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BELNUC LIEGE 2019 SYMPOSIUM: MED 01

Abstract category:
- Medical

Title:
Utility of baseline and interim volumetric ⁶⁸Ga-DOTATOC uptake parameters and inflammation-based index in neuroendocrine tumor patients treated with ⁹⁰Y-DOTATOC

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Abstract body:

Aim:
Peptide receptor radionuclide therapy (PRRT) is an evidence-based treatment for patients with inoperable/disseminated well-differentiated neuroendocrine tumors (NET) and will likely be more widely used in the future. Predictive tools to stratify patients will therefore become increasingly important. In this regard, we retrospectively investigated the utility of tumor uptake and tumor volume (TV) on pre-therapeutic and early interim ⁶⁸Ga-DOTATOC PET/CT, and a recently proposed biomarker for PRRT outcome prediction, the inflammation-based index (IBI), in NET patients treated with ⁹⁰Y-DOTATOC in the setting of a prospective phase II trial.

Materials and methods:
Forty-three NET patients received up to four cycles of 1.85 GBq/m²/cycle ⁹⁰Y-DOTATOC with a maximal kidney biologic effective dose of 37 Gy. All patients underwent a ⁶⁸Ga-DOTATOC PET/CT at baseline and seven weeks after the first PRRT cycle (interim PET). ⁶⁸Ga-DOTATOC-avid tumor lesions were semi-automatically delineated using a customized standardized uptake value (SUV) threshold-based approach. SUVmax, SUVmean and ⁶⁸Ga-DOTATOC-avid TV were determined for each scan. Baseline IBI was derived from serum C-reactive protein (CRP) and albumin values (score 0-2; 1 point for each abnormal parameter; CRP ≥10 mg/l, albumin ≤35 g/l). The primary endpoint was overall survival (OS). Kaplan-Meier survival curves with log-rank tests were used to compare different groups (quartiles for PET-derived values). Cox proportional hazards models were applied to estimate hazard ratios (HR) and 95% confidence intervals.

Results:
Median OS was 22.3 months (range: 3.0–97.4). A SUVmean higher than 14 (Q3) was associated with better survival (HR 0.45; p=0.024), while a TV higher than 578 ml (Q3) was associated with worse OS (HR 2.18; p=0.037). For SUVmax no significant correlations were found. An elevated baseline IBI was associated with worse OS (HR 3.90; p=0.001). Multivariate analysis corroborated independent associations between OS and SUVmean (p=0.016) and IBI (p=0.015). On interim PET, a significant decrease in SUVmax and SUVmean were observed (p<0.001), whereas TV remained unchanged. Survival analysis revealed that a decrease in SUVmean of more than 17% (Q3) was associated with worse survival (HR 2.29; p=0.024).

Conclusion:
Normal baseline IBI and high ⁶⁸Ga-DOTATOC tumor uptake (SUVmean>14) predict better outcome in NET patients treated with ⁹⁰Y-DOTATOC. Interim ⁶⁸Ga-DOTATOC PET did not allow to identify patients with poorer prognosis that would justify a change in treatment strategy.
Figure: Survival analysis according to baseline (A) inflammation-based index (IBI), (B) mean standardized uptake value (SUVmean) and (C) tumor volume, and (D) decrease in SUVmean between interim and baseline PET. HR: hazard ratio, CI: confidence interval.
Abstract category:
☒ Medical

Title:
A direct prospective comparison of [18F]FDG-PET and arterial spin labeling using simultaneous PET/MR in patients referred for differential diagnosis of dementia

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Abstract body:

Aim:
[18F]FDG-PET is an established tool to assist the clinical diagnosis and differentiation in the main forms of dementia syndromes, namely Alzheimer’s disease (AD), frontotemporal dementia (FTD), Lewy body dementia (LBD), and vascular dementia. Arterial spin labeling (ASL) magnetic resonance imaging has been proposed as practical alternative for measuring neural dysfunction. In this study, we directly compared [18F]FDG-PET to ASL in the accuracy for differential diagnosis of dementia in a clinical prospective set of patients referred for differentiation of a dementing disorder.

Materials and methods:
Twenty-seven consecutive patients (64.3±11.2 years, 14 M/13 F, MMSE 11-30) with suspected neurodegenerative dementia were referred for a clinical 30-min brain [18F]FDG-PET-CT scan. Subsequently all patients underwent a novel 20 min PET-MR scan, with additional acquisition of enhanced ASL images, on a simultaneous GE Signa PET-MR system. This group was compared to an age- and gender-matched control group of 30 carefully screened healthy controls (CON; 63.9±10.6 years; 14 M/16 F; MMSE 28-30; 40-60 min p.i static scan). [18F]FDG-PET and ASL images were compared by visual qualitative and semiquantitative volume-of-interest (VOI) analysis by two experienced nuclear medicine physicians. Voxel-based (t-test and 2nd level) analyses were performed to determine group differences in glucose metabolism and blood flow, and to investigate the differences in statistical sensitivity and pattern deduction for both techniques.

Results:
The working diagnosis for the patient group consisted of 8 AD, 2 FTD, 1 LBD, 1 multiple system atrophy of the cerebellar type, 1 motor neuron disorder, 1 traumatic brain injury and 13 patients with no clear pre-PET arguments for a neurodegenerative cause for the cognitive complaints. The visual analysis resulted in equal specificity (0.70) for differentiating normal and abnormal images between the two modalities, but in a higher sensitivity and confidence rating of the readers for FDG-PET (0.87) compared to ASL (0.60). Both VOI- and voxel-based analyses revealed reduced regional and quantitative hypometabolism and hypoperfusion between CON and the patient group, although the pattern was more pronounced with FDG-PET (pFWE<0.05 at cluster level) (Figure 1) and assessable on each individual patient.

Conclusion:
Overall, in a direct head-to-head comparison, FDG-PET has higher accuracy and confidence when differentiating patients referred for potential neurodegenerative causes, both visually as well as semiquantitatively (larger effect size).
Figure: Results of the voxel-based (SPM) group comparison for AD and FTD versus CON with FDG-PET (at left) and ASL images (at right), at cluster level of PFWE-corrected<0.05, with a peak height threshold of pheight<0.01, extent threshold of 20 voxels.
Title: Head-to-head comparison between DAT \([^{123}\text{I}]\text{FP-CIT SPECT}\) and \([^{18}\text{F}]\text{FE-PE2I PET}\) in Parkinson’s disease

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Abstract body:

Aim:
Dopamine transporter (DAT) SPECT imaging with \([^{123}\text{I}]\text{FP-CIT}\) is widely used in the diagnostic work-up of clinically uncertain parkinsonian syndromes. \([^{18}\text{F}]\text{FE-PE2I}\) is a recently developed PET radioligand with equal affinity but much higher (>1000-fold) DAT selectivity\textsuperscript{1}. Apart from improved spatial resolution (PET), \([^{18}\text{F}]\text{FE-PE2I}\) also shows fast kinetics allowing short static \([^{18}\text{F}]\text{FE-PE2I}\) imaging protocol within the hour after injection. Here, we compared discriminatory power and effect size (ES) of \([^{18}\text{F}]\text{FE-PE2I}\) PET versus \([^{123}\text{I}]\text{FP-CIT}\) in early Parkinson’s disease (PD).

Materials and methods:
Twelve PD patients (64.2±7.0y, 7F, motor UPDRS: 20.8±9.3 (medication on n=9, off n=3), H&Y stage I/II) and 23 HV (57.7±9.7y, 16F) were scanned with 150 MBq \([^{18}\text{F}]\text{FE-PE2I}\) on a GE Signa PET/MR. Static PET data (50-60 min postinjection) were reconstructed using OSEM (28 subsets, 4 iterations) and Zero-Echo Time (ZTE)-based attenuation maps. PD patients had also undergone clinical \([^{123}\text{I}]\text{FP-CIT}\) on GE-Discovery SPECT-CT (time interval : 6.6±3.6 months, range 1.6-13.0; injected activity 185 MBq). Additionally, in 16 historical HV (53.5±16.8y, 9F) \([^{123}\text{I}]\text{FP-CIT}\) was performed on similar dual-head SPECT (E-CAM, Siemens). SPECT data were reconstructed with identical parameters (OSEM, 5x8/1x4/1x2/1x1 iterations x subsets, with uniform attenuation 0.15/cm). Spatial normalization and identical VOI delineation was performed in PMOD v3.7 using individual structural MRIs. An occipital VOI centered in the midtransverse plane was used as reference region to calculate BPND(= SUVR-1) values. In case of lateralized clinical motor function, images were flipped to the left as most affected side. ES was calculated as ((meanHV–meanPD)/SDHV). Correlations were assessed using Spearman’s r. The discriminative diagnostic power of both tracers was investigated using receiver operating characteristics (ROC).

Results:
Contralateral putamen binding in PD was 29.4±16.0 % decreased compared to HV for \([^{123}\text{I}]\text{FP-CIT}\) and 51.7±21.0% for \([^{18}\text{F}]\text{FE-PE2I}\). Substantia nigra \([^{18}\text{F}]\text{FE-PE2I}\) binding was decreased 12.7±11.1% in PD compared to HV. ES for contralateral putamen, striatum and caudate were 1.6, 2.1 and 1.7 for \([^{123}\text{I}]\text{FP-CIT}\) and 3.1, 2.5 and 1.4 for \([^{18}\text{F}]\text{FE-PE2I}\). The decreases in \([^{123}\text{I}]\text{FP-CIT}\) and \([^{18}\text{F}]\text{FE-PE2I}\) binding for contralateral putamen, striatum and caudate were significantly correlated, with Π=0.87, 0.91 and 0.72. ROC analysis showed an accuracy of 0.87 for \([^{123}\text{I}]\text{FP-CIT}\) and 0.95 for \([^{18}\text{F}]\text{FE-PE2I}\) for contralateral putamen binding.

Conclusion:
High diagnostic correspondence was observed between \([^{18}\text{F}]\text{FE-PE2I}\) and \([^{123}\text{I}]\text{FP-CIT}\), but \([^{18}\text{F}]\text{FE-PE2I}\) outperforms \([^{123}\text{I}]\text{FP-CIT}\) in ES and diagnostic accuracy and allows SN DAT assessment. Overall, \([^{18}\text{F}]\text{FE-PE2I}\) is highly promising for early assessment of DAT binding in PD, on an improved patient friendly basis (faster kinetics, shorter scan duration) and superior image quality.

\textsuperscript{1}Jakobsen Mo\textit{S.} et al. EJNMMIRes2018.
Figure 1: $^{[123]}$I-FP-CIT (upper row) and $^{[18F]}$FE-PE2I (lower row) images of a 67 y old Parkinson’s Disease (PD) patient (Hoehn and Yahr 2), and healthy volunteers (HV) (45 y old for $^{[123]}$I-FP-CIT, 52 y old for $^{[18F]}$FE-PE2I). Images in radiological orientation. The red arrow points to the uptake in the substantia nigra.
Title: Personalised selective internal radiation therapy improves overall survival in unresectable and refractory intra-hepatic cholangiocarcinoma: a European multicenter study

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Abstract body:

Aim
In refractory intra-hepatic-Cholangiocarcinoma (IH-CCA) patients treated with selective-internal-radiation-therapy (SIRT), contrasting results enlightens the lack of prognostic/predictive biomarkers for patient stratification and treatment optimization.

This study aim was firstly to determine predictive value of pretherapeutic clinical, biological and imaging biomarkers of unresectable and refractory IH-CCA patients treated with SIRT, and secondly to compare treatment efficacy using partition-model (PM) over standard and widely used Body-Surface-Area (BSA) method for calculating the 90Y-microspheres activity to administer.

Materials and methods
This retrospective multicenter study enrolled 58 IH-CCA patients, refractory to surgery and/or chemotherapy, treated with resin 90Y-microsphere, in 4 European SIRT expert centers. Clinicopathologic data were collected from patient’s records. Metabolic parameters as well as presence of hypermetabolic-lymph-nodes were measured at baseline FDG-PET/CT. Lesions were delineated on baseline FDG-PET/CT and then projected on the anatomically registered 99mTc-MAA-SPECT/CT. MAA lesion to non-tumoral-liver uptake ratio (TLRMAA) was computed for each lesion. Univariate associations between variables and OS were examined by the log rank test. Continuous variables were dichotomized by using their respective median as cut-off value. Multivariate Cox’s proportional hazards model was then performed to determine the independent predictive significance of each parameter.

