusion:** We have created a database supported, multipurpose verification system, which enable the failures of the MiniPET-II scanner to be detected in a reliable way. Besides, the software speeds up the development of image reconstruction components in the M3I environment.

#### **P9**

## REGISTRATION OF LOW-DOSE AND DIAGNOSTIC CHEST CT SCANS BASED ON SKELETAL AND BRONCHUS SURFACE MODELS

T. Spisák, M. Koselák, G. Opposits, S. A. Kis, L. Galuska, M. Emri

Department of Nuclear Medicine, Medical and Health Science Center, University of Debrecen, Debrecen, Hungary

**Background:** For the postprocessing of clinical PET data acquired from PET/CT studies of the human chest in some cases it is necessary to produce the fusion of the diagnostic CT and PET images. Due to the various scanning protocols different CT scans of the same subject may represent different morphological states of the target area. This effect makes the comparison of diagnostic and low-dose CT scans complicated. The purpose of this work is to develop an intrasubject chest CT registration method based on skeletal and bronchus surface models.

**Material and methods:** For both the diagnostic and low-dose CT scans, dedicated algorithms were developed for segmenting the regions of sternum, backbone and bronchus. Former problems were solved by a simple intensity-threshold based procedure, latter was performed by a particular adaptive region growing algorithm. Using the surface models and landmark points retrieved from the segmented regions, a complex transformation and deformation method was constructed, which solves the problem of the CT registration accurately in the important regions. In areas being less relevant, the criterion of registration accuracy is weaker.

**Results:** The developed method enables the local nonlinear registration of the diagnostic and low-dose CT scan of the same subject. Due to the nature of the method, the accuracy of the registration is highest in the featured environment of the skeleton and bronchus. The PET/CT data of 3 subjects was used in the testing and development of the proposed approach. The clinical validation of the method is in progress within the confines of the institutional virtual bronchoscopy project.

**Conclusion:** One possible application of the elaborated registration method is the PET-assisted virtual bronchoscopy. The method according to the primary registration tests proved to be effective, however the clinical validation is still in progress.

#### P10

### INVESTIGATION OF SYNGENIC RODENT TUMOR MODELS USING MINIPET-II SCANNER

Gy. Trencsényi<sup>1</sup>, I. Lajtos<sup>1</sup>, F. Bakó<sup>1</sup>, I. Jószai<sup>1</sup>, L. Balkay<sup>1</sup>, M. Emri<sup>1</sup>, P. Kertai<sup>2</sup>, P. Mikecz<sup>1</sup>, L. Galuska<sup>1</sup>, T. Márián<sup>1</sup>

<sup>1</sup>Department of Nuclear Medicine, University of Debrecen, Debrecen, Hungary

<sup>2</sup>Department of Preventive Medicine, University of Debrecen, Debrecen, Hungary

**Background:** Earlier examinations showed, that carbohydrate and amino acid metabolism in cancer cells are more dynamic than in normal cells. To estimate the tumorogenic potential, the 18FDG uptake and expression of facilitative glucose transporters have been suggested. It is also well known that 11C-methionine is a useful radiotracer for the investigation of amino acid transport and metabolism in the living body. In our experiments, we wished to prove with MiniPET-II scanner that these radiotracers and modern PET imaging technics are useful tools to follow the growing of implanted tumor cells and metastases in different rodent models.

**Material and methods:** Rats were injected subcutaneously or intravenously with  $5 \times 106$  rat hepatocellular carcinoma (He/De) and myelomonocytic leukemia (My/De) cells. In other experiments  $5 \times 106$  He/De and My/De cells were placed under the left renal capsule by surgical procedure. After the implantation 18FDG and 11C-methionine scans were repeated at different time points. Control and tumor-bearing rats were injected *i.v.* with  $5.5 \pm 0.3$  MBg 18FDG or  $10.0 \pm 0.5$  (mean  $\pm$  SD) MBg 11C-methionine.

50 min (18FDG) and 30 min (11C-methionine) after tracer injection animal were anaesthetized by 3% isoflurane. 10 minutes PET scans were acquired in each bed positions using a small animal PET scanner (MiniPET-II, Department of Nuclear Medicine, Debrecen) to visualize the primary tumor and the metastasis. The MiniPET-II consists of 12 detector modules in one ring with LYSO scintillator crystal blocks. The axial and the radial field of view (FOV) are 48 mm and 106 mm, respectively and the system absolute sensitivity is 10.14% (NEMA-NU4 2008). The 18FDG and 11C-methionine uptake were expressed in terms of standardised uptake values (SUVs) and tumour to muscle (T/M) ratios.

**Results:** By taking the SUV values from the MiniPET-II images the majority of the radioactivity (18FDG and 11C-methionine) was accumulated in the primary tumors: He/De 18FDG-SUVmean:  $10.2\pm3.0$ , 11C-methionine-SUVmean:  $3.2\pm1.0$ ; My/De 18FDG-SUVmean:  $4.7\pm1.2$ , 11C-methionine-SUVmean:  $3.2\pm0.8$ . Two weeks after the implantation in rats bearing primary tumors under the renal capsule we found metastases at the parathymic lymph nodes (PTLN): He/De 18FDG-SUVmean:  $3.5\pm0.6$ , 11C-methionine-SUVmean:  $1.7\pm0.2$ ; My/De 18FDG-SUVmean:  $3.2\pm0.7$ , 11C-methionine-SUVmean:  $1.8\pm0.5$ . In the subcutaneous models after two weeks only primary tumors (He/De — SUVmean:  $9.0\pm2.6$ , My/De — SUVmean:  $9.0\pm2.6$ , and no metastases were found by 18FDG scans. Three weeks after intravenous injection of He/De cells metastatic lesions were found by 18FDG scans in the liver and lungs with SUVmean  $9.0\pm0.7$  and  $9.0\pm0.3$ 0. Tespectively.

**Conclusion:** This preclinical study showed that tumor cells implanted under the capsule of the kidney generate metastases in the PTLN. The renal capsule-parathymic lymph node complex seems to be suitable for the isolated *in vivo* examination of metastatic development. MiniPET-II scanner and the animal models are helpful appliances in preclinical research and drug development research.

#### P11

## DEVELOPMENT OF WEB TECHNOLOGY SUPPORTED MULTIMODAL IMAGE PROCESSING SERVICES AT THE UNIVERSITY OF DEBRECEN

L. Pohubi, G. Opposits, S. A. Kis, L. Trón, M. Emri

University of Debrecen, Medical School and Health Science Center, Debrecen, Hungary

**Background:** Our aim was to develop a web-based software environment that offers image processing services for our research partners, using the imaging infrastructure of the Institute of Nuclear Medicine. As important considerations we have defined ease of use, realization of automatic notification points in the co-operation process, centralized availability and management of information and state of data

Material and methods: The core of this service is the MultiModal Medical Imaging software system developed in the institute. Furthermore, database tools are provided on the R&D website (www.minipetct.hu) of our institute to manage the data flow and data states. The flexibility and scalability provided by the CMS (Content Management System) is utilized to generate the web pages dynamically. Analysis and modeling of the co-operation process and life cycle of the data packages had been performed. Points were identified in the process where the system notifies the participants via email. We have also examined the workflow of co-operation and identified the services that should be supported by web interface.

**Results:** As a result we can provide database supported image processing infrastructure for our partners that can be used effectively for research projects without advanced knowledge on the field of informatics. Our virtual bronchoscopy project is used to validate the web service and its infrastructure.

Conclusion: The web services provided for the clinical research projects and supported by the infrastructure developed in our institute simplifies the collaboration and increases its efficiency. Thus we can provide uniform communication system for our upcoming, long-term clinical projects with standardized image procession; the tasks can be performed in an efficient and controllable way.