Results
Median OS post-SIRT of the entire cohort was 10.3 months. Biomarkers associated with significant differences in terms of OS were albumin (median-OS=15.1 vs 6.6 months, hazard-ratio(HR)=2.78, p=0.002), total-bilirubin (median-OS=14.9 vs 7.2 months, HR=2.17, p=0.009), aspartate-aminotransferase (median-OS=15.1 vs 5.9 months, HR=2.96, p<0.001), alanine-aminotransferase (median-OS=12.5 vs 9.4 months, HR=2.02, p=0.01) and γ-GT (median-OS=15.1 vs 5.2 months, HR=2.61, p<0.001). Absence of hypermetabolic-lymph-nodes was associated to a longer OS (median-OS=14.9 vs 5.5 months, HR=2.35, p=0.008), as well as a TLRMAA≥1.87 (median-OS=14.9 vs 5.5 months, HR=2.92, p=0.009). No other metabolic parameters were found to be associated with OS. Finally, OS was significantly higher in patients treated according to PM (median-OS=14.9 vs 5.5 months, HR=2.52, p<0.001).

Conclusion
In unresectable and refractory IH-CCA patient treated with SIRT several baseline biological biomarkers could be used for patient stratification (Total-Bilirubin, Aspartate aminotransferase and γ-GT). Importantly, 90Y-microsphere activity to administer should be determined using a more personalised approach: Partition-Model instead of BSA-method, as our study demonstrated that personalised SIRT improved outcome.
Abstract

Aim
In refractory intra-hepatic Cholangiocarcinoma (IH-CCA) patients treated with selective internal radiation therapy (SIRT), contrasting results enlighten the lack of prognostic/predictive biomarkers for patient stratification and treatment optimization.

This study aimed to determine the predictive value of pretherapeutic clinical, biological, and imaging biomarkers of unresectable and refractory IH-CCA patients treated with SIRT, and secondly to compare treatment efficacy using partition-model (PM) over standard and widely used Body-Surface-Area (BSA) method for calculating the 90Y-microspheres activity to administer.

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Median OS post-SIRT of the entire cohort was 10.3 months. Biomarkers associated with significant differences in terms of OS were albumin (median-OS=15.1 vs 6.6 months, hazard ratio (HR)=2.78, p=0.002), total bilirubin (median-OS=14.9 vs 7.2 months, HR=2.17, p=0.009), aspartate aminotransferase (median-OS=15.1 vs 5.9 months, HR=2.96, p<0.001), alanine aminotransferase (median-OS=12.5 vs 9.4 months, HR=2.02, p=0.01) and γ-GT (median-OS=15.1 vs 5.2 months, HR=2.61, p<0.001). Absence of hypermetabolic lymph nodes was associated with a longer OS (median-OS=14.9 vs 5.5 months, HR=2.35, p=0.008), as well as a TLRMAA≥1.87 (median-OS=14.9 vs 5.5 months, HR=2.92, p=0.009). No other metabolic parameters were found to be associated with OS.

Finally, OS was significantly higher in patients treated according to PM (median-OS=14.9 vs 5.5 months, HR=2.52, p<0.001). Multivariate analysis showed that Total-Bilirubin, Aspartate aminotransferase, and γ-GT were statistically significant with p of 0.03, 0.006, and 0.01 respectively. Statistical significance of the method of calculation of individual activity was also retained, even after adjustment for standard biological parameters (Total-Bilirubin, Aspartate aminotransferase and γ-GT) with HR=2.26 and p=0.03.

Conclusion
In unresectable and refractory IH-CCA patients treated with SIRT, several baseline biological biomarkers can be used for patient stratification (Total-Bilirubin, Aspartate aminotransferase, and γ-GT). Importantly, 90Y-microsphere activity to administer should be determined using a more personalized approach: Partition-Model instead of BSA-method, as our study demonstrated that personalized SIRT improves outcome.

Figure 1. OS curves estimated by the Kaplan-Meier method stratified by absence or presence of hypermetabolic lymph nodes (A), TLRMAA (B) and the calculation of individual activity method (BSA vs. PM) (C).
Title: Lowering threshold to 15% for early metabolic response assessment using 18F-FDG PET/CT in metastatic colorectal cancer: results from prospective studies with external validation cohort.

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Abstract body:
Aim: Assessing the 15% response threshold for early metabolic response in large development and validation cohorts of metastatic colorectal cancer (mCRC) patients treated with multikinase inhibitors or chemotherapy.

Materials and Methods:
The development cohort included 224 chemorefractory mCRC patients enrolled in two prospective multicenter non-randomized trials evaluating sorafenib/regorafenib as last line therapy. The validation cohort included 122 mCRC patients from another center treated with chemotherapy and bevacizumab as first line. 216/224 and 102/122 patients were analyzed. Standardized baseline and early 18F-FDG PET/CT scans were performed within 2 weeks before treatment and 2-3 weeks after the beginning of the therapy. EORTC criteria (15% threshold), PERCIST (with 15 and 30% thresholds), and CONSIST method (non-responder patient identified when at least one target lesion showed no significant decrease of SUVmax (<15%) were tested. Univariate analyses for overall survival (OS) were performed to assess the predictive values of these different response criteria and multivariate analyses to assess their prognostic independency along with well-known clinical factors (i.e. age, gender, BMI, ECOG performance status, time since diagnosis, previous use of bevacizumab, KRAS mutation, and use of sorafenib vs. regorafenib).

Results:
In the development cohort, univariate analyses showed that early 18F-FDG PET/CT response was strongly related to outcome whatever the criteria used (HR: 1.65, P < 0.001 for CONSIST 15%; HR: 1.48, P = 0.005 for PERCIST with 15% threshold and HR: 1.48, P = 0.006 for PERCIST 30%). Early 18F-FDG PET/CT response was identified by multivariate analyses as independent predictor of OS along with clinical factors for the different response criteria (HR: 1.62, P = 0.001 for CONSIST 15%; HR: 1.45, P = 0.01 for PERCIST 15%; and, HR: 1.44, P = 0.02 for PERCIST 30%). In the validation cohort, only early 18F-FDG PET/CT response using the 15% threshold was confirmed to be strongly related to outcome (HR: 2.05, P = 0.002 for CONSIST 15%; HR: 2.08, P = 0.003 for EORTC 15%; and, HR: 2.13, P = 0.002 for PERCIST 15%). PERCIST with 30% threshold was not significantly related to outcome (HR: 1.55, P = 0.055).

Conclusion:
This prospective study based on a development and a validation cohort validates the strong predictive value of early 18F-FDG PET/CT response for OS in mCRC patients treated with different treatment modalities. A lowered metabolic response threshold of 15% was validated as the most appropriate method for OS prediction in a setting of early metabolic response assessment.
Figure: Survival curves with a different median OS for responder and non-responder patients of the validation cohort identified by the early ¹⁸F-FDG PET/CT response assessment using CONSIST method with a 15% threshold.
Title: Comparative dosimetry between 99mTc-MAA SPECT/CT and 90Y PET/CT in primary and metastatic liver tumours.

Authors (name and surname) and affiliation number (presenter author underlined):
Alexandre Jadoul1 MD, Claire Bernard1 Ir, Pierre Lovinfosse1 MD PhD, Laurent Gérard2 MD, Henri Lillet1 MD, Olivier Cornet2 MD, Roland Hustinx1 MD PhD

Authors affiliation:
1. Division of Nuclear Medicine and oncological imaging, University Hospital of Liege, Belgium
2. Division of Radiology, University Hospital of Liege, Belgium

Abstract body:

Introduction
The aim of this study is to determine whether 99mTc-MAA SPECT/CT-based dosimetry could predict the actual absorbed dose in hepatocellular carcinoma (HCC) or liver metastases, treated by glass or resin microspheres.

Material and methods
Fifty-seven patients who underwent selective internal radiation therapy (SIRT) were retrospectively included in the study, for a total of 59 treatments. Nineteen HCC were treated by resin microspheres (HCC-SIR), 20 HCC with glass microspheres (HCC-Thera) and 20 liver metastases with resin microspheres (Metastases-SIR). The mean absorbed doses in tumoral liver (Dm) and non-tumoral liver (DmNTL) were determined on the 99mTc-MAA SPECT/CT and the 90Y PET/CT, and compared to each other.

Results
DmNTL was <50Gy in the 3 groups, with a strong correlation in all population, albeit slightly lower in Metastases-SIR than HCC-SIR and HCC-Thera (ICC: 0.81, 0.94 and 0.96, respectively). In tumoral liver, Dm was higher in HCC than metastases (159±117Gy versus 63±31Gy). 99mTc-MAA SPECT/CT proved to be a better indicator of Dm in HCC compared to metastases, with similar 99mTc-MAA-90Y concordance in resin and glass microspheres (ICC HCC-SIR: 0.82, ICC HCC-Thera: 0.83 and ICC Metastases-SIR: 0.52).

Conclusion
99mTc-MAA SPECT/CT is a reliable tool for predicting the dose to the non-tumoral liver in both HCC and metastases, regardless of the type of microspheres. It is also highly reliable for predicting the tumor dose in HCC, again regardless of the type of spheres.
Figure: Correlation of mean doses in non-tumoral liver (left column) and in tumoral lesions (right column) between $^{99m}$Tc-MAA (Dm NTL MAA) and $^{90}$Y (Dm NTL Y90). The red line depicts the perfect concordance and the dotted line represents the observed regression line.
Title:
The differentiation of low- and high-grade gliomas using PET- and MRI-derived \([^{18}F]\)FET PET parameters

Authors (name and surname) and affiliation number:
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Authors affiliation:
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Abstract body:

Aim
Gliomas are the most frequent malignant primary brain tumours in adults and can be classified into either low-grade gliomas (LGG, WHO grades I-II) or high-grade gliomas (HGG, WHO grades III-IV). The overall survival rate of HGG is poor (several months) when compared with LGG (years). This distinction makes an accurate and early diagnosis, for which histopathology is the gold standard, of utmost importance to determine the optimal treatment procedure(s). However, biopsy and resection present certain risks, which ought to be avoided when possible, and since histopathological tumour evaluation is prone to bias due to tumour heterogeneity and observer variability, there is an increasing interest in non-invasive diagnostic methods to support preoperative treatment planning. In this retrospective cohort study, the role of different positron-emission tomography (PET)-based, and magnetic resonance imaging (MRI)-based O-(2-[18F]fluoroethyl)-L-tyrosine (\([^{18}F]\)FET) PET parameters in discriminating HGG from LGG was investigated.

Materials and methods
A pre-treatment \([^{18}F]\)FET PET scan and an anatomical MRI were performed in 30 patients (14 LGG and 16 HGG). Twenty-four PET-derived parameters, e.g. metabolic tumour volume (MTV), total lesion uptake (TLU) and tumour-to-background ratio (TBR), were calculated using various standardized uptake value (SUV) thresholds. Subsequently, an in-house developed and segmentation algorithm was used to label different tissue categories on both contrast-enhanced T1-weighted and FLAIR MR images: necrosis (N), oedema (OE), non-enhancing tumour (NET) and contrast-enhancing tumour (CET). MR-derived tumour masks were applied to the PET images to calculate 55 PET parameters. PET- and MR-derived PET parameters were compared between HGG and LGG. Significantly different parameters were analysed by receiver-operating characteristics (ROC) analysis, yielding area under the curve (AUC) values. Pathological diagnosis served as the reference.

Results
Significant differences between HGG and LGG were found for 13 out of 24 and 17 out of 55 parameters for respectively the PET- and MR-derived PET parameters. PET parameters significantly differing between HGG and LGG with an AUC value greater than 0.80 are shown in Table 1.

Conclusion
This study illustrates that various PET- and MRI tumour-derived \([^{18}F]\)FET PET parameters, among which MTV\(_1\).\(_5\) and TLU\(_1\).\(_5\), are significantly different between HGG and LGG. Hence, PET and MRI of brain tumours may aid the pre-treatment diagnostic classification of gliomas. Further studies are needed to investigate whether PET-MR may serve as a surrogate for biopsies. Also, the combination of multiple parameters into one diagnostic tool for precise differentiation of LGG and HGG.
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Table 1. AUC values (> 0.80) for significantly different PET- and MR-derived $[^{18}F]FET$ PET parameters between HGG and LGG.
Abstract category
Medical

Title:
Cost-effectiveness of \(^{18}\text{F}\)FET for therapy assessment of temozolomide in patients with glioblastoma

Authors (name and surname) and affiliation number:
Tristan Baguet\(^1\), Jeroen Verhoeven\(^1\), Filip De Vos\(^1\), Ingeborg Goethals\(^2\)

Authors affiliation:
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2. Department of Nuclear Medicine, University Hospital Ghent

Abstract body:
Glioblastomas represent the most aggressive tumors among all gliomas. Classified as grade IV tumors by the World Health Organization (WHO), prognosis is poor. Combined treatment including surgery, radio- and chemotherapy shows variable outcome and is expensive. Faced with increasing costs of healthcare, society demands that medical expenses are justified. Therefore, the cost-effectiveness of \(^{18}\text{F}\)FET PET based follow-up was calculated in patients with glioblastoma after surgery and before the start of maintenance TMZ.