#### P12

## METHODOLOGICAL DEVELOPMENTS FOR AUTOMATED REGION ANALYSIS OF BRAIN SPECT AND PET EXAMINATIONS

G. Opposits¹, T. Spisák¹, M. Koselák¹, L. Pohubi¹, L. Galuska¹, A. Jakab², E. Berényi², M. Emri¹

<sup>1</sup>Institute of Nuclear Medicine, Medical and Health Science Centre, University of Debrecen, Debrecen, Hungary <sup>2</sup>Department of Biomedical Laboratory and Imaging Science, Medical and Health Science Centre, University of Debrecen, Debrecen, Hungary

**Background:** The infrastructure for automated region analysis of brain PET and SPECT examinations was partly available in our institute, which was developed for image registration processes earlier. We broadened this automated process by software components, which were developed along the development of BrainLOC, made it possible to join these components to the automated image processing thread.

Materials and methods: We have used the MultiModal Medical Imaging software system to develop the main software components required by the automated regional analysis service: pre-defined functional and anatomical brain structures as part of the VOI database of the BrainLOC application;  $3^{\rm rd}$  party (MNI, FSL) and in-house developed mulimodal registration and standardization software; utilities for ROI analysis. We have also developed the DicomBBox software to receive and convert images, which is built on the basis of the DICOM server in our institute. Processing and monitoring services are available through the interfaces developed for the R + D web site of our institute.

**Results:** In contrast with our goals, a completely automated software system was developed to evaluate regional analysis of brain PET and SPECT data using arbitrary regional definitions of various brain atlases. The user requesting this service could select regions from more than 20 brain atlases and for spatial standardization T1-weighted MRI, PET or SPECT templates. The results of analysis carried out on the images received by our DICOM server can be accessed by email or through the web site of the institute. The standardization was carried out by the automated system.

**Conclusion:** We expanded the automated image processing in our institute with a service of automated region analysis of brain PET and SPECT examination. This service can be accessed by other institutes who does not have this kind of image processing infrastructure.

#### P13

## INTEGRATION OF PET-CT IN THE MANAGEMENT OF PATIENTS' TREATED WITH RADIOSURGERY: DEBRECEN'S EXPERIENCES

B. Szücs<sup>1</sup>, Zs. Hascsi<sup>1</sup>, J. Dobai<sup>2</sup>, L. Bognár<sup>2</sup>, I. Garai<sup>1</sup>

<sup>1</sup>ScanoMed Nuclear Medicine Centers, Debrecen, Hungary <sup>2</sup>Rotating Gamma Institute, Debrecen, Hungary

Background: The first hungarian gamma radiosurgery center was opened at 2007 in Debrecen. Until now 1500 patients have been treated. Radiosurgery is based on different imaging modalities that are used for targetting. In the currenct clinical practise we use contrast-enhanced CT and T1 weighted contrast-enhaced,3D SPGR MR sequences.We report our clinilcal experience with the combined use of metabolic (18F-FDG-PET-CT, 11C-MET-PET) and anatomic ( CT,MR ) images for the radiosurgical treatment of patients, to determine whether these imaging methods can be useful for further clinical management.

**Material and methods:** Four patients with brain metastases were treated with stereotactic radiosurgery. MRI and 11C-Met-PET examinations were done before the treatment and 2 and 6 months following the radiosurgical procedure. PET/MR fusions were also conducted. In the PET-scans we measured the size of the lesions and the tumor activity. Data was compared to the MRI findings. In one brain metastatic case radiosurgeons used 11C-MET-PET/contrast-enhanced CT fused images for treatment planning.

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In another case of recurrent nasopharyngeal carcinoma 18F-FDG-PET/MR fusion was used to determine the target.

**Results:** All PET-guided radiotherapy was succesful. Using fused images the delineation of viable tumor tissue was more accurate. All the four followed patients displayed good regression, decreased lesion size and tracer uptake. In one case we didn't find any metabolic activity in the treated metastases after 2 months following radiosurgical treatment. We compared our data to the MR-scans and it seemed to be useful in differentiation of radionecrossis from residual/recurrenct viable tumor tissue.

**Conclusion:** The integration of PET in radiosurgery provides additional information that opens new perspectives for the optimization of the treatment and follow-up stereotactically treated patients. Our results requires confirmation by further clinical study with larger patient group and a longer follow-up period.

#### P14

## THE EFFECT OF COMBINED TREATMENT BLOCKING P-GLYCOPROTEIN FUNCTION MEASURED USING MINIPET IN XENOGRAFT TUMOR MODEL

T. Márián¹, Gy. Trencsenyi¹, K. Goda², G. Szalóki², I. Juhász³, L. Vízkeleti⁴, A. Szöllösi⁵, I. Lajtos¹, P. Mikecz¹, Z. Krasznai², G. Szabó², Z.T. Krasznai⁶

<sup>1</sup>Department of Nuclear Medicine, University of Debrecen, Debrecen, Hungary

<sup>2</sup>Department of Biophysics and Cell Biology, University of Debrecen, Debrecen, Hungary

<sup>3</sup>Department of Dermatology, University of Debrecen, Debrecen, Hungary <sup>4</sup>Department of Preventive Medicine, University of Debrecen, Debrecen, Hungary

<sup>5</sup>Department of Physiology, University of Debrecen, Debrecen, Hungary <sup>6</sup>Department of Obstetrics and Gynecology, University of Debrecen, Debrecen, Hungary

Background: P-glycoprotein (Pgp) is one of the active efflux pumps that are able to extrude a large variety of chemotherapeutic drugs from the cells, causing multidrug resistance. It has been shown earlier that the combined application of a class of modulators used at low concentrations and UIC2 antibody is a novel, specific, and effective way of blocking P-glycoprotein (Pgp) function. *In vivo* study of this combined treatment was developed using xenograft multidrog resistant and sensitive human tumors model. The effect of this combined treatment by Pgp modulator and UIC2 antibody was monitored using MiniPET-II camera and tumor diagnostic PET tracers.

Material and methods: Female SCID mice were injected subcutaneously with KB-3-1 (Pgp negative) cells on the left and KB-V-1 (Pgp positive) cell on the right side. Four days after the injection mice were treated with doxorubicin (5 mg/kg, i.v.) combined with UIC2 monoclonal antibody (5 mg/kg, i.v.) and cyclosporine A (10 mg/kg, i.p.). After the implantation 18FDG/PET and 18F-FLT/PET scans were repeated at different time points. Control and tumor-bearing mice were injected i.v. with 5.5  $\pm$  0.2 MBg 18FDG or 18F-FLT. 40 min after tracer injection animal were anaesthetized by 3% isoflurane and 20 minutes PET scans were acquired using a small animal PET scanner to visualize the tumors. The 18FDG and 18F-FLT uptake were expressed in terms of standardised uptake values (SUVs) and tumour to muscle (T/M) ratios. Results: In the non-treated mice palpable tumors developed 4 days after the implantation. By taking the SUV values from the MiniPET-II images a higher 18F-FLT uptake was observed in the Pgp positive (SUVmean: 4; SUVmax: 5-7) than in the Pgp negative tumors (SUVmean: 3; SUVmax: 4). The FDG accumulation rate of the tumors showed a similar trend as FLT. In the Doxorubicin-UIC2-CSA treated group the regression of tumors was observed. The size of tumor, the accumulation rate of 18FDG and 18F-FLT was decreased significantly. In the KB-V-1 tumors high expression of Pgp was found by immunohistochemical analysis.

**Conclusion:** Combined treatment with UIC2 antibody and low concentrations of Pgp modulators effectively blocked the function of the Pgp pump in human epidermoid carcinoma tumors and this effect could be followed *in vivo* by using 18F-FLT and 18FDG tumor-diagnostic tracers and MiniPET-II camera.

#### P15

#### ISOLATION, DIFFERENTIATION AND RADIOLABELLING STUDIES OF CANINE ADIPOSE TISSUE DERIVED MESENCHYMAL STEM CELLS (CAD-MSC) — THE VERY PRELIMINARIES

V. Haász<sup>1</sup>, Z. Pöstényi<sup>1</sup>, A. Polyák<sup>1</sup>, P. Tátrai<sup>2</sup>, K. Németh<sup>2</sup>, F. Uher<sup>2</sup>, Gy. Janoki<sup>3</sup>, G. Janoki<sup>3</sup>, R. Török<sup>3</sup>, J. Thuróczy<sup>4</sup>, L. Balogh<sup>1</sup>

1"Frédéric Joliot-Curie" NRIRR, Budapest, Hungary

<sup>2</sup>National Blood Transfusion Service, Budapest, Hungary

<sup>3</sup>Radiopharmacy Lab. Ltd., Budaörs, Hungary

<sup>4</sup>Szent István University, Budapest, Hungary

**Background:** Dogs (Canis lupus familiaris) are a reliable model of human diseases in a wide variety of disorders. The autologous adipose-derived stem cell therapy (cAD-MSC) can be a promising new treatment in the field of regenerative medicine and tissue engineering for both human and veterinary medicine. Our aim was to develop stem cell therapy for veterinary patients suffering diseases and parallelly to prove the usefulness of canine model for human biomedical tasks.

Material and methods: The subcutaneous adipose tissue was harvested from the thoracic fat depots of Beagle dogs using standard sterile surgical procedures. The SVF (Stromal Vascular Fraction) was obtained by digestion with collagenase. Following centrifugation and washing of the pellet, cells were incubated in Dulbecco modified Eagle's medium (DMEM) supplemented with 10% Fetal Bovine Serum (FBS), in incubator supplied with humidified air and 5% CO2. Mesenchymal stem cells may also be represented in cell mixture. To evaluate this hypothesis the cells were successfully differentiated towards adipogenic, osteogenic and chondrogenic lineages. Moreover, FACS measurements are carried out to identify the expression of the appropriate cell surface markers. Radiolabelling (99mTc-HMPAO, Leuco-Scint® kit) method was performed following the producer's (Medi-Radiopharma Ltd) instructions.

**Results:** The adipose derived MSC cells — similarly to the human adipose derived cells — showed fibroblast-like morphology in light microscope. The phenotype of the isolated cAD-MSC was identified by detecting cell surface markers with flow cytometry (FACS); that is we successfully isolated canine adipose derived stem cells. The induced differentiation, further FACS measurements are in progress. Non-specific radiolabelling with 99mTc-HMPAO (Leuco-Scint®, Medi-Radiopharma Ltd.) resulted high labelling efficiency with retained functional abilities so that labelled MSCs are available for reinjecting and further SPECT/CT imaging.

**Conclusions:** Our preliminary results suggest that isolation-, identification-, differentiation- and radiolabelling of cAD-MSC are feasible. Canine adipose tissue represents an easily available source for veterinary stem cell therapies. Beside dog proved to be a promising biomedical model for evaluation of novel therapies such as applying stem cells.

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#### P16

### INVESTIGATION OF PGP PUMP FUNCTIONS WITH PET RADIOTRACER 11C-VERAPAMIL

P. Szabó¹, Gy. Trencsényi¹, T. Nagy¹, P. Mikecz¹, E. Németh¹, T. Miklovicz¹, I. Lajtos¹, Z.T. Krasznai², M. Emri¹, L. Galuska¹, T. Márián¹

<sup>1</sup>Institute of Nuclear Medicine

<sup>2</sup>Department of Obstetrics and Gynecology, University of Debrecen, Medical and Health Science Centre, Debrecen, Hungary

**Background:** Chemotherapy failure due to multidrug resistance (MDR) is a common problem in cancer treatment, because of the overexpression of the drug efflux pump P-glycoprotein (Pgp). Detection of the Pgp pump functions is an essential aspect in the treatment of cancer patients. The 11C-verapamil — substrate of the Pgp pump — could be a useful *in vivo* 

PET radiotracer. The Aim of our study was the evaluation of the uptake of the radiotracer 11C-verapamil in Pgp negative and Pgp positive cells. **Material and methods:** For *in vitro* study human epidermoid carcinoma KB-3.1 Pgp negative and KB-V-1 Pgp positive cell lines were used. The accumulation of the 11C-verapamil was measured by a calibrated gamma-counter. The Pgp functions were tested with rhodamine 123 by flow-cytometry. The pump functions were attested in an *in vivo* mouse model by MiniPET-II scanner.

Results: We found that 11C-verapamil accumulation were higher in Pgp negative than in Pgp positive cells. The accumulation was decreased in Pgp positive cells in a time dependent manner. The treatment with ciklosporin A (CSA) — which is a Pgp inhibitor — increased the 11C-verapamil uptake in Pgp positive cells but it did not modulate the uptake in Pgp negative cells. In the presence of verapamil the 11C-verapamil uptake was lower in both cell lines than that by the verapamil-untreated cells. Norverapamil — the precursor of 11C-verapamil — influenced the 11C-verapamil uptake in both Pgp positive and negative cells. 1  $\mu M$  Norverapamil treatment increased the uptake to 70% while incubation with 10  $\mu$ M norverapamil reduced 11C-verapamil uptake to 25%. The Pgp pump functions were studied in vivo by MiniPET-II scanner. The main function of the Pgp pump in the blood-brain barrier is to protect the brain against of the accumulation of toxic chemical agents. In our in vivo experiments by analysing the MiniPet-II images we found that there was no 11C-verapamil accumulation in the brain. When we inhibited the Pgp pump functions with CSA we measured an increased 11C-verapamil uptake in the brain.

**Conclusion:** From our measurements we concluded that 11C-verapamil can serve as a useful tool in *in vivo* and *in vitro* demonstration of Pgp pump functions.

#### P17

### [11C]CHOLINE SYNTHESIS WITH THE NEW SYNTHESIS MODULE

T. Miklovicz, E. Németh, D. Szikra, I. Jószai, L. Galuska, P. Mikecz

Department of Nuclear Medicine, University of Debrecen, Debrecen, Hungary

**Background:** [11C]Choline has been reported to be useful for the detection and differential diagnosis not only of prostate cancer, but also in case of brain tumors, lung cancer and esophageal cancer, whereas generally used [18F]FDG lacks of specificity or sensitivity. In order for [11C]Choline to become available for human PET investigation marketing authorization is needed from the National Institute of Pharmacy. For this purpose a new synthesis module has been created which is suitable for the aseptic production of [11C]Choline and the optimal parameters of the process were also investigated. With the new module we started to compile the registration documentation which will be submitted to the authority this year.

Material and methods: In our Institute [11C]Choline production was started many years ago for biological experiments. The synthesis module used was not suitable in aseptic conditions therefore a new module was created using the experience acquired during the development of the 11Cmethionine module. The quality of the materials used for the production were if possible of GMP standard pharmaceutical quality the production and dispensing were done in aseptic conditions. The 11CO2 content of the irradiated target gas was first converted into [11C]methyl iodide in a gas phase reaction and then it passed into the new module where the [11C]methyl iodide reacted with the precursor that had been loaded into a solid phase cartridge. The main goal of the solid phase method is that both the methylation of the precursor and the cleaning procedure take place on the solid phase cartridge and then the product was eluted. At the end of the process the isotonic solution was moved into the dispensing unit and dispensed into sterile vials. The process was simplified according to the literature and the optimal parameters were determined. The examination of the quality of the product can be found in the literature and in the Draft of [11C]Choline in the European Pharmacopeia. The radiochemical purity was measured by using the HPLC method: LiChrospher NH2 column, eluent MeCN/KH2PO4 pH:4 80/20, UV:205 nm. The chemical purity (precursor and ethanol content) was measured with gas chromatography: Carbowax amine column, sample/internal standard 20/1.