Methods:
To determine the cost-effectiveness, clinical data published by Galldik et al. were used and the costs were calculated in the Belgian healthcare setting. Sensitivity analyses in the form of one-way deterministic analysis and Monte Carlo analysis on the obtained ratios were done.

Results:
The decision tree based on overall survival showed 57.14% more non-responders identified with PET than with conventional MRI. A comparable 57.50% increase was seen in the decision tree built on progression free survival. The cost calculation yielded a cost of 780.50 euro per patient for two PET scans necessary during follow-up. Two cost-effectiveness ratios were determined based on overall survival and progression free survival. Both yielded very similar results with an incremental cost-effectiveness ratio of 1 365.86 euro per non-responder identified based on overall survival and 1 357.38 euro per non-responder identified based on progression free survival. The sensitivity analysis supported the calculations and showed that the obtained data were robust.

Conclusion:
\(^{18}\text{F}\)FET PET is a valuable tool that allows the prediction of treatment outcome before the start of maintenance TMZ in GB patients in a cost-effective way when compared with conventional MRI. \(^{18}\text{F}\)FET PET enables the prediction of the clinical outcome accurately and at a low cost. In addition, the sensitivity analyses show that this can be achieved with acceptable certainty given the robustness of the data.
Figure 1: Decision tree based on overall survival patients. 23 patients were available for PET analysis and 21 for MRI analysis. N1 & N2 gave chance node to be responder (R) for respectively PET and MRI. Chance nodes N3 & N5 gave the chance to be a real responder (RR) with PET and MRI. N4 and N6 gave the chance to be real non-responder (RNR) for PET and MRI. Non-responder (NR); false responder (FR) and false non-responder (FNR) are equal to 1 minus the chance to be R; RR and RNR. N = number patients. P in most right transparent framework gives the total chance to this event (is calculated by multiplying the previous two chance nodes).
Title: Value of $^{99m}$Tc-MAA SPECT-CT based dosimetry before radioembolization of liver tumors.

Authors (name and surname) and affiliation number:
Philippe d’Abadie\(^1\), Stephan Walrand\(^1\), Michel Hesse\(^1\), Nadia Amini\(^2\), Pierre Goffette\(^2\), Ivan Borbath\(^3\), Renaud Lhomme\(^1\), Francois Jamar\(^1\)

Authors affiliation:
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3. Gastro entology department, Cliniques Universitaires Saint Luc, UCL

Abstract body:

$^{99m}$Tc- macroaggregated albumin SPECT/CT($^{99m}$Tc-MAA) is performed before $^{90}$Y liver radioembolization (RE) for evaluating lung shunt, ruling out extrahepatic deposition and sometimes for calculating the delivered activity for treatment using the partition model. $^{99m}$Tc-MAA is then considered as a surrogate to $^{90}$Y-microspheres to predict tumor and liver absorbed doses.

The aim of this study is to assess the value of the dosimetry based on $^{99m}$Tc-MAA SPECT-CT compared to the real distribution of $^{90}$Y-microspheres observed with $^{90}$Y PET-CT.

Methods:
Patients treated by RE in our institution between 2011 and 2018 for hepatocellular carcinoma and cholangiocarcinoma were studied. 53 treatments and 136 lesions were analyzed. Tumor volumes of interest (VOIs) were delineated using the baseline imaging (arterial contrast enhanced MRI ou CT scan). VOIs were fused with $^{99m}$Tc-MAA SPECT and $^{90}$Y PET using PMOD 3.7 for calculation of a tumor to total liver ratio (T/L). Mean doses (DY90 and DMAA) and Dose Volume histogram (DVH) were calculated using the MIRD formula with input of the delivered activity of $^{90}$Y microspheres and of the ratio T/L (MAA or $^{90}$Y).

Using DVH, the minimal dose deposited in 66% of the tumor volume (D66) was calculated. Patients were categorized as a function of the catheter’s position during the $^{99m}$Tc-MAA and $^{90}$Y microspheres injections. Correlations were analyzed using the Spearman’s coefficient (R) and the accuracy of the prediction was studied using standard error of the estimate (SEE).

Results:
Regarding only treatments realized in the same angiographic conditions (25 treatments, 58 treatments), the correlation was strong (R=0.78) but the linear regression demonstrates a significant risk of error (SEE=76 Gy). A better correlation was found after exclusion of angiographies with injections in the proximity of an arterial bifurcation (R=0.88, SEE=56 Gy). Using DVH and D66, results were quite similar in both conditions (R=0.71, SEE=57 Gy and R=0.82, SEE=51 Gy).

Conclusion:
Despite good catheter positioning, the accuracy of $^{99m}$Tc-MAA dosimetry remains limited. $^{99m}$Tc-MAA SPECT/CT allows to estimate tumor doses with an unacceptable accuracy. In clinical practice, this dose estimation would not guarantee to avoid liver toxicity in case of dose escalation based on the partition model.
BELNUC LIEGE 2019 SYMPOSIUM: MED POSTER #4

Abstract category
☒ Medical

Title:
Characterization of the FDOPA uptake of the brainstem in parkinsonian syndromes by PET / MRI

Authors (name and surname) and affiliation number:
Demonceau Quentin1, Demonceau Georges1 2, Lebon Vincent1 3

Authors affiliation:
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2. Bois de l’Abbaye Liège
3. Université Paris Sud

Abstract body:

Aim:
FDOPA PET / CT is commonly used for the investigation of dopaminergic denervation, the diagnosis being based on striatal uptake. But other brain structures, including monoaminergic neurons of the brainstem, metabolize FDOPA and are likely to be affected. Using the values automatically generated by a PET / MRI atlas of the brainstem, we looked for alterations in the FDOPA uptake in parkinsonian syndromes. We retrospectively selected 35 patients who underwent FDOPA PET / MRI examination, 15 with Parkinson’s syndrome according to clinical and scintigraphic data, 20 others considered very unlikely to have this condition.

Method:
The T1 images of each patient were registered on the T1 images of a model where 28 anatomical regions had been previously identified. The adjustment parameters were then applied to FDOPA images. In each region VOIs of different sizes were then generated: 1 voxel (1mm³), 27 voxels or a volume adapted to the size of the region to be studied. The average voxel value, alone or compared to that of the other regions, was used to distinguish the 2 groups, by the way of a Student’s test.

The results were similar, using different sizes of VOIs. In the parkinsonian group, a significant reduction in SUV was thus observed in the substantia nigra (p = 0.03) and pulvinar (p = 0.04). Subtracting from the measured values the average value of the median raphe increases the number of significant regions: hypothalamus (p = 0.003), reticular nuclei (p = 0.006), substantia nigra (p = 0.008) and pulvinar (p = 0.01). We did not observe any significant difference in the midbrain, the A8 zone, the median raphe per se or the epiphysis. In the supratentorial area, the occipital region was also not affected, in contrast to the striatum and amygdala (both p = 0.002).

Results:
The best discriminations between parkinsonian and control groups, obtained by combining the activities of different regions, were provided by the difference between the average activities of, on the one hand, the putamen and, on the other hand, the substantia nigra (p = 2 10-11), pulvinar (p = 1.010-10) or amygdala (p = 2 10-9). The left side was significantly more affected than the right one.

Conclusion:
for the first time in nuclear medicine, we have been able to show automatically the involvement of brainstem nuclei in Parkinson’s syndrome. This opens perspectives in terms of early detection, staging and differential diagnosis of this disease.
Abstract category
☒ Medical

Title:
Exclusion of subclinical kidney allograft rejection by FDG PET/CT imaging systematically performed at 3 months post kidney transplantation

Authors (name and surname) and affiliation number:
Lovinfosse Pierre1, Hanssen Oriane2, Weekers Laurent2, Jadoul Alexandre1, Huynen Alexandre3, Catherine Bonvoisin2, Antoine Bouquegneau2, Roland Hustinx1 and Jouret François2,4

Authors affiliation:
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2. Division of Nephrology, Department of Internal Medicine, University of Liège Hospital, Liège, Belgium
3. Structural Engineering Division, Faculty of Applied Sciences, University of Liège, Liège, Belgium
4. Groupe Interdisciplinaire de Géno-protéomique Appliquée, Cardiovascular Sciences, University of Liège, Liège, Belgium

Abstract body:

Background
Kidney transplant recipients (KTR) are at risk for acute kidney allograft rejection (AR). By definition, “subclinical” AR (SCR) corresponds to AR in a stable patient, fortuitously evidenced by surveillance kidney biopsy. We hypothesize that FDG PET/CT detects SCR, which may help avoid the need for invasive systematic biopsies in KTR.

Material and methods
From 2015 to 2018, we prospectively performed FDG PET/CT in 95 adult KTR who underwent surveillance transplant biopsy ~3 months after transplantation. Banff-2017 classification was used to assess the presence of AR on kidney samples. Four volumes of interest (VOI) were distributed in the upper and lower poles of kidney cortex and the average value of the 4 SUVmean (mSUV) was obtained. Statistics (ANOVA, t-test and ROC curves) were performed using Python library SciP.

Results
Three patients were excluded for PCR-proven BK nephropathy (n=2) or uninterpretable histology (n=1). Based on the histology, the population was categorized into 3 groups: normal (n=70), borderline (n=16) and SCR (n=6). There were no clinical or biological differences between the groups. A significant difference of mSUV was observed across the 3 groups (normal 1.49 ± 0.32, borderline 1.64 ± 0.34 and SCR 1.77 ± 0.35) (p=0.05), and the mSUV was significantly higher in AR versus normal groups (p=0.04). Using a threshold of mSUV of 1.6 for identifying AR, the area under the ROC curve was 0.71, with 66% sensitivity, 62% specificity and 96% negative predictive value. Finally, mSUV was positively correlated with total inflammation score (p=0.02, r2=0.06) and with the acute composite of the Banff score (p=0.03, r2=0.05).

Conclusion
Our pilot study suggests that FDG-PET/CT could non-invasively detect SCR, with an excellent negative predictive value.
Abstract category
☒ Medical

Title: The metabolic clinical risk score (mCRS) as a new prognostic model for surgical decision in patients with colorectal liver metastases

Authors (name and surname) and affiliation number:
Ivan Duran Derijckere1, Hugo Levillain1, Ali Bohlok2, Celine Mathey3, Jonathan Nezri2, Raoul Muteganya1, Valerio Lucidi4, Fikri Bouazza2, Gaetan Van Simaeys5, Serge Goldman3, Alain Hendlisz5, Patrick Flamen1, Vincent Donckier2

Authors affiliation:
1. Institut Jules Bordet - Université Libre de Bruxelles (ULB) - Nuclear Medicine
2. Institut Jules Bordet - Université Libre de Bruxelles (ULB) - Surgical Oncology
3. Hôpital Erasme, Université Libre de Bruxelles - Nuclear Medicine
4. Hôpital Erasme, Université Libre de Bruxelles - Abdominal Surgery
5. Institut Jules Bordet - Université Libre de Bruxelles (ULB) - Digestive Oncology

Abstract body:

Aim: Accurate selection for surgery in patients with colorectal-liver-metastases (CRLM) remains challenging as predictive clinicopathologic factors and scores lack prognostic accuracy. Metabolic characteristics of CRLM, evaluated by 18FDG-PET/CT could contribute to better characterization of tumor biology and improve surgical selection.

The aim of our study was to evaluate if metabolic baseline characteristics of CRLM assessed with 18FDG-PET/CT at the time of diagnosis, before any preoperative treatment, could predict the benefit of surgery and furthermore to evaluate the impact of combining these metabolic data with standard Clinical Risk Score (CRS).