**Results:** It was found in the optimisation experiments that the precursor can be loaded into the system more easily (in the top of the cation exchange cartridge, without using a second cartridge). The amount of the precursor was decreased without the yield decreasing and the optimal reaction time was determined (2 minutes). The [11C]Choline yield with the new module was  $814\pm89$  MBq/ $\mu$ Ah (n = 9) in 18 minutes. The radiochemical purity was more than 98% in all experiments, the content of precursor and ethanol was below the set limits. **Conclusion:** [11C]Choline can be synthesised quickly and effectively with the new synthesis module. After the registration procedure [11C]Choline injection will be available for human PET investigation.

#### P18

## PET AND MR INVESTIGATION OF NOVEL SUPERPARAMAGNETIC NANOCOMPOSED CONTRAST AGENT

I. Hajdu<sup>,4</sup>, Gy. Trencsényi<sup>2</sup>, Zs. Csikós<sup>4</sup>, M. Emri<sup>2</sup>, Gy. Vámosi<sup>3</sup>, T. Márián<sup>2</sup>, M. Bodnár<sup>4</sup>, J. Borbély<sup>4</sup>, J. Kollár<sup>1</sup>

<sup>1</sup>Department of Radilogy, University of Debrecen, Debrecen, Hungary <sup>2</sup>Department of Nuclear Medicine, University of Debrecen, Debrecen, Hungary <sup>3</sup>Department of Biophysics and Cellbiology, University of Debrecen, Debrecen, Hungary

<sup>4</sup>BBS Nanotechnology Ltd., Debrecen, Hungary

Background: Non-invasive diagnostic tools, such as MRI (magnetic resonance imaging), CT (computer tomography) and PET (positron emission tomography) have become the most important methodologies in the field of medical diagnostics. In radiology, contrast means the difference between the darkest and lightest points of the image. In optimal case, contrast facilitates the diagnosis of different diseases, which could be enhanced using contrast agents. The aim of our research work was to develop a novel, tumor specific, nanocomposed superparamagnetic MR contrast agent using biocompatible, biodegradable, non-immunogenic macromolecules. Material and methods: Physico-chemical characterization was performed using dynamic light scattering, electron microscope and surface charge measurements. For in vitro experiments, tumor cells incubated with the nanoparticles were studied using confocal microscope and flow cytometer. In vivo experiments were performed on a Fischer rat model. A total of 5 × 106 HeDe (hepatocellular carcinoma) cells were placed under the left renal capsule of rat xenografts by surgical procedure. Nanoparticulate contrast agent was added intravenously to the rats on the 9th day after implantation. PET and MRI investigations were performed within 24 h after injection. When taking multimodal images PET measurement was performed right before MR scanning in anesthesia, placing the animal in a fixed position for both experiments. For PET investigations rats were injected i.v. with  $5.5 \pm 0.3$ MBq 18FDG. After one hour incubation 10-minute PET scans were acquired in each bed position using a small animal PET scanner.

Results: Targeted nanoparticles containing superparamagnetic iron oxide (SPION) were prepared, which could specifically accumulate in the tumor cells overexpressing folate receptors. These nanoparticles reduce the T2 relaxation time, change the signal intensity and cause considerable contrast enhancement. In our research work, SPION-loaded nanoparticles were prepared. First folic acid as targeting ligand was conjugated to the poly-gamma-glutamic acid (PGA) and then SPION was synthesized in the presence of this modified biopolymer. Stable nanoparticles were produced by self-assembly of the SPION-loaded PGA and chitosan. One of the main advantages of this system, that the biopolymers maintain their favorable biological properties due to the lack of new covalent bonds. Physico-chemical characterization of nanoparticles was performed by investigation of concentration and ratio of biopolymes, sequence of their mixing and the SPION concentration in the nanoparticles. The effect of the reaction conditions on the formation and parameters (e.g. surface charge, size, size distribution) of self-assembled nanoparticles was also studied. In vitro experiments were performed using several tumor cell lines, which overexpress folate receptors (e.g., HeLa, Jimt-1, A2780, AD2780, and HeDe). Confocal microscopic images show that the nanoparticles internalize into the targeted tumor cells, and accumulate in them. Flow cytometry results demonstrate that the selectivity of nanoparticles is about 100%, whereas the number of cells that do not contain nanoparticulate contrast agent is negligible. Cell suspensions treated with nanoparticulated contrast agent were measured **Abstracts** 

by MRI, and images clearly show a remarkable decrease of T2 relaxation time values as expected. These results confirmed that the targeted tumor cells internalize and accumulate the novel T2 contrast agent.

Conclusion: Based on the results, it can be established that the primary tumor and the metastasis could be visualized and fusion images of PET and MRI results could be made. The development of this contrast agent opens many opportunities for localization and early diagnosis of solid tumors.

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#### P19

#### PET/CT IMAGING IN DOGS AND CATS - THE FEASIBILITY AND RADIOTOXICOLOGICAL ASPECTS

Z. Pöstényi<sup>1</sup>, L. Balogh<sup>1</sup>, V. Haász<sup>1</sup>, A. Polyák<sup>1</sup>, T. Márián<sup>2</sup>, I Garai<sup>2</sup>, L. Galuska<sup>2</sup>, L. Balkay<sup>2</sup>, Gy. Trencsényi<sup>2</sup>, T. Nagy<sup>2</sup>, J. Trencsényi<sup>2</sup>, Gy. Janoki<sup>3</sup>, G. Janoki<sup>3</sup>, R. Török<sup>3</sup>, J. Thuróczy<sup>4</sup>

<sup>1</sup>National Research Inst. for Radiobiology and Radiohygiene, Budapest, Hungary

<sup>2</sup>Department of Nuclear Medicine, University of Debrecen, Debrecen,

3Radiopharmacy Ltd., Budaörs, Hungary

4Veterinary Faculty, Szt. I. University, Budapest, Hungary

Background: In this study we present an overview of the impact and advantages of PET/CT fusion imaging in the practice of veterinary oncology. FDG-PET imaging is useful and essential in disease staging, monitoring response to treatment, planning and choosing appropriate therapies, detecting recurrence and predicting prognosis.

Material and methods: Between December 2009 and February 2011 75 PET/CT examinations were performed in 60 referred client-owned dogs and cats in the Department of Nuclear Medicine, University of Debrecen. Pets were sedated and injected iv. with 18F-fluoro-deoxy-glucose (FDG) 15 MBg/bwkg and one hour later after the injection whole body fusion images were taken. We also collected blood samples from patients to check the haematological and biochemical parameters.

Results: A number of neoplastic diseases have been recognised in this study; include soft tissue sarcoma (16%), mastocytoma (11%), mammary tumours (10%), osteosarcoma (11%), lymphoma (3%) and squamous cell carcinoma (25%). In 6 cases we performed follow-up examinations to monitor response to treatment or to detect recurrence. Meanwhile the applied method proved to be well-tolerated in even late stage diseases. Conclusion: This diagnostic imaging technique is non-invasive and provides important information to veterinary clinicians and biomedical researchers. The relatively high incidence rate of some cancers, similar biological behaviour, large body size, comparable response to chemotherapeutic agents, shorter overall lifespan and shorter latency period are the factors that contribute to the advantages of the companion animals as a model for human neoplastic diseases.

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#### P20

#### TC-99M LABELED SELF-ASSEMBLED BIOPOLYMER BASED NANOPARTICLES FOR IMAGING RECEPTOR MEDIATED UPTAKE AND APPLICATION IN TUMOR DIAGNOSIS

A. Polyák<sup>1</sup>, I. Hajdu<sup>2</sup>, M. Bodnár<sup>2</sup>, Z. Pöstényi<sup>1</sup>, V. Haász<sup>1</sup>, G. Jánoki<sup>3</sup>, R. Török³, Gy. A. Jánoki⁴, L. Balogh¹, J. Borbély²

<sup>1</sup>National "F.J.C." Research Institute for Radiobiology and Radiohygiene (NRIRR), Budapest, Hungary

2BBS Nanotechnology Ltd., Debrecen, Hungary

3Radiopharmacy Laboratories Ltd., Budaörs, Hungary

<sup>4</sup>Medi-radiopharma Ltd., Budapest, Hungary

Background: A new biocompatible and biodegradable self-assembling nanoparticulate product was investigated as a potential new SPECT ima-

ging agent. Previously this new polyelectrolyte was investigated as a novel nanoscale drug carrier system and then presented as a new folate receptor targeting MRI contrast agent. In present study we examined possibility of application of these nanoparticles in SPECT imaging of folate receptor overexpressing tumors using technetium-99m. The aim of our preliminary in vitro and in vivo examinations was to verify that nanoparticles can labeled and followed up with Tc-99m with appropriate radiochemical stability, and they show the proper distribution according to their particle size and stability. Material and methods: Nanoparticles with a hydrodynamic size of 150 nm were prepared by self assembly. Particle sizes were measured by dynamic light scattering (Malvern Zetasizer Nano, Malvern Instruments) before and after labeling. SnCl2 was used to reduction of 900 MBq [Tc-99m] pertechnetate solution for labeling in 3 ml total volume. In vitro radiochemical purity was examined by thin layer chromatography (ITLC-SG developed in MEK and saline) up to 24 hours after labeling. Biodistribution values were determined by scintigraphic imaging studies in healthy Beagle dogs and Wistar rats. Images were taken by gamma camera at several times and organ uptakes were estimated by quantitative ROI analysis.

Results: Radiolabeled products showed high degree and durable labeling efficiency (99%) during 24h in vitro radiochemical stability follow-up. In vitro measured particle size distributions were stable before and after the labeling up to 24h. The in vivo biodistribution examinations of nanoparticles had close correlation to earlier described products which have similar particle size distributions. Images and calculated injected dose percentage values validated that in vivo radiolabeling efficiency and particle diameters were relative stable and constant after IV application. In the Beagle dogs and Wistar rats the injected labeled compound showed retained blood-background, liver, kidnevs, urinary bladder and slight bone-marrow uptake was seen in the scans. Conclusions: Our preliminary examinations verified that the self assembled nanoparticles are able to label and follow-up using technetium-99m isotope and gamma-camera. In our further examinations Tc-99m-radiolabeled nanoparticles were followed-up in folate receptor overexpressing tumor cell lines in biological experiments.

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#### P21

#### SYNTHESIS OF FLUORINE-18 LABELED RHODAMINE B: A POTENTIAL PET MYOCARDIAL PERFUSION IMAGING **AGENT**

L. Kárpáti, I. Kertész

Department of Nuclear Medicine, University of Debrecen, Debrecen. Hungary

Background: There is considerable interest in developing an 18F-labeled PET myocardial perfusion agent. Rhodamine dyes share several properties with 99mTc-MIBI, the most commonly used single-photon myocardial perfusion agent, suggesting that an 18F-labeled rhodamine dye might prove useful for this application. In addition being lipophilic cation, like 99mTc-MIBI, rhodamine dyes are known to accumulate in the myocardium and are substrates for Pgp, the protein implicated in MDR1 multidrug resistance. Fluorine-18-labeled rhodamine B was developed as a potential positron emission tomography (PET) tracer for the evaluation of myocardial perfusion. Material and methods: Rhodamine B was chosen as the prototype compound for development of the synthesis because the ethyl substituents on the amine moieties of rhodamine B protect them from side reactions, thus eliminating the need to include (and subsequently remove) protecting groups. The 2'-[18F] fluoroethyl ester of rhodamine B was synthesized by heating rhodamine B lactone with [18F] fluoroethyltosylate in 1-butyl-3-methylimidazolium tetrafluoroborate at 165°C for 15 min. [18F] fluoroethyltosylate was prepared by the reaction of ethyleneglycol ditosylate with Kryptofix 2.2.2, K2CO3, and [18F] in acetonitrile for 5 min at 80°C. The internal and the final product were purified by semi-preparative HPLC.

**Results:** We produced the 2'-[18F] fluoroethylester in > 98% radiochemical purity and a total synthesis time of 150 min.

**Conclusion:** The synthesized 18F-labeled rhodamine will be a promising candidate for more extensive evaluation as PET tracers for the evaluation of myocardial perfusion.

#### **P22**

#### SELECTIVE OH SCAVENGERS WITH HIGH KOH EFFECTIVELY STABILIZE [18F]FDG AGAINST RADIOLYSIS

I. Jószai, M. Svidró, N. Potári, P. Mikecz, L. Galuska

Department of Nuclear Medicine, University of Debrecen, Debrecen, Hungary

**Background:** The radiochemical purity of [18F]FDG at high radioactive concentrations decreases in time rapidly due to active species formed during the radiolysis of water. In this study we intended to clarify the effect of selective scavengers of hydroxyl radicals and hydrated electrons on the stability of [18F]FDG. Our goal was also to examine the stabilization effect of various salts, B-vitamins, sugars and amino acids, which are effective hydroxyl radical scavengers.

**Material and methods:** We studied the impact of stabilizers using 50–100  $\mu$ L of samples of [18F]FDG treated with reagents to the concentrations of 50 mmol/L. The initial radioactive concentrations of samples were approximately 2 GBq/ml. Both treated and untreated [18F]FDG samples were stored at room temperature (25°C). Stability was tested by analyzing the samples at appropriate time intervals. We determined the radiochemical purity of [18F]FDG samples by thin layer chromatography method: Merck TLC Silica gel 60, acetonitrile/water 95/5V/V%, 18F Rf = 0, [18F]FDG Rf = 0.45, Acetyl-[18F]FDG Rf = 0.65.

Results: We found that the radiochemical purity of the untreated [18F] FDG sample after 210 minutes decreased to 94.70%. In the presence of ammonium formate (selective hydroxyl radical scavenger) and sodium nitrate (selective scavenger of hydrated electrons) the radiochemical purities were 96.76% and 95.35%, respectively. On the other hand the [18F] FDG sample treated with the mixture of formate and nitrate had a purity of 96,13%. Consequently, selective hydroxyl radical scavengers are the most effective stabilizers for [18F]FDG. We also investigated the relationship between the effectiveness of stabilizers and the rate constants of their reactions with hydroxyl radicals (kOH). We found that the purity of samples treated with selective OH scavengers, namely with potassium iodide (kOH: 1.1·1010 L·mol-1·s-1), ethanol (kOH: 1.9·109 L·mol-1·s-1) and sodium acetate (kOH: 7.4·107 L·mol-1·s-1) were 98.90%, 98.74% and 97.96%, respectively. Consequently, the higher the kOH of the stabilizer the more effective for stabilizing [18F]FDG. In addition we found that several OH radical scavengers effectively suppress the radiolytic decomposition of [18F]FDG. For instance, the purity of samples treated with glucose, thiamine and methionine decreased with 1.5%.

**Conclusion:** Selective OH scavengers with high kOH should be chosen to effectively stabilize [18F]FDG against radiolysis. Among the examined stabilizers glucose could be ideal, as it meets the above mentioned requirements and there is no need for a new analytical method for its quantification, since the HPLC method recommended by the Ph. Eur.6.2 for the determination of radiochemical purity of [18F]FDG can be used for this purpose.