Material and methods: In a series of 450 patients operated for CRLM, we retrospectively identified two groups 1) long-term survival group (LTS), as defined by a postoperative recurrence-free survival (RFS) ≥5 years, i.e. the patients who benefited of surgery, and 2) early relapse group (ER), as defined by a RFS <1 year, i.e. the patients who did not benefit of surgery. 18FDG-PET/CT was to be performed at the time of diagnosis of CRLM before any preoperative treatment.

A total of 53 patients were analyzed, including 23 patients in the LTS group and 30 in the ER group. Clinicopathologic characteristics, CRS and baseline 18FDG-PET/CT metabolic parameters were analyzed. Low and high-risk CRS were defined by scores of ≤2 and ≥3, respectively.

Metabolic CRS (mCRS) was implemented, using 1 additional point to the standard 5-points CRS when the highest tumor standardized uptake value (SUVmax) and normal liver mean SUV (SUVmean(liver)) ratio was >4.3. Low and high-risk mCRS were defined by scores of ≤2 and ≥3 to 6, respectively.

Results: No difference was observed between LTS (n=23) and ER (n=30) groups for clinicopathologic characteristics, CRS and baseline 18FDG-PET/CT metabolic parameters were analyzed. Low and high-risk CRS were defined by scores of ≤2 and ≥3, respectively.

Metabolic CRS (mCRS) was implemented, using 1 additional point to the standard 5-points CRS when the highest tumor standardized uptake value (SUVmax) and normal liver mean SUV (SUVmean(liver)) ratio was >4.3. Low and high-risk mCRS were defined by scores of ≤2 and ≥3 to 6, respectively.

Results: No difference was observed between LTS (n=23) and ER (n=30) groups for clinicopathologic parameters, CRS and rates of low/high-risk CRS. All metabolic parameters, except for MTV, were significantly higher in ER patients, the ratio SUVmax/SUVmean(liver) being the most significantly different (median ER=4.21 vs LTS=2.82, p=0.008).

Taken individually, neither CRS nor the rate of metastatic SUVmax/SUVmean(liver) ratio >4.3 were significantly different between LTS and ER groups (p=0.120 and p=0.159 respectively). In contrast, mCRS was significantly different between LTS and ER groups (p=0.024). The rates of low and high-risk mCRS were also significantly distributed among LTS and ER groups, 60.9% of the LTS patients having a low risk score and 73.3% of the ER having a high risk mCRS (p=0.023).

Conclusions: Baseline 18FDG-PET/CT tumor characteristics and derived mCRS could represent additional tools to improve the selection in patients with CRLM candidate for surgery.
Figure 1. A. Patients with early relapse showed a significantly higher $\text{SUV}_{\text{max}}/\text{SUV}_{\text{mean(liver)}}$ ratio (Median LTS=2.8 vs ER=4.2, $p=0.008$). B. A higher proportion of early relapses were identified as high-risk at baseline using mCRS (CRS=53% vs mCRS=73%).
Abstract category
☒ Medical

Title:
Selective internal radiation therapy (SIRT) absorbed doses influences the nature of tumor-infiltrating lymphocytes in hepatocellular carcinoma

Authors (name and surname) and affiliation number:
Ligia Craciun1, Roland de Wind1, Pieter Demetter1,2, Valerio Lucidi3, Ali Bohlok4, Sébastien Michiels5, Michael Vouche6, Ilario Tancredi6, Gontran Verset7, Soizic Garaud8, Céline Naveaux8, Maria Gomez Galdon1, Karen Willard Gallo9, Alain Hendlisz6, Ivan Duran Derijckere10, Patrick Flamen10, Denis Larsimont1, Vincent Donckier4

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5. Radiology, Institut Jules Bordet, Université Libre de Bruxelles
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7. Gastroenterology and Medical Oncology, Hôpital Erasme, Université Libre de Bruxelles
8. Molecular Immunology Unit, Institut Jules Bordet, Université Libre de Bruxelles
9. Medical Oncology, Institut Jules Bordet, Université Libre de Bruxelles
10. Nuclear Medicine, Institut Jules Bordet, Université Libre de Bruxelles

Abstract body:

Aim
Selective internal radiation therapy with 90Yttrium (SIRT) is an effective locoregional treatment for hepatocellular carcinoma (HCC), leading to radiation-induced cellular necrosis. HCC have been shown as immune sensitive tumors and high levels of tumor-infiltrating lymphocytes (TILs) are associated with a better prognosis. We hypothesized that SIRT may modify immune tumor microenvironment in a dose dependent manner, by leading to different mechanisms of immunogenic cell death.

The aim of our study was to evaluate and compare TILs characteristics in patients treated with high doses (HD) or low doses (LD) of SIRT before partial hepatectomy for HCC.

Methods
All patients were included in a prospective trial to evaluate the feasibility and safety of SIRT before partial hepatectomy for HCC (clinicaltrials.gov NCT01686880). Lesion dosimetry was performed either on pre-therapeutic 99Tc-MAA SPECT/CT images or post-therapeutic 90Y-PET/CT using PMOD® (Technologies Ltd; Zurich, Switzerland). Lesions were manually delineated on anatomical images by an experienced physician and co-registered with either pre-therapeutic or post-therapeutic images. The median value of delivered doses was used as cut-off value to dichotomize between HD and LD.

Sections for digital image analysis (DIA) were prepared from paraffin blocks obtained from 11 patients treated with SIRT before partial hepatectomy. Immunohistochemistry stains were performed for CD3, CD4, CD8, CD20 and Granzyme B. The slides were scanned and analyzed with DIA Visiopharm software®. After exclusion of necrotic zones, TILs were quantified as percentages of positive cells/analyzed area within the tumor and stromal areas defined by a pathologist for each digital image and compared between LD and HD groups.

Results
All patients were CHILD score A without significant portal hypertension. Median number of tumors was 1 and median size 40mm. Median elapsed time between SIRT and partial hepatectomy was 16 weeks. Mean and median delivered doses were 130Gy and 112Gy respectively.

Preoperative SIRT significantly increased CD3+ TILs in peri-tumoral area in patients treated with LD (p=0.004), whereas a higher ratio of intra-tumoral CD4+ cells was observed in patients treated with HD (p=0.030). The other T-cell populations and GZB expression were not significantly modulated according to different absorbed doses.

Conclusion
Our results suggest that the type of immune responses induced by SIRT are variable depending on the administered radiation dose. Clinical development of therapeutic approaches combining SIRT and immunotherapy must take into account the tumor’s absorbed doses in order to optimize therapy.
Figure 1 Significantly increased peri-tumoral CD3+ cells in patients treated with lower doses (left) and intra-tumoral CD4+ in patients treated with higher doses (right).
Abstract category
☒ Medical

Title:
The use of 18F-FDG-PET/CT in an organ preservation protocol for patients with locally advanced rectal cancer.

Authors (name and surname) and affiliation number:
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Authors affiliation:
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2. Abdominal Surgery, University Hospital Leuven, Leuven, Belgium
3. Digestive Oncology, University Hospital Leuven, Leuven, Belgium
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5. Radiology, University Hospital Leuven, Leuven, Belgium
6. Nuclear Medicine, University Hospital Leuven, Leuven, Belgium

Abstract body:

Objective
Omission of surgery after chemoradiation is appealing in patients with rectal cancer with a clinical complete response (cCR). To improve patient selection for organ preservation, we compare the value of 18F-FDG-PET parameters according to treatment stratification and to response.

Methods
In forty patients with rectal cancer, assessment for cCR after chemoradiation, based on clinical findings and imaging, directed patients towards surgery or a watch-and-wait protocol. 18F-FDG-PET was performed before and six weeks after chemoradiation. Mean, median, maximum and peak standardized uptake value (SUV), tumour diameter, tumour volume and total lesion glycolysis (TLG) were measured. Using a Wilcoxon signed-rank test with a significance level of ☒ = 0.05, PET parameters were compared according to treatment and according to response defined as ypT0-1N0 or sustained cCR.

Results
Sixteen out of 40 patients underwent surgery and 24/40 patients entered a watch-and-wait protocol, of which 7 received salvage surgery for local regrowth. Eighteen out of 40 patients achieved a response as defined above and 22/40 did not. SUVmean, SUVmedian, SUVmax, SUVpeak and TLG were significantly lower in non-operated patients 6 weeks after chemoradiation. Furthermore, relative decrease in SUVmean, SUVmedian and SUVmax was significantly higher in these patients. In responding patients, SUVmedian, SUVpeak, TLG and volume were lower than in non-responding patients at baseline. Although no significant differences in relative change in parameters were seen, we observed a lower TLG six weeks after chemoradiation in responding patients.

Conclusion
18F-FDG-PET parameters differ between operated and non-operated rectal cancer patients after chemoradiation. The higher relative decrease in SUV in non-operated patients is a consequence of the fact that visual 18F-FDG-PET assessment is part of the response assessment after chemoradiation, upon which the decision for surgery relies. Responding patients have smaller tumours and lower SUVs at baseline. Six weeks after chemoradiation, TLG is a strong predictor of response, showing that documentation of residual tumor after treatment is more important than the relative decrease. These findings can contribute to better patient selection for an organ-sparing treatment for rectal cancer.
### Table 1.

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18F-FDG-PET was performed before and 6 weeks after chemoradiation. Responder = ypT0-1N0 or sustained cCR. Data are Median [Interquartile Range]. Δ indicates relative change in value between both scans.
BELNUC LIEGE 2019 SYMPOSIUM: MED POSTER #9

Abstract category
☒ Medical

Title:
Influence of pretreatment with everolimus and sunitinib on the acute hematotoxicity of 177Lu-Dotatate PRRT

Authors (name and surname) and affiliation number:
Eva Medaer, MD1; Chris Verslype, MD, PhD2; Eric Van Cutsem, MD, PhD2; Jeroen Dekervel, MD, PhD2; Paul Clement, MD, PhD2; Kristiaan Nackaerts, MD, PhD2; Olivier Gheyssens, MD, PhD2; Karolien Goffin, MD, PhD2; Sander Jentjens, MD2; Koen Van Laere, MD, PhD, DrSc1; Christophe M. Deroose, MD, PhD1.

Authors affiliation:
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3. Medical Oncology, University Hospitals Leuven, Leuven, Belgium.
4. Respiratory Oncology, University Hospitals Leuven, Leuven, Belgium.

Abstract body:

Background and aim
Peptide receptor radionuclide therapy is a validated treatment for somatostatin receptor overexpressing neuroendocrine tumors. The phase III NETTER-1 trial has demonstrated a pronounced effect on progression-free survival compared to high dose somatostatin agonists, with a strong tendency towards overall survival benefit. In Belgium, 177Lu-Dotatate is not yet reimbursed, but it is made available by the RIZIV/INAMI Special Solidarity Fund, for patients pretreated with all approved medical agents. The PRRT cohort in UZ Leuven is largely pretreated with targeted agents, in contrast to many other published cohorts. Everolimus is approved for primary pancreatic, lung and non-functional intestinal NETs, sunitinib for primary pancreatic NETs.

The aim of this work is to determine the influence of pretreatment with everolimus and/or sunitinib on acute hematotoxicity of PRRT.

Materials and methods
We analyzed the records of 90 consecutive patients treated with 177Lu-Dotatate PRRT (1 to 4 cycles) at the University Hospital Leuven, between November 2013 and July 2018. Six patients were excluded (incomplete data). All 84 included patients were assigned to 2 groups, according to their pretreatment: no targeted agents (naive), or pretreated (with everolimus, sunitinib or both). The end point was the acute hematotoxicity, defined as the nadir value during PRRT and the 6-months’ follow-up period after the last PRRT administration (using the CTCAE 4.03 classification). For clinical relevance, severe hematological toxicity (grade 3 + 4) was shown separately (see figure).

Results
No statistically significant differences in acute hematological toxicity were seen in the cohort pretreated with everolimus/sunitinib vs. the naive cohort respectively (all p > 0.05) for hemoglobin (any grade: 95% vs. 88%; grade 3/4: 21% vs. 15%), neither for the leucocytes (any grade: 65% vs. 59%; grade 3/4: 7% vs. 12%), nor for the neutrophils (any grade: 58% vs. 59%; grade 3/4: 7% vs. 7%), the lymphocytes (any grade: 91% vs. 98%; grade 3/4: 40% vs. 46%) or the platelets (any grade: 63% vs. 61%; grade 3/4: 16% vs. 17%). Our reported acute toxicity grades were more pronounced when compared to the NETTER-1 trial results, but possible confounding factors, such as subsequent chemotherapy or cardiac surgery for valve involvement during the follow-up period were not yet taken into account. Further analysis of these confounding factors will be presented at the congress.