#### P23

#### EXAMINATIONS OF DIFFERENT SIZED DOXORUBICIN-LOADED NANOPARTICLES AND COLLOIDS

A. Polyák¹, Z. Pöstényi¹, V. Haász¹, G. Jánoki², R. Török², Gy. A. Jánoki³, L. Balogh¹

<sup>1</sup>National "F.J.C." Research Institute for Radiobiology and Radiohygiene (NRIRR) Budapest, Hungary

<sup>2</sup>Radiopharmacy Laboratories Ltd., Budaörs, Hungary

3Medi-radiopharma Ltd., Budapest, Hungary

**Background:** Nanoparticles represent promising drug carrier systems. In the case of cytostatics such as doxorubicin, carrier colloid nanoparticles may increase their therapeutical efficiency, decrease their side-effects (toxicity) and any potential multidrug resistance. In present study, doxorubicin,

as a widely used antineoplastic agent, was incorporated into the matrix of human serum albumin and three different particle-sized doxorubicin-loaded HSA nanoparticles were prepared. The three prepared colloids were labeled by technetium (Tc-99m) to *in vivo* examinations and they were tested for their physicochemical, colloidal quality, fluctuations and radiochemical stability. The aim of *in vivo* examinations was to verify that colloid carriers have right stability, insignificant size fluctuations after an intravenous application and they show the proper distribution according to their particle size.

Material and methods: Particle sizes and their stabilities, fluctuations were measured by dynamic light scattering and examinations were reinforced by TEM images. Radiochemical purity was examined by thin layer chromatography. Biodistributions of different-sized, radiolabeled colloids were determined by means of scintigraphic imaging studies in healthy male Wistar rats. Images were taken by gamma camera at several times and organ uptakes were estimated by quantitative ROI analysis.

Results: Non-adsorbed doxorubicin quota was checked and followed-up respectively, until 7 days after preparation and verified that more than 95% of doxorubicin proportion was permanently adsorbed to human serum albumin. Mean diameters of the prepared doxorubicin-loaded fractions were 180 nm, 430 nm and 1800 nm. Products were radiolabeled with Tc-99m with high-degree and durable labeling efficiency (99%) as in vitro radiochemical stability measurements demonstrated. Particle size was observed for 1 week. Each product showed a high degree of colloid size-stability: diameters and polydispersities of particle fractions were fluctuating within a relatively narrow range and changes were not unidirectional, nor trend-like. The in vivo biodistribution data of doxorubicin-loaded radiocolloids had a very close correlation to earlier described results. Images and calculated injected dose percentage values emphasized that directly post-injection, the greatest particle-sized compounds were located especially in the lungs and they slowly disaggregated. The smaller particle fractions were relocated mainly in the liver and they also had slow elimination.

**Conclusions:** Doxorubicin or different cytostatics loading in these nanoparticulate and colloid formulations can lead to an improvement of cancer therapy. Moreover the methods of nuclear medicine can provide useful possibilities for follow-up colloid carrier systems. Our examinations verified that manufacturing stable different sized HSA colloid carriers for cytostatics is possible. In addition different sizes of particles can raise the question of different application possibilities.

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#### P24

## PREPARATION OF HIGH SPECIFIC ACTIVITY 11C ISOTOPE LABELLED VERAPAMIL SUITABLE FOR BIOLOGICAL TESTING

E. Németh, T. Miklovicz, J. P. Szabó, T. Márián, L. Galuska, P. Mikecz

Nuclear Medicine Institute, University Medical School of Debrecen, Debrecen, Hungary

**Background:** 11C labelled tracer molecules are often used in PET examination. In most cases the labelling procedure is methylation with [11C] methyl-iodide reagent. In most cases the labelled compound used to the receptor investigations requires high specific activity, to avoid pharmacological effects. Objective: In this study our aim was the synthesis of 11C labelled verapamil with the most optimal parameters: high purity and specific activity. The verapamil is a calcium antagonist, what prevents Ca ions to diffuse across the membrane into the cell. In biological investigation it can be used for examination of multidrug resistance in the presence of Pgp pump.

**Material and methods:** The 11C radionuclide was produced by the 14N(p,  $\alpha$ )11C nuclear reaction and the PETtrace Mel MicroLab synthesis module manufactured by GE was used to synthesize [11C]CH3I, for methylation. In the literature different reaction parameters can be found, such as the amount of the precursor, solvent, temperature, HPLC method. We tried to find the optimum of these parameters in our system. In our work we prepared a process control panel which helps us to control the

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parameters of reaction and flow of materials from outside of the hot cell. The starting material was norverapamil, dissolved in it in acetonitrile. The [11C] CH3I bubbled (50 ml/min flow) in this solvent. The efficiency of the reaction was enhanced by using aluminium oxide/potassium-fluoride catalyst. The reaction mixture was heated for 10 minutes, when the reaction took place, then the reaction mixture was diluted with HPLC eluent and filtered from the catalyst. The generated [11C]verapamil was separated on preparative HPLC from other impurities and from the precursor. The collected fractions of [11C]verapamil was diluted with water and adsorbed on a C18 column. For elution small volume of ethanol was used to get concentrated solution, what later can be diluted with saline for biological investigation.

Results: In receptor binding studies the specific activity of [11C]verapamil is very important. In our experiments 100  $\pm$  20 GBg/ $\mu$ mol was achieved, with the radiochemical purity of more than 98%. We had got large problem the separation from the precursor, because it can reduce the acummulation of radioactive verapamil in cells. We had optimized the separation what resulted of greater purity of the product.

#### **P26**

#### **OVERWEIGHT IN DOGS AND IN HUMANS** - WHAT DIFFERS?

L. Müller<sup>1</sup>, E. Kollár<sup>1</sup>, Zs. Várnay<sup>1</sup>, J. Thuróczy<sup>1</sup>, L. Balogh<sup>2</sup>, Z. Pöstényi<sup>2</sup>, V. Haász<sup>2</sup>, A. Polyák<sup>2</sup>, T. Márián<sup>3</sup>, I. Garai<sup>3</sup>, L. Galuska<sup>3</sup>, L. Balkay<sup>3</sup>, Gy. Trencsényi<sup>3</sup>, T. Nagy<sup>3</sup>, J. Szabó<sup>3</sup>, Gy. Jánoki<sup>4</sup>, G. Jánoki<sup>4</sup>, R. Török<sup>4</sup>

<sup>1</sup>Veterinary Faculty, Szt. I. University, Budapest, Hungary

<sup>2</sup>National Research Inst. for Radiobiology and Radiohygiene, Budapest, Hungary

<sup>3</sup>Department of Nuclear Medicine, University of Debrecen, Debrecen, Hungary

4Radiopharmacy Ltd., Budaörs, Hungary

Background: Obesity is an enlarging problem is companion animals (dogs, cats) too similarly to the tendency observed in human population. Nowadays veterinary clinicians take a special emphasis to reach an early diagnosis and preceed in obesity diseases and metabolic disorders that develop as consequences. Parallely investigators often use the canine model in obes research based on genetical and physiological similarities. As in human beings also in dogs could be important to develop novel methods for measuring type-, and regionality obesitas, subcutaneous and visceral distribution of fat deposits. Not even in human obes patients is clear the distribution of fat in different deposits and their correlations to many metabolic disorders. However references are not perfectly consistent in the task, several data showed that quantity of abdominal fat deposits correlate closer with insulin resistency and insulin-resistency based metabolic disorders while subcutan fat sizes better correlate with serum leptin levels. In this present study we goaled to work-out a method available to examine the regional distribution of fat deposits and their metabolic effects in canine obes patients.

Material and methods: Suspected oncological patients altogether 25 dogs were underwent PET/CT whole body examinations and blood sampling for measuring the metabolic status. Following earlier published data we also choosed 2<sup>nd</sup>-3<sup>rd</sup> lumbal transversal slices to measure the subcutan fat diameter calculated the subcutan/visceral fat deposit rates too. Metabolic status was evaluated as follows: after 12 hours fasten glucose-, insulin-, thyroxin-, cortisol- and leptin levels were measured from serum samples. HOMA index was choosed to evaluate the level of insulin resistency in our patients. Results: Our data showed basic differences in regionality of fat deposits. Canine obes patients had either visceral or subcutan type-deposits where major part of fat stayed. Serum leptin levels varied between 0.4-20.1 ng/ml. Elevated serum leptin levels correlated closely with visceral fat deposit quantities but not with subcutan ones. HOMA-IR index did not showed correlation with regionality neither with total fat quantities. It is clear that dogs having visceral-type fat deposits insulin sensitivity is worse (HOMA-IR: 0.15-2.42), and insulin level is higher (0.66–11.65  $\mu$ U/ml). This tendency is higher (however not significantly) if we measure subcutaneous deposit at 3rd lumbal transversal images. Similar tendency (significant!) is seen in thyroxin levels (3.19–250 nmol/l) but in cortisol-, and leptin levels there is no correlation.

Conclusion: Further histopathological work to measure the fat cell sizes and leptin-receptor immunohistochemistry and blood chemistry is still ongoing for better understand the effects of fat deposit sizes and the regionality in doas.

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#### **P27**

#### INITIAL EXPERIENCES WITH MEDICHECK Q.C. KIT

T. Pásztor

Kenézy Hospital, Debrecen, Hungary

Background: The aim of the study was to look over the experiences with application of MEDICHECK Q. C. kit.

Material and methods: In the department prepared radiopharmaceuticals werre by a preliminary determined system examined.

Results: The examined radiofarmaceuticals generally fill regiurements. The study is under way, for this reason it is impossible to give numerical data. Conclusion: The MEDICHECK Q. C. kit seems an adequat tool in quality controll of radiofarmaceuticals.

#### **P28**

#### RADIOGUIDED LYMPH NODE BIOPSY OF A CHEMORESISTANT LYMPH NODE DETECTED ON INTERIM FDG PET-CT IN HODGKIN LYMPHOMA

T. Györke<sup>1,6</sup>, A. Kollár<sup>2</sup>, Gy. Bottlik<sup>3</sup>, Á. Szepesi<sup>4</sup>, I. Bodó<sup>5</sup>, T. Masszi<sup>5</sup>, V. Bérczi2, I. Garai6

<sup>1</sup>Department of Nuclear Medicine, Semmelweis University, Budapest, Hungary

<sup>2</sup>Department of Diagnostic Radiology and Oncotherapy, Semmelweis

University, Budapest, Hungary

Department of Dermatology, Dermatooncology and Venerology, Semmelweis University, Budapest, Hungary

<sup>41st</sup> Department of Pathology and Experimental Cancer Research,

Budapest, Hungary

5Department of Haematology and Stem Cell Transplantation, St. István and St. László Hospital of Budapest, Budapest, Hungary ScanoMed Ltd., Budapest, Hungary

Background: Interim FDG PET has high prognostic value in Hodgkin lymphoma and can detect early inadequate therapy response. Positive findings may require histological clarification for further therapy guidance. However nonpalpable lesions may be difficult to localise intraoperatively. This case report presents the successful surgical biopsy with the Radioguided Occult Lesion Localisation (ROLL) technique of a chemoresistant lymph node detected by interim FDG PET-CT.

Material and methods: A 32 years old male patient was diagnosed with nodular lymphocyte-predominant Hodgkin lymphoma. Staging FDG PET-CT detected large right axillary lymph node conglomerate and splenic manifestation. Interim PET-CT following two cycles of ABVD chemotherapy revealed good metabolic response with the exception of one single axillary lymph node. A second "interim" PET-CT after two further cycles had similar result. A biopsy of the metabolically active nonpalpable lymph node was performed by using the ROLL technique with ultrasound guidance.

Results: The lymph node was successfully removed with a minimal invasive procedure. Histological evaluation revealed a transformation into T cell rich diffuse large B cell lymphoma. Based on this finding a relevant therapy

Conclusion: The ROLL technique is an appropriate method for the biopsy of chemoresistant non palpable lymph nodes suspected by interim PET-CT. The anatomic information given by the CT part of the combined PET-CT method has great relevance for a multimodality approach i.e. ultrasound guidance during ROLL procedure.

#### P29

## PREOPERATIVE SCINTIGRAPHYC PARATHYROID GLAND LOCALISATION IN SECONDARY HYPERPARATHYROID PATIETS TREATED WITH DIALYSIS

L. Szabados<sup>1</sup>, L. Krakomperger<sup>2</sup>, Z. Tóth<sup>1</sup>, J. Mátyus<sup>2</sup>, I. Garai<sup>1</sup>

<sup>1</sup>ScanoMed Ltd, Debrecen, Debrecen, Hungary <sup>2</sup>1st Department of Internal Medicine, University of Debrecen, Debrecen, Hungary

**Background:** The most important pathology associated with chronic renal failure patients requiring dialysis is secondary hyperparathyreosis which sometimes need surgical treatment removing three and a half glands. The histological examination finds hyperplasia or adenoma in these hyperfunctioning glands. We aimed to locate the most normal parathyroid gland using parathyroid scintigraphy.

Material and methods: 36 patients with secondary hyperparathyreosis were examined before parathyroidectomy. 99m-Tc MIBI and pertechnetate subtraction was used. This method uses a reference ROI for proportional subtraction. Four ROIs were used as reference: thyroid tissue (thyroid gland without the parathyroid), whole thyroid gland and right and left lobes separately. We determined the mean counts per pixel in the regions of the parathyroid lobes and compared the results with the histological findings. Results: The least active gland in a certain patient had a 3% probability to contain adenoma. Considering a gland positive if the mean count per pixel is above 10 the sensitivity, specificity, NPV and PPV are 77%, 100%, 77% and 100% respectively.

**Conclusion:** The 99m-Tc MIBI-pertechnetate subtraction parathyroid scintigraphy is a very reliable tool to choose the one parathyroid lobe which must be retained. The best reference ROI for the proportional subtraction method is the thyroid gland without the parathyroid glands.

#### P31

### THE ROLE OF NUCLEAR MEDICINE IN THE DIAGNOSTICS OF DIABETIC FOOT

T. Pásztoi

Department of Nuclear Medicine, Kenézy Hospital Ltd., Debrecen, Hungary

**Background:** To present in basics literary facts and own experiences the role of nuclear medicine in the diagnostics of diabetic foot.

Material and methods: Scintigraphy with 99mTc-HMPAO labelled autolog leukocytes or immunscintigraphy.

**Results:** It was made in 10 years period 41 leukocytescintigraphy and 47 immunscintigraphy because of suspicion a muskuloskeletal disease, out of these in 3-3 cases was the probably diagnosis diabetic foot.

**Conclusion:** In the authors opinion — on basisc literary facts — it is needed more often nuclear methods to apply in the diagnostics of diabetic foot.

#### P32

## EVALUATION OF PATIENT DOSES RELATED TO THE NUCLEAR MEDICINE INVESTIGATIONS IN THE PAST 20 YEARS IN HUNGARY

T. Séra<sup>1</sup>, M. Papós<sup>1</sup>, S. Pellet<sup>2</sup>, L. Pávics<sup>1</sup>

<sup>1</sup>Department of Nuclear Medicine, University of Szeged, Szeged, Hungary <sup>2</sup>National Institute of Public Health, Budapest, Hungary

Background: International reports dealing with the exposure of the population to radiation from medical sources describe a continuous increase during recent years due to the increase in the number of medical investigations (CT scans, interventional radiological examinations, unnecessarily repeated investigations, etc.). The radiation protection scientific committees are making great efforts to assess the patient doses, to follow up the cases, and, if possible, to decrease these doses. The aim of our study was to evaluate the patient doses in nuclear medicine in Hungary in representative years during the past two decades.