Conclusion
In a 177Lu-Dotatate PRRT patients’ cohort that is largely pretreated with targeted agents, no significant influence of everolimus or sunitinib on the acute hematotoxicity of 177Lu-Dotatate PRRT was observed.
Belnuc Liege 2019 Symposium: Med Poster #10

**Abstract category**
- Medical

**Title:**
90Y-PET/CT-based dosimetry after selective internal radiation therapy predicts outcome in patients with liver metastases from colorectal cancer

**Authors (name and surname) and affiliation number:**
Hugo Levillain¹, Ivan Duran Derijckere¹, Gwennaëlle Marin², Thomas Guiot¹, Michaël Vouche¹, Nick Reynaert¹, Alain Hendlisz², Bruno Vanderlinden¹ and Patrick Flamen¹

**Authors affiliation:**
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2. Department of Medical Physics, Jules Bordet Institute, Université Libre de Bruxelles, Rue Héger-Bordet 1, B-1000 Brussels, Belgium.
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4. Department of Digestive Oncology, Jules Bordet Institute, Université Libre de Bruxelles, Rue Héger-Bordet 1, B-1000 Brussels, Belgium.

**Abstract body:**

**Aim**
Selective internal radiation therapy (SIRT) based on intra-arterial embolization of yttrium-90 (⁹⁰Y)-labelled resin microspheres is an established treatment of primitive or metastatic liver disease. Recent preliminary data indicated that post-SIRT dosimetry correlated with FDG-PET-based metabolic response assessment performed 6–8 weeks after SIRT. The feasibility of ⁹⁰Y imaging with PET in the hours following SIRT has recently been assessed as well as its quantitative performance. Therefore, post-SIRT dosimetry, if related to patient outcome, could become a valuable tool for early post-SIRT treatment adaptation.

The aim of this study was to confirm that post-SIRT ⁹⁰Y-PET/CT-based dosimetry correlates with lesion metabolic response and to determine its relationship with overall survival (OS) in liver-only metastases from colorectal cancer (mCRC) patients treated with SIRT.

**Materials and methods**
Twenty-four mCRC patients underwent pre/post-SIRT FDG-PET/CT and post-SIRT ⁹⁰Y-PET/CT. Lesions delineated on pre/post-SIRT FDG-PET/CT were classified as non-metabolic responders (total lesion glycolysis (TLG)-decrease < 15%) and high-metabolic responders (TLG-decrease ≥ 50%). Lesion delineations were projected on the anatomically registered ⁹⁰Y-PET/CT. Voxel-based 3D dosimetry was performed on the ⁹⁰Y-PET/CT and lesions’ mean absorbed dose (Dmean) was measured. The coefficient of correlation between Dmean and TLG-decrease was calculated. The ability of lesion Dmean to predict non-metabolic response and high-metabolic response was tested and two cutoff values (Dmean-under-treated and Dmean-well-treated) were determined using ROC analysis. Patients were dichotomized between the “treated” group (all the lesions received a Dmean > Dmean-under-treated) and the “under-treated” group (at least one lesion received a Dmean < Dmean-under-treated). Kaplan-Meier product limit method was used to describe OS curves.

**Results**
Fifty-seven evaluable mCRC lesions were included. The coefficient of correlation between Dmean and TLG-decrease was 0.82. Two lesions Dmean cut-offs of 40 Gy (sensitivity 80%, specificity 95%, predictive-positive-value 86% and negative-predictive-value 92%) and 60 Gy (sensitivity 70%, specificity 95%, predictive positive-value 96% and negative-predictive-value 63%) were defined to predict non-metabolic response and high-metabolic response respectively. Patients with all lesions Dmean > 40 Gy had a significantly longer OS (13 months) than patients with at least one lesion Dmean < 40 Gy (OS = 5 months) (p = 0.012; hazard-ratio, 2.6 (95% CI 0.98–7.00)).

**Conclusions**
In chemorefractory mCRC patients treated with SIRT, lesion Dmean determined on post-SIRT ⁹⁰Y-PET/CT correlates with metabolic response and higher lesion Dmean is associated with prolonged OS.
Figure 1 Regression analysis between post-treatment mean absorbed dose and the metabolic response assessed by TLG-decrease on a lesion by lesion basis ($R^2 = 0.82$). Red and green lines represents post-treatment mean absorbed dose cutoff values for predicting respectively non-metabolic responders (39 Gy) and high-metabolic responders (60 Gy).
Abstract category
☒ Medical

Title:
Inter-observer variability assessment for hepatic function measurement based on hepatobiliary-scintigraphy

Authors (name and surname) and affiliation number:
Hugo Levillain1, Ivan Duran Derijckere1, Gwennaëlle Marin2, Alessandro Desy2, Nicolas Gohimont1, Erwin Woff1, Carlos Artigas1, Nick Reynaert2, Vincent Donckier3, Alain Hendlisz4, Bruno Vanderlinden2, Patrick Flamen1

Authors affiliation:
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4. Department of Digestive Oncology, Jules Bordet Institute, Université Libre de Bruxelles, Rue Héger-Bordet 1, B-1000 Brussels, Belgium

Abstract body:

Aim
In patients addressed for liver direct therapy, the underlying liver pathology and prior treatments may decrease functional hepatic reserve to critical levels with risk of post-treatment liver failure. In this context hepatobiliary-scintigraphy (HBS) enables hepatic function (HF) measurement. Eligibility for therapy is assessed with a recently validated cut-off value of 2.7 %/min/m2 as HF lowest limit.

This study aims at defining the inter-observer variability of HF measurement based on HBS.

Materials and Methods
20 patients, who underwent HBS, were retrospectively evaluated by 4 experienced nuclear medicine physicians using dedicated commercial software (SyngoMI-V-A60C).
Dynamic planar acquisition (10×36 seconds during 360 seconds) was performed immediately after intravenous injection of 200 MBq of 99mTc-mebrofenin.
Three time-activity curves (TAC) were generated for three regions of interest on geometric mean images: liver, heart (plus large vessels) and total field of view. HF was calculated using TAC derived values acquired between 150 and 350 seconds after injection. Finally HF was normalised by patient’s body-surface-area for inter-patient comparison.
The largest inter-observer HF difference was computed for each patient. Then, both maximum and average values were determined for all patients.
To avoid inter-patient variability, HF were normalised by the respective mean value of each patient for all physicians (mean value=1). Standard deviation (SD) was computed for the normalised HF. The 95% confidence interval (95%CI) of HF measurement was computed with 1.96xSD, assuming Gaussian-distribution (N=80).

Results
The largest difference observed between two physicians in HF measurement was 24.1%. On the average the largest inter-observer variability on the whole cohort was 12.3%. The SD of the normalised HFs was 5.6%. The 95%CI taking into account the inter-observer variability was HF ± (0.11×HF).

Conclusion:
Our study demonstrates that the method for determining patient’s HF based on HBS was reproducible and that safe HF could be defined as HF - (0.11×HF). HBS is an interesting tool to evaluate functional hepatic reserve and could be used to assess patient’s eligibility before hepatotoxic therapy.
Abstract category
☒ Medical

Title:
Towards dose-response relationship in gastro-entero-pancreatic neuroendocrine tumours (GEP-NETs) treated with 177Lu-DOTATATE peptide receptor radionuclide therapy (PRRT)

Authors (name and surname) and affiliation number:
Gwennaëlle Marin1,3, Ioannis Karfis2, Clémentine Marin1, Hugo Levillain1, Nick Reynaert1, Stefaan Vandenbergh3, Bruno Vanderlinden1, Patrick Flamen4

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Abstract body:

Aim
PRRT with 177Lu-DOTATATE is an established treatment for metastatic well-differentiated GEP-NETs. Despite the fact that combining patients with different GEP-NET primary sites could improve the statistical power, dose–response relationship might depend on the tumour primary site.
This work aims to study the relationship between absorbed dose at first 177Lu-DOTATATE administration D1A, tumour primary site and GEP-NET response to PRRT.

Materials and methods
This retrospective study was based on 15 well-differentiated GEP-NET patients treated with 177Lu-DOTATATE (3 to 5 administrations) who underwent 3 post-PRRT-SPECT/CT (4, 24, 168 h post-administration). Baseline and end-of-treatment 68Ga-DOTATATE-PET/CT were performed; image quality was assessed using predefined criteria.
GEP-NET patients were classified in three groups—pancreatic, intestinal or rectal—depending on tumour primary site.
Lesion-based dosimetry was performed on three post-PRRT-SPECT/CT (PMOD® 3.4). Peak specific activity was measured in a sphere surrounding the lesion on each image. These values were fitted over time with a bi-exponential function. Dose in each lesion was computed considering local energy deposition and homogenous specific activity.
Response assessment was performed on baseline and end-of-treatment 68Ga-DOTATATE-PET/CT (AWserver 3.2, GE-Healthcare®). Lesions were delineated with a threshold equal to the baseline normal kidney cortex uptake measured in a 2 cm diameter sphere (Marin et al, EANM 2016). The lesion-based response to PRRT was assessed by lesion-uptake-volume (LU-V)-decrease.
Data normality was checked with D’Agostino-Pearson normality test. The variability of D1A and LUV-decrease in function of GEP-NET group was evaluated with Kruskal-Wallis and one-way ANOVA test respectively according to normality test results (GraphPad 7.1, Prism®).

Results
This study included 61 GEP-NET lesions of which 20, 25 and 16 were classified respectively as pancreatic, intestinal and rectal.
D1A did not pass normality test. [First quartile; median; third quartile] was [19.8; 38.5; 59.5], [22.5; 48.6; 68.1] and [24.0; 72.4; 105.3] Gy respectively for pancreatic, intestinal and rectal GEP-NETs. D1A distributions were not significantly different (P=0.19).
LUV-decrease passed normality test. Mean±SD was 58.8±41.6, 33.8±30.6 and 79.5±21.6 % respectively for pancreatic, intestinal and rectal GEP-NETs. LUV-decrease distributions were significantly different (P<0.001). Pancreatic and rectal GEP-NET LUV-decreases were significantly different from intestinal (P<0.05 and P<0.001 respectively) but the difference between pancreatic and rectal LUV-decreases was not statistically significant (P=0.3).

Conclusion
This study indicates that GEP-NET response to PRRT strongly depends on tumour primary site despite similar lesion absorbed doses at first administration. It highlights the importance of classifying GEP-NETs in function of their primary site when assessing dose-response relationship.
Figure 1: In GEP-NET patients, lesion-uptake-volume (LUV)-decrease after PRRT strongly depends on tumour primary site ($P<0.001$) despite similar tumour absorbed doses at first administration ($P=0.19$).
BELNUC LIEGE 2019 SYMPOSIUM: MED POSTER #13

Abstract category
☒ Medical

Title:
Development and Validation of a Prognostic Score for Overall Survival Integrating Baseline Metabolically Active Tumor Volume measured by 18F-FDG PET/CT and Clinical Factors for Metastatic Colorectal Cancer Patients.

Authors (name and surname) and affiliation number:
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3. Medical Oncology Department, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy.
4. Department of Translational Research and New Technologies in Medicine and Surgery, Unit of Medical Oncology 2, Azienda Ospedaliera Universitaria Pisana, Pisa, Italy.
5. Nuclear Medicine Department, Fondazione Toscana «Gabriele Monasterio», Pisa, Italy.
6. Data centre, Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium.

Abstract body:

Aim:
This study aimed to develop and validate a prognostic score integrating baseline metabolically active tumor volume (MATV) and clinical factors in metastatic colorectal cancer (mCRC) patients.

Materials and Methods:
The development cohort included chemorefractory mCRC patients enrolled in two prospective multicenter non-randomized trials evaluating sorafenib/regorafenib as last line therapy. The validation cohort included mCRC patients from another center, treated with chemotherapy and bevacizumab as first line. Baseline MATV was defined as the sum of the metabolically active volumes of all target lesions identified on the baseline 18F-FDG PET/CT. MATV optimal cutoff for OS prediction was determined from the development cohort with the Contal and O’Quigley’s method. MATV, age, gender, BMI, ECOG PS, years since diagnosis, and KRAS status were included in a multivariate analysis. A prognostic score to predict OS was developed from the development cohort based on the regression coefficients from the final Cox proportional hazards model.

Results:
MATV and clinical factors were evaluable respectively in 155 and 122 patients of the development and the validation cohorts. In univariate analysis, MATV with cutoff set at 100 cm³ identified two risk groups with different median OS (mOS) in both the development (4.5 vs 10.9 months, HR: 2.64; p<0.001) and the validation cohorts (20.9 vs 42.9 months, HR: 2.39; p<0.001). A multivariate analysis identified four independent negative predictors of OS (high MATV, short time since diagnosis, poor PS, BMI<25). Combining these factors in a prognostic score for OS (best cutoff:-2) allowed to identify two risk groups with different mOS in the development (4.4 vs 13.4 months, HR: 3.67; p<0.001) and the validation cohorts (25 vs 63.8 months, HR: 2.5; p=0.001).

Conclusion:
In mCRC patients, the high prognostic value of baseline MATV found in the development cohort was confirmed by external validation, independently of patients’ treatment. In both the development and validation cohorts the prognostic score for OS allowed to identify two risk groups of mCRC patients with significantly different mOS. MATV and our prognostic score for OS should provide a firm basis for risk stratification, in clinical practice and research trials.
Figure: Prognostic score for OS allowed to identify in the development cohort (A) and in the validation cohort (B) two risk groups with different median OS.
Abstract category
☒ Medical

Title:
Impaired kidney function is associated with higher dose to organs-at-risk in $^{177}$Lu-DOTATATE peptide receptor radionuclide therapy (PRRT)

Authors (name and surname) and affiliation number:
Gwennaëlle Marin1,3, Ioannis Karfis2, Hugo Levillain1, Nick Reynaert1, Stefaan Vandenberghhe3, Bruno Vanderlinden1, Patrick Flamen1

Authors affiliation:
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2. Department of Nuclear Medicine, Jules Bordet Institute, Université Libre de Bruxelles
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Abstract body:

Aim
In patients addressed for PRRT, prior treatments or underlying pathology may decrease kidney function. In PRRT, kidneys and bone marrow (BM) are classically considered as dose limiting organs. Impaired kidney function might be associated with higher doses to organs-at-risk (OAR) due to reduced $^{177}$Lu-DOTATATE renal clearance.

This work aims to study the impact of renal function, assessed by glomerular filtration rate (GFR), on absorbed dose to OAR in $^{177}$Lu-DOTATATE PRRT of patients with neuroendocrine tumours (NETs).

Materials and methods
This retrospective study was based on 26 NET patients treated with $^{177}$Lu-DOTATATE (3 to 5 administrations). $^{177}$Lu-DOTATATE was administered intravenously every 12 weeks with four-hours concomitant nephroprotective aminoacid solution.

Patients underwent $^{51}$Cr-EDTA test before each administration for renal function assessment (GFR) and 3 post-PRRT-SPECT/CT (4, 24, 168 h post-administration) and 5 post-PRRT blood samples (0, 1, 4, 24, 168 h post-administration) for dosimetry purpose.

Activity in the kidneys was computed by multiplying specific activity measured on SPECT images by the anatomical CT volume (PMOD® 3.4 software). For BM, specific activity measured in blood samples was multiplied by OLINDA BM volume normalized by patient height. Measures were fitted over time with a bi-exponential function. Absorbed doses were computed following MIRD formalism (OLINDA/EXM 1.1 software) and normalized by injected activity.

Mean values over PRRT administrations for GFR (GFR_mean) and dose per injected activity (D_mean) were computed for each patient. Descriptive statistics [first quartile; median; third quartile] were performed. Correlation coefficients ($R^2$) between GFR_mean and both kidney and BM D_mean were computed using linear regression model (GraphPad 7.01, Prism®).

Results
Descriptive statistics for GFR_mean, kidney D_mean and BM D_mean were [64.0; 71.8; 87.4] ml/min/1.73m²/day, [0.72; 0.97; 1.2] Gy/GBq and [0.023; 0.281; 0.033] Gy/GBq respectively.

GFR_mean was linearly correlated with D_mean in kidneys ($R^2$=0.24) and D_mean in BM ($R^2$=0.43). Linear regressions had a negative slope significantly different from zero (P=0.01 for kidneys and P=0.0003 for BM).

Conclusion:
This study demonstrates that impaired kidney function (lower GFR) is correlated with higher absorbed doses to kidneys and BM in patients treated with $^{177}$Lu-DOTATATE. This might be explained by a decreased $^{177}$Lu-DOTATATE clearance from blood and can suggest a potential predictive value of GFR for OAR toxicity.
Figure 1: In patients treated with $^{177}$Lu-DOTATATE, impaired kidney function (lower GFR) is linearly correlated with higher absorbed doses to bone marrow ($R^2=0.43$) and to kidneys ($R^2=0.24$). Linear regressions have a negative slope significantly different from zero ($P=0.0003$ for bone marrow and $P=0.01$ for kidneys).
Bayesian Penalized-Likelihood reconstruction algorithm: Noise reduction study on a 15 cm axial field-of-view PET/CT Scanner

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2. Department of Nuclear Medicine – Ghent University Hospital, Belgium
3. Division of Nuclear Medicine and Molecular Imaging – UZ/KU Leuven, Belgium

Abstract body:

Background:
Block sequential regularized expectation maximization (BSREM) is a Bayesian penalized-likelihood reconstruction algorithm which improves image quality by controlling noise amplification during image reconstruction. In this study, the performance of BSREM was compared to ordered-subset expectation maximization (OSEM) for both phantom and patient data acquired on a state of the art TOF PET/CT. The aim was to determine if the noise level can be reduced without a loss in image quality.

Methods:
The NEMA IQ phantom (6 fillable spheres: 10-37 mm) and a whole-body patient acquisition were acquired on a 15 cm axial-FOV GE Discovery MI (SiPM-based TOF PET/CT) system in listmode. From these acquisitions, different datasets with varying count levels were generated. These were reconstructed using BSREM with different regularization $\beta$-factors of 300, 500, 750, 1000, 1500 and 3000 and as well reconstructed using OSEM with 5 iterations and 17 subsets for different Gaussian post-filter with a full width at half maximum (FWHM) of 4.5, 5.0, 6.0, 7.0, 8.0, 9.0 and 10 mm. All reconstructions included attenuation and scatter correction based on CT, point spread function (PSF) compensation and TOF. The optimal choices of the beta parameter of both reconstructed image data were analyzed. Recovery coefficients (RC), and background noise levels (coefficient of variation, CoV) were used to determine the performance in the phantom data. These conclusions were checked on a clinical patient scan. In patient studies SUV and lesion metabolic activity was evaluated. The liver was used as the background region.

Results:
For the same count statistics BSREM resulted in lower background variability than OSEM for any choice of the regularization parameter. For values of the regularization parameter lower than 750 also a higher contrast was observed. With the phantom data, the number of counts can be reduced by a factor 2-4 using BSREM instead of OSEM. For the patient data, similar trends are seen and the possible count level reduction was at least a factor of 2.

Conclusion:
Noise reduction is possible by introducing regularization in the image reconstruction without a loss in image quality. This reduction can be used to lower the injected dose or shorten the acquisition time.
Figure 1 Right background variability of OSEM (5mm postfilter) and BSREM for a volume of 26.52 ml at different scan time. Left: comparison in terms of SUVmean (red), SUVmax (black) and metabolic lesion activity (green) for the 0.52 and 26.52 ml lesions (arrows).
Abstract category
Physics and engineering

Title:
GE Signa integrated PET/MR system: results of the NEMA NU 2–2007 tests and a GATE Monte Carlo study of the clinically available isotopes

Authors (name and surname) and affiliation number (presenter author underlined):
André Diogo1,2, Paulo Caribé1, Michael Koole3, Yves D’Asseler1, Stefaan Vandenberghe1

Authors affiliation:
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2. Faculty of Sciences of the University of Lisbon (FCUL), Portugal
3. Division of Nuclear Medicine and Molecular Imaging, UZ/KU Leuven, Belgium

Abstract body:

Background:
Fully integrated PET/MR systems are being used frequently in clinical research and routine, rising the need to better understand how clinically used isotopes behave in such scanners. To study this issue, a realistic model of the GE Signa integrated PET/MR was implemented on GATE for Monte Carlo simulations to estimate the performance of the scanners and the effect of magnetic fields on the positron range of different radioisotopes.

Methods:
The NEMA sensitivity and noise equivalent count rate (NECR) performance measurements were acquired on a GE Signa 3T PET/MR scanner installed in UZ/KU Leuven using 18F. A realistic model of the GE Signa integrated PET/MR was implemented on GATE for Monte Carlo simulations. The geometry was modelled using the cylindrical PET system, considering the MRI RF coils, foam, plastic and copper shielding between the field of view and the detectors. We applied the NEMA protocols to estimate absolute sensitivity and NECR and the results were compared with the published and measured values. Data analysis was done via ROOT and MATLAB following the protocols for each test as described by NEMA publications. In addition, we investigate the effect of the 3T MR field on positron range of 18F, 11C, 13N, 15O, 68Ga and 82Rb for different tissue types. To characterize the effect of 3T MR field on positron range, 3 million events were simulated.

Results:
The positron range of the more energetic radioisotopes was substantially affected by the 3T magnetic field in the z-direction. This effect is more noticeable for high positron energy emitters, such as 15O, 68Ga and 82Rb, increase in z-direction by a factor 4 when compared to the range in x/y direction in the lung tissue. The positron range values are shown on Table 1. The NEMA simulated sensitivity test for 18F was 20.73cps/kBq, which is slightly lower than both the one measured, 21.5cps/kBq and 22.5cps/kBq sensitivity value provided by GE Healthcare. The simulated peak NECR value for 18F was equivalent to the measured, 215.0 and 216.8kcps, respectively, although the difference is less than 1%.

Conclusion:
In this study, we have performed and simulated the NEMA sensitivity and NECR tests on the GE Signa PET/MR. Sensitivity and NECR results obtained with the GATE Monte Carlo simulated model matched with measured and published values. The positron range is a tissue-dependent and increase in z-direction by a factor 4 when compared to the range in x/y direction in the lung tissue for 68Ga and 82Rb.
<table>
<thead>
<tr>
<th></th>
<th>$^{18}\text{F}$</th>
<th>$^{11}\text{C}$</th>
<th>$^{13}\text{N}$</th>
<th>$^{15}\text{O}$</th>
<th>$^{68}\text{Ga}$</th>
<th>$^{82}\text{Rb}$</th>
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<tr>
<td><strong>Maximum Energy (keV)</strong></td>
<td>633.5</td>
<td>960.2</td>
<td>1198.5</td>
<td>1732.0</td>
<td>1899.0</td>
<td>3378.0</td>
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<tr>
<td><strong>$T_{1/2} \text{(min)}$</strong></td>
<td>109.8</td>
<td>20.4</td>
<td>10.0</td>
<td>2.0</td>
<td>67.7</td>
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<td><strong>Branching Ratio (%)</strong></td>
<td>99.86</td>
<td>99.75</td>
<td>99.82</td>
<td>99.89</td>
<td>88.88</td>
<td>95.45</td>
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<td><strong>Positron Range @ 3T (mm)</strong></td>
<td></td>
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<tr>
<td>Mean 3D range</td>
<td>0.52</td>
<td>0.96</td>
<td>1.01</td>
<td>1.66</td>
<td>2.04</td>
<td>3.82</td>
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<tr>
<td>Lung</td>
<td>1.70</td>
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<td>2.63</td>
<td>4.28</td>
<td>4.59</td>
<td>10.12</td>
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<td>Mean x (or y) range</td>
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<td>0.49</td>
<td>0.77</td>
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<tr>
<td>Lung</td>
<td>0.73</td>
<td>0.63</td>
<td>0.74</td>
<td>0.97</td>
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<td>Bone</td>
<td>0.17</td>
<td>0.25</td>
<td>0.34</td>
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<td>Mean z range</td>
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<td>0.54</td>
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<tr>
<td>Lung</td>
<td>1.08</td>
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<td>0.17</td>
<td>0.26</td>
<td>0.35</td>
<td>0.61</td>
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<td><strong>NEMA Performance Measurements</strong></td>
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<td>Sensitivity (cps/kBq)</td>
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<td>-</td>
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<td>Simulated</td>
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<tr>
<td>Peak NECR (kBq/ml)</td>
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<td>-</td>
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</tr>
<tr>
<td>Simulated</td>
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<tr>
<td>Measured</td>
<td>216.8</td>
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Table 1: Isotope characteristics, positron range simulation results and NEMA tests results.
BELNUC LIEGE 2019 SYMPOSIUM: PHYS 03

Abstract category
Physics and engineering

Title:
Cellular dosimetry of $[^{177}\text{Lu}]$DOTATATE radionuclide therapy: the impact of modelling assumptions on the correlations with in vitro cytotoxicity

Authors (name and surname) and affiliation number (presenter author underlined):

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2. Radiobiology Unit, Belgian Nuclear Research Centre (SCK·CEN), Mol, Belgium.
3. Department of Radiology & Nuclear Medicine, Erasmus MC, University Medical Center Rotterdam, The Netherlands.
4. INSTEC, Higher Institute of Technologies and Applied Sciences, Havana, Cuba.

Abstract body:

Aim:
Targeted radionuclide therapy (TRNT) is a promising technique for treating metastasized cancers. Correlating absorbed doses in the nucleus to biological responses is fundamental to optimize treatment planning for TRNT. However, only simplified in vitro dosimetry models are available, leading to inaccurate linear-quadratic model fitting parameters. Therefore, we modeled cellular dosimetry of $[^{177}\text{Lu}]$DOTATATE, accounting for the alleged translocation of $^{177}$Lu to the Golgi and we assessed the impact of different modelling assumptions on the final correlation with experimental survival fractions.

Material and methods:
Time-integrated activity curves from uptake experiments in medium, membrane-bound and internalized fractions over 6 days and clonogenic survival assays for the corresponding added activity (0.1-2.5 MBq/ml) were generated. Confocal microscopy 3D images (stained for cytoplasm, nucleus and Golgi) were used as reference for developing 9 polygonal meshes (PM) in 3DsMax to properly model the cellular and organelle geometry. Geant4 Monte Carlo toolkit was used to calculate absorbed dose rate $S\text{-values}$ for different subcellular radioactivity distributions. The geometrical set-up of the 6-day survival fraction experiment was modelled, including dynamic changes in proliferation, proximity variations and cell death. The absorbed dose to the nucleus of radioactive cell (selfdose) and neighboring cells (crossdose) was calculated applying the MIRD scheme ($D=\sum S_{\text{org}}\times A(s)$) to (1) MIRDcell sphere geometry, (2) truncated cone-shaped constructive solid geometry (CSG) and (3) realistic PM models. Finally, the correlation between survival fraction and calculated dose was fitted using a linear dose-response curve for different assumptions, related to cellular shape and localization of the internalized fraction of activity (Golgi, cytoplasm).

Results:
The absorbed doses to the nucleus were on average significantly lower when modeling the cells realistically using PMs (1.12±0.19Gy-2.17±0.31Gy) as compared to CSG (1.71-3.15Gy) and MIRD (3.39-6.15Gy). When translocating the internalized activity to the Golgi for the PM cells the dose slightly increased to 1.64±0.38Gy-3.03±0.63Gy. The experimental survival fractions ranged between 60%-40%. Linear dose response curves revealed higher alpha values for PM when compared to CSG and MIRD: $SF_{\text{PM}}= e^{-0.43\pm0.03}$, $SF_{\text{CSG}}= e^{-0.32\pm0.02}$, $SF_{\text{MIRD}}= e^{-0.17\pm0.01}$, ($\alpha/\beta>100$ Gy) (Fig. 1). Furthermore, assuming the translocation of the internalized vector to the Golgi affected the dose-response correlation significantly decreasing the alpha value ($SF_{\text{PM}}= e^{-0.31\pm0.02}$), which demonstrates that modeling the Golgi apparatus, neglected in MIRDcell or any other cellular dosimetry model, is crucial.

Conclusion:
Our results show that specific cell line features and geometry are crucial to perform accurate dosimetry. These results suggest dose overestimation when planning therapy based on generalized dosimetry models.
Fig. 1 Dose-response curve corresponding to 3 geometrical assumptions: spheres (blue), CSG (green) and PM (orange).
Abstract category
- Physics and engineering

Title:
Standardisation of 68Ga PET/CT imaging resolution for multi-centre study

Authors (name and surname) and affiliation number (presenter author underlined):
Clémentine Marin1, Gwennaëlle Marin1, Bruno Vanderlinden1, Hugo Levillain1, Thomas Guiot1, Nick Reynaert1, Patrick Flamen2

Authors affiliation:
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2. Department of Nuclear Medicine, Jules Bordet Institute, Université Libre de Bruxelles, 1 rue Héger-Bordet, 1000 Brussels, Belgium.

Abstract body:

Aim:
Gallium-68 PET/CT imaging is an emerging modality not yet standardised for multi-centre studies. The aim of this work was to study the impact of resolution on recovery coefficients (RCs) and propose a method to standardise PET spatial resolution for inter-centre comparison.

Materials and methods:
A 20cm-diameter uniform cylinder with 68Ga specific activity of 18 kBq/ml and three NEMA-2012/IEC-2008 phantoms with 68Ga specific activity of 8, 13 and 23 kBq/ml in spheres and water without activity in background were prepared and acquired on a GE Discovery 690 PET/CT with EARL accreditation parameters (two 5-minutes steps overlapping on spheres). The uniform cylinder was acquired with a low angle with respect to the PET/CT z-axis for fine sampling of edge spread function and resolution determination. Images were reconstructed with the 3D OSEM algorithm (3 iterations, 18 subsets, TOF and resolution recovery correction) using different Gaussian post-filters with full width at half maximum (FWHM)=[0, 4.0, 6.8, 11.1, 13.6] mm. Voxel dimensions were 2.73×2.73×3.27 mm3.

Resolution, characterised by FWHM of a Gaussian point spread function, was determined by fitting of edge spread functions from the uniform cylinder for all filters. RCs were measured with Pmod 3.4 in spheres delineated on NEMA phantom PET images according to constructor volumes. Mean RCs were computed from the three NEMA phantoms for each filter. Assuming that partial volume effect is proportional to sphere surface, mean RCs were plotted as a function of inverse sphere radius. The correlation of RC slope with PET resolution was also investigated, using a linear model.

NEMA phantom PET images without statistical noise were simulated with Scilab 6.0.0 in order to mimic experimental measurements (same voxel size and post-filtering) and validate results.

Results
The resolution measured on the uniform cylinder PET images for the five filters was FWHM=4.0, 5.7, 7.5, 11.8 and 14.8 mm. The linear relationship between RC and inverse sphere radius was demonstrated for each resolution (R2≥0.99). RC line slopes were linearly correlated to image resolution (R²=0.97). These relationships were confirmed by the Scilab simulations.

Conclusion:
Linearisation of RC curves and quadratic sum of Gaussian FWHMs allowed direct determination of spatial resolution and of the needed post-reconstruction filter to reach comparable resolution for multi-centre studies, a first step towards 68Ga PET/CT standardisation.
Figure 1: Linear relationship between mean RCs and inverse sphere radius for each resolution

- $y = -507x + 101$
- $y = -562x + 99$
- $y = -217x + 101$
- $y = -391x + 102$

Resolution:
- × 4.0mm
- ♦ 5.7mm
- □ 7.5mm
- ▲ 11.8mm
- ■ 14.8mm
Abstract category
• Physics and engineering

Title:
Quantification of 131I activity in mouse kidneys using micro-SPECT and ex vivo gamma counting: experimental evaluation of uncertainties.

Authors (name and surname) and affiliation number (presenter author underlined):
Clarita Saldarriaga Vargas¹², Lara Struelens¹, Matthias D’Huyvetter², Jos L. Eersels², Vicky Caveliers², Peter Covens²

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Abstract body:

As opposed to conventional external gamma counting (GC) of dissected tissues, micro-SPECT offers the possibility to perform in vivo longitudinal studies on the same animal. In order to derive the pharmacokinetic parameters necessary for tissue dosimetry and the evaluation of the dose dependence of biological response, micro-SPECT must be quantitative and allow an accurate and reproducible assessment of the radiopharmaceutical activity in the relevant tissue.

This study aims to evaluate the accuracy and reproducibility associated with the pharmacokinetic assessment of 131I-labeled single-domain antibody fragments (sdAb) in mice using micro-SPECT, against ex vivo biodistribution studies using GC. The focus is on the kidneys, where uptake of the 131I-labeled sdAb is significant.

Biodistribution studies were done on healthy C57BL/6 mice. The pharmacokinetic profile of 131I-labeled sdAbs in the kidneys was determined from tissue activity measurements at different time points post injection of the radiolabeled compound, both with micro-SPECT and GC. SPECT/CT acquisitions were performed with a VECTor micro-SPECT/PET/CT (MiLabs). Following the last SPECT acquisition, the activity of dissected tissues was assessed in a NaI(Tl) scintillation counter. Several sources of uncertainties were evaluated experimentally for each technique. For SPECT: system performance in terms of activity recovery coefficients (phantom study) and measurement reproducibility, mouse inter-variability, and size of the regions of interest (ROI) used for image quantification. For GC: device performance in terms of measurement reproducibility, cross-talk, sample volume effects and response linearity; as well as mouse inter-variability. Additionally, the accuracy and reproducibility of the activity calibration factors determined for each technique were evaluated.

For GC, the uncertainties due to device performance are mostly below 5% when using an appropriate measurement protocol. For SPECT, errors due to partial recovery of activity account for an underestimation of at least 20% of the kidney activity. Also the ROI size has a large impact on SPECT image quantification. SPECT measurements resulted in lower variability between time-specific kidney activities of different mice than GC, and resulted also in a lower variability in the estimated residence time (±10%, vs ±20% for GC). SPECT was also less prone to large (>15%) errors in the determination of the activity calibration factor. When using an appropriate SPECT ROI size, kidney activities from SPECT and GC agreed mostly within 20%.

Micro-SPECT allows reproducible and reasonably accurate quantification of 131I in murine kidneys. This opens the possibility to perform longitudinal biodistribution studies and kidney dosimetry for the same animals used for long-term toxicity studies.
The differentiation of low- and high-grade gliomas using radiomics and machine learning on [18F]FET PET and T1ce MRI

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Aim
Gliomas are the most frequent malignant primary brain tumour in adults and can be classified into low-grade (LGG) and high-grade glioma (HGG). Due to the importance of an accurate and early diagnosis, for which histopathology is the gold standard, there is an increasing interest in image-based automated classification. This study evaluates automatic segmentation and radiomics features from [18F]FET PET and contrast-enhanced T1-weighted (T1ce) MRI images for discrimination between LGG and HGG.

Materials and methods
Pretreatment [18F]FET PET scans and anatomical MRI were performed in 30 patients (14 LGG and 16 HGG). An in-house developed segmentation algorithm was used to automatically delineate different tumour tissues on T1ce and FLAIR MRI: necrosis, oedema, non-enhancing tumour, and contrast-enhancing tumour.

These different tumour masks were used to extract 2913 quantitative radiomics features per patient from the T1ce and PET images. Next, forward sequential selection and five-fold cross-validation were implemented to identify up to 15 features that are able to make the optimal distinction between LGG and HGG using Random Forest classification model.

Results
Results are shown in Table 1. The best result is obtained when combining features from T1ce and [18F]FET PET. This model achieves excellent discrimination between LGG and HGG (AUC = 0.951).

Conclusion
This study illustrates that automatic tumour segmentation and extraction of radiomics features from combined [18F]FET PET and T1ce MRI scans are able to discriminate between LGG and HGG with high accuracy.

<table>
<thead>
<tr>
<th>Features</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MR-based</td>
<td>86.6</td>
</tr>
<tr>
<td>PET-based</td>
<td>83.3</td>
</tr>
<tr>
<td>Combined</td>
<td>96.7</td>
</tr>
</tbody>
</table>

Table 1. Accuracy for the classification tasks using MRI-based, PET-based, and combined features
Abstract category
- Physics and engineering

Title:
Feasibility of a brainstem and diencephalon atlas in FDOPA PET / MRI imaging

Authors (name and surname) and affiliation number:
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Authors affiliation:
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Abstract body:

Aim:
In the diagnosis of neurodegenerative diseases, only striatal uptake of FDOPA is analyzed, the brainstem and the diencephalon being ignored. Indeed, the position of the stem with respect to the cortex varies between patients, preventing accurate registration of MRI or PET images on cerebral atlases. The use of a hybrid PET / MRI camera overcomes this problem. In this context, our objective was to constitute an atlas of FDOPA uptake in the brainstem and diencephalon.

Methods:
We retrospectively selected 35 patients who underwent FDOPA PET / MRI: 15 considered as positive for dopaminergic denervation, 20 considered as normal. The T1 images of each patient were registered on the T1 images of a reference model where several anatomical regions had been previously identified. The registration was carried out in a progressive way, in non-deformable and then deformable mode, after creation of a mask including the brainstem, the diencephalon and the striatum. The registration parameters were then applied to the FDOPA images. The choice of the optimal method of registration was based on the analysis of the dispersion of the activity in the summed image of the control group. We finally investigated the correlation between the scores of 70 deformable registrations and the ability of specific brain regions to discriminate, using those registrations, the parkinsonian from the normal patients.

Results:
The whole processing takes about 4 minutes to be complete. Visually the images of the brainstem, diencephalon and striatum are correctly replaced after registration in all patients, without deformation. A significant inverse correlation (Pearson’s coefficient; p-values less than 0,0001) was found between the 70 scores and the corresponding p-values of a Student t-test comparing the control and patient groups in 5 non-striatal regions: the epiphysis, the hypothalamus, the pulvinar, the raphe nuclei and the substantia nigra. Furthermore, using the registration method with the highest score, two of those regions (the substantia nigra and the hypothalamus) exceeded the level of signification. Those statistical characters were also observed in well validated regions in Parkinson’s disease, the caudate and the putamen.

Conclusion:
Using the hybrid PET / MRI technique, it is possible to reliably achieve an automatic analysis of FDOPA uptake in brainstem and diencephalon nuclei. The method is independent of the injected tracer, which broadens its scope.
Abstract category
☒ Physics and engineering

Title:
Monte Carlo simulations of pre-clinical SPECT systems with $^{99m}$Tc and 188Re sources

Authors (name and surname) and affiliation number:
Marek Beliš1,2, Karen Van Hecke1, Thomas Cardinaels1,3, Stefaan Vandenberghe2

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Abstract body:

Introduction:
Rhenium-188 (188Re) is a β- emitting radionuclide (T1/2 = 17.0 h, Emax = 2.1 MeV), suitable for radiotherapeutic applications. In addition, it emits a 155 keV γ ray (15 %), which can be used for imaging with current SPECT (single-photon emission computed tomography) systems. However, several high-energy γ rays in emission spectrum of 188Re, together with radiation produced by β- particles (Bremsstrahlung), may complicate quantitative imaging. The aim of our research is to simulate the spectra of detected events with 188Re sources and compare to the SPECT gold standard, technetium-99m (99mTc). These simulations provide useful information about the amount of contamination, their origin, the scatter fraction and the detection efficiency with various parameters of a collimator.

Methods:
GATE software (Geant4 Application for Tomographic Emission) was used to execute Monte Carlo simulations. Point and volume sources of $^{99m}$Tc and 188Re were used in the simulations, either directly or wrapped in water-filled phantoms. Single-crystal NaI detectors (50×50×4 mm) were positioned at 7 cm from the center of the system (at the center of the detector plane). Various setups were simulated, with no collimator present in the system, or using simplified tungsten collimator plates with a thickness of 4 cm. The collimator plates had 1 or 20 lothole openings (a gradual change from a circular aperture to a rectangular end).

Results:
First results show a small effect of the high-energy γ-rays from the 188Re emission spectrum in the optimal energy window around 155 keV. However, a decrease of the spatial resolution in these small systems may be caused by penetration of high-energy photons or by the primary β- particles reaching the detector. Scatter of the photons in phantoms (8 % of the detected events in the energy window 155 ± 20 keV), crystal detectors (13 %) or the back compartment of the gamma-camera (5 %) is more important than the scatter in the collimator (2 %). These results will be confirmed by simulations with higher number of simulated particles and by phantom studies on small animal imaging SPECT systems.

Conclusion:
Obtained results are promising for usage of 188Re as a theranostic agent - both for the therapy and imaging - without the necessity of administration radiopharmaceuticals with pure diagnostic radionuclides.
Title: Effective dose estimation and relation to BMI in FDG PET/CT scans.

Aim: To determine the relationship of body mass index (BMI) with patient effective dose in FDG PET/CT scans.

Methods: The PET/CT images of 112 consecutive patients were reviewed. The study focused on diagnostic high-dose CTs of trunk (neck, chest, abdomen and pelvis) and head-trunk. Eighty-four patients of 112 were included in the study, subdivided in 42 trunk and 42 head-trunk scans. To obtain the total patient PET/CT effective dose (PET/CT-ED), we calculated the PET effective dose (PET-ED) from the administered activity (MBq), given both by the Medrad® Intego FDG Infusion System and calculation with the conversion factor from ICRP-106.[2] The CT effective dose (CT-ED) was calculated using the dose-length product (DLP) and the conversion factors for CT from ICRP-103.[1] BMI was documented for each patient and was compared with the effective dose.

Results: The mean BMI was 26.7 kg/m². The mean PET-ED, CT-ED and PET/CT-ED were 3.5 mSv, 13.3 mSv and 16.7 mSv respectively. In all three, the effective dose increased linear with increasing BMI (P < 0.001). By analyzing the graphs, we noticed that the difference in PET-ED, CT-ED and PET/CT-ED between the lowest BMI and highest BMI was factor 3 in head-trunk scans and factor 3.5 in trunk scans. The ratio CT-ED / PET-ED approaches 4.5:1 in head-trunk scans and 4:1 in trunk scans and CT-ED is responsible for 4/5 of the PET/CT-ED in (head-)trunk scans.

Discussion: The difference between Medrad®-PET-ED and manually calculated PET-ED is significant (P < 0.001). An update of the conversion methods for the infusion system is absolutely necessary. Furthermore, caution has to be taken to compare the calculated ED from CT and PET, since both were calculated with other conversion factors, ICRP-103 and ICRP-106 respectively. Nevertheless, it seems that CT could be responsible for 4/5 of the ED in patients undergoing diagnostic PET/CT investigations. We expect that in patients who had a recent diagnostic CT, a low dose non-diagnostic CT scan could help lowering the patient dose with limited impact on the diagnostic performance, but this was not yet the primary objective of this abstract.

Conclusion: Increasing BMI significantly increases the effective dose received from PET, CT and PET/CT trunk and head-trunk scans. More data should be collected we can subdivide our patient group in a normal weight, overweight and obese category for evaluating if there is a significant difference in effective dose between those groups.
Fig 1: PET/CT effective dose against BMI in head and trunk scans

Fig 2: PET/CT effective dose against BMI in trunk scans


Abstract category
☒ Radiochemistry & radiopharmacy

Title:
Labeling of an anti-HER2 nanobody with the α-particle emitter bismuth-213: in vitro and in vivo evaluation

Authors (name and surname) and affiliation number (presenting author underlined):

Yana Dekempeneer¹,², Vicky Caveliers²,³, Dominic Maertens¹, Mireille Gysemans¹, Maarten Ooms¹, Tony Lahoutte²,³, Catarina Xavier⁴, Peter Covens⁵, Frank Bruchertseifer⁶, Alfred Morgenstern⁵, Thomas Cardinaels¹,⁴*, Matthias D’Huyvetter⁵.

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Abstract body:

This study investigates a novel targeted therapy which combines the α-emitter bismuth-213 (213Bi) and a HER2-targeting nanobody (Nb) to selectively kill HER2pos metastases in breast- and ovarian cancer. The use of Nbs as vehicles in TAT is promising due to their excellent in vivo properties, high target affinity and specificity, and their fast diffusion and clearance kinetics. Moreover, Nbs show good tumor penetration due to their small size of about 15 kDa. The aim of this study is to develop and evaluate the in vitro binding characteristics, the in vitro stability and cytotoxicity and the in vivo biodistribution of [213Bi]DTPA-Nb.

Methods:
First, a 213Bi-labeled-Nb was developed using an 225Ac/213Bi generator where the 225Ac was obtained from a Th-source of SCK•CEN and from the Institute for Transuranium Elements (Karlsruhe). p-SCN-Bn-CHX-A”–DTPA was used as bifunctional chelator for complexing 213Bi and conjugating the complex to the anti-HER2 Nb. In vitro saturation binding assay, clonogenic assay, IncuCyte® live cell imaging and double strand break ex vivo immunofluorescence staining were performed on HER2pos cells to determine the affinity and cytotoxicity of [213Bi]DTPA-Nb. The biodistribution of [213Bi]DTPA-Nb was analyzed in relevant mouse models. Results: Under optimized labeling conditions, [213Bi]DTPA-Nb remained stable up to 100min with a radiochemical purity ≥95% in PBS at room temperature and 37 °C. In vitro, [213Bi]DTPA-Nb bound HER2pos SKOV-3 cells in a HER2-specific way (KD of 5.06 ± 1.19 nM). High tumor uptake (4.5 ± 0.7%ID/g) was reached 15 min after injection of [213Bi]DTPA-Nb in HER2+ tumor-bearing mice. Extremely low uptake values were observed in normal tissues at all time points. [213Bi]DTPA-Nb was excreted via the kidney into the urine, leading to significant kidney retention of the radioconjugate of 59.9 ± 5.1%ID/g after 60 min (Fig. 1A). Co-infusion of 150mg/kg gelofusine resulted in a 2-fold reduction in kidney uptake (Fig. 1B). The injection of unlabeled anti-HER2 Nb 30 min prior to injection of [213Bi]DTPA-Nb reduced the tumor uptake by 50% and a significant decrease in double strand DNA damage was observed compared to the group that did not receive a pre-injection.

Conclusion:

Here we describe for the very first time the successful labeling of an anti-HER2 Nb with an α-emitter, 213Bi, using a DTPA derivative, resulting in high yields with excellent preservation of affinity for its HER2 target and high in vivo stability and high tumor-to-background ratios. Future work will aim at further characterizing [213Bi]DTPA-Nb with regard to defining the maximum tolerated dose, short- and long-term toxicity as well as therapeutic efficacy studies.
Figure: In vivo biodistribution of [213Bi]DTPA-Nb (A) and of [213Bi]DTPA-Nb + coinfusion of gelofusine (B) 15 min, 30 min, 60 min and 90 min after injection. A more detailed comparison between [213Bi]DTPA-Nb with and without gelofusine for kidney, tumor and blood (C).
BelNuc Liege 2019 Symposium: PHARM 02

Abstract category
Radiochemistry & radiopharmacy

Title:
Understanding the radiobiology of targeted radionuclide therapy with ¹⁷⁷Lu-DOTATATE

Authors (name and surname) and affiliation number (presenter author underlined):
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Abstract body:

Aim
Several parameters affecting radiosensitivity have been investigated, namely proliferation rate, metabolism, cell cycle, DNA repair, chromatin compaction, hypoxia and oxidative stress. Their importance in radiobiology stems from external beam radiotherapy (EBRT) studies and is mostly related to direct DNA damage. However, when using targeted radionuclide therapy with low-LET β- emitter (e.g., Lutetium-177 (¹⁷⁷Lu)), generation of ROS is more likely to occur hence also affecting cell redox-balance and viability. Our aim is to investigate whether these parameters are predictors of sensitivity to ¹⁷⁷Lu-DOTATATE in somatostatin receptors (SSTR) expressing tumors.

Materials & Methods
Human cancer cell lines were selected for their different intrinsic radiosensitivities to EBRT: HBL and MM162 (melanoma-radioresistant), COLO-677 and EJM (multiple myeloma-radiosensitive), MIA-PACA-2 and HT-29 (pancreatic and colon carcinoma-intermediate radioresistance). SSTR expression was assessed by qRT-PCR and immunocytochemistry and its functionality by binding/uptake assays with ¹⁷⁷Lu-DOTATATE. The radiosensitivity parameters were evaluated by means of MTT assay, 18FDG uptake, qRT-PCR of antioxidant enzymes and glutathione and ROS quantification. Effect of ¹⁷⁷Lu-DOTATATE on cell viability was assessed at day 1-3-6 using MTT assay.

Results
SSTR expression and ¹⁷⁷Lu-DOTATATE uptake was present in all cell lines. Cell survival after ¹⁷⁷Lu-DOTATATE treatment was time and radioactivity dependent. At day 6 it was significantly reduced in all cell lines (COLO-677: 64±9%, EJM: 41±20%, MIA-PACA-2: 50±15%, HBL: 22±9%, MM162: 24±6%) except in HT-29 (2±13%). Interestingly, MM162 and HT-29 had either the highest expression of antioxidant enzymes (HT-29) or the highest glutathione level (MM162) compared to the other cell lines. In addition, H2O2 was not able to induce ROS in MM162 and HT-29, whereas ROS levels were doubled in the most sensitive cell line COLO-677. The other radiosensitivity parameters were not found to be significantly associated with cell survival.

Conclusion
Our results showed