**Material and methods:** For the calculation of the effective doses, we used the mSv/MBq values from the ICRP 53. Publication; the data relating to the different types of nuclear medicine examinations were provided by the Hungarian College of Nuclear Medicine and the National Registry.

**Results:** During the analysed years 1991, 1997, 2004, 2005, 2007 and 2009; the total number of investigations was 155682, 177208, 173385, 187184, 156534, and 171846, respectively, while the collective effective doses (man Sv) were 471, 1025, 1010, 1016, 812 and 835, respectively. The total numbers of bone, lung, brain, kidney, thyroid (between 2004 and 2009), inflammation and tumour investigations exhibited good correlations (R2 = 0.9) with the corresponding effective doses; for cardiology and gastroenterology, R2 was 0.6; and for all different types of examinations combined, R2 was 0.8. **Conclusions:** during the past 20 years, the patient doses in nuclear medicine in Hungary have varied in proportion to the total number of investigations and did not display a continuous increase.

#### P33

## THE IMPORTANCE OF RENOGRAPHY IN FOLLOWING OF RENAL TOXICITY CAUSED BY RADIOTHERAPY IN GASTRIC CANCER PATIENTS

Zs. Feies<sup>1,2</sup>, A. Maráz<sup>3</sup>, M. Lázár<sup>1,2</sup>, L. Pávics<sup>1,2</sup>

<sup>1</sup>Euromedic Diagnostics Hungary Ltd., Szeged, Hungary <sup>2</sup>Department of Nuclear Medicine, Faculty of Medicine, University of Szeged, Szeged, Hungary

<sup>3</sup>Department of Oncotherapy, Faculty of Medicine, University of Szeged, Szeged, Hungary

**Background:** Postoperative chemoradiotherapy in gastric cancer improves locoregional control and survival. Renal toxicity is one of the most serious complications in upper abdominal radiotherapy; we prospectively analyzed kidney function in patients, who underwent postoperative chemoradiotherapy for gastric cancer.

**Material and methods:** In 25 patients (age 39–81, average age: 61.4) renography was performed after the surgery, but before the postoperative chemoradiotherapy. In 20 patients the control renography was performed within 6–24 months, in 10 patients within 24–60 months after postoperative chemoradiotherapy. In 5 patients it was performed during both time intervals. The kidney in-damage to kidney in-safe (D/S) ratio was used as an index of the relative kidney function.

**Results:** for patients in the first group the D/S ratio decreased according to pre-radiotherapy investigation from 0.95 to 0.79 (p < 0.05). In the second group, where the control investigation were 24–60 month after the chemotherapy, the decline of D/S ratio was more significant, from 1.03 to 0.6 (p < 0.01).

**Conclusion:** The relative function impairment of the damaged kidney in patients after postoperative chemoradiotherapy for gastric cancer is demonstrated. In case of long survival, renography is recommended to monitor the state of the damaged kidney after years of radiotherapy.

#### P34

### PET-CT APPEARANCE OF RELEVANT RADIOLOGICAL PULMONARY FINDINGS IN PATIENTS WITH LYMPHOMA

N. Fedinecz<sup>1</sup>, S. Barna<sup>1</sup>, F. Magyari<sup>2</sup>, Zs. Miltenyi<sup>2</sup>, A. Illes<sup>2</sup>, I. Garai<sup>1</sup>

¹ScanoMed Nuclear Medicine Centers, Debrecen, Hungary ²3rd Department of Internal Medicine, University of Debrecen, Debrecen, Hungary

**Background:** Pulmonary abnormalities are not uncommon on 18FDG PET-CT in patients diagnosed with lymphoma and may often cause differential diagnostic problems. These abnormalities may represent manifestation of lymphoma, inflammation, other pathology or might be clinically irrelevant. The aim of our retrospective study was the evaluation of relevant pulmonary findings with a follow-up period of 1-24 months.

**Material and methods:** The analysis involved 1085 PET-CT examinations of 721 lymphoma patients. Pulmonary nodules smaller than 5 mm and fibrotic

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changes were regarded as radiologically irrelevant. A distinction was made between infiltrative and solid lesions based on their radiological appearance, and lesions were further characterised by their FDG-PET positivity. Differential diagnosis was made according to histology, clinical course of the disease, laboratory and microbiology results.

Results: Relevant radiological abnormalities were found in 116 patients (10.7%), of which 36 were diagnosed with Hodgkin (HL) and 80 with non-Hodgkin lymphoma (NHL). There were 45 infiltrative (8 FDG negative and 37 FDG positive) and 59 solid lesions (19 FDG negative and 40 FDG positive). Twelve patients were lost to follow-up. With regard to PET negative pathologies other than inflammation or lymphoma, there were 2 benign pulmonary nodules and interstitial lung disease was found in one case. Apart from the non-neoplastic cases, there were 2 primary lung tumours amongst the PET positive cases. The pulmonary manifestation of NHL was found to be solid PET-positive in all cases in our study, whereas infiltrative PET-positive finding was twice as common as the solid appearance in HL patients.

**Conclusions:** Our results draw attention to the different appearances of pulmonary manifestations of lymphoma, which can be very useful for the correct staging of the disease.

#### P35

### INEFFECTIVNESS OF BONE PAIN PALLIATION THERAPY WITH RADIONUCLIDES

S. Takács, Z. Nagy

Department of Nuclear Medicine, Hospital Irgalmasrendi, Budapest, Hungary

Department of Radiology, Zalaegerszeg Hospital

**Background:** We experienced a growing number of ineffective bone pain paliation therapy with radionuclides in the last years. We examined the reasons of this in a retrospective study.

**Material and methods:** In the last 8 years 191 patient with multiple bone metastasis were treated with radionuclides for pain palliation. We split the group in two parts: the first group results(135 patients) were reported in a study in 2007. The second group (51 patients) were treated in the last 3 years. The patients age: 21-87, average: 57,3 years, man: 85 women: 101. Treated tumor types: breast 73 (47 + 21), prostate: 71 (52 + 19), other: 47 (36 + 11). The applied radiopharmaceuticals: 80 - 153 Multibone 161 (125 + 36), Y-90 Multibone 161 (125 + 36), Y-90 Multibone 161 (125 + 36), Y-90 Multibone 161 (126 + 19), with repeated terapies if needed. The patients were questioned in detail about the pain scale, blood results and about the applied other oncological therapies and about the alternative methods which were widespread used in the last years: special diets, vitamins, flavins, Avemar, Culevit, water types, mushrooms. We compared the data of the first group patients with the data of the second group.

**Results:** In case of breast tumors previously in the first group 95% of patients became painless, in the second group 76% of patients became pain free. In case of prostate cancer the first result was: 85%, the second result: 78%. In the first group we did not found patients with increasing pain but in the second group 4% of patients with breast tumor and 8% of the patients with prostate cancer reported increase of the bone pain after radionuclide therapy. Analizing the patients with ineffective therapy we found the following results: out of 7 patients with breast tumor 5 had increasing pain, 2 were with constant pain, from the group of prostate cancer 4 had increasing pain, 2 were with constant pain. Out of 7 patient with breast tumor 2 rejected the chemotherapy, 3 rejected the bisphosphonate and hormone therapy. Out of patients with prostate cancer 2 rejected the hormone therapy and 4 the bisphosphonate therapy. 5 patients used only alternative therapy and 20% of patients used the alternative therapy in combination with the usual oncological protocols.

**Conclusions:** analyzing the results of the patients with bone palliation therapy with radionuclides we found an increasing number of ineffective pain palliation. According to our results the reason of this ineffective cases were that patients ignored the traditional oncological protocolls and there were a widespread use of the alternative methods.

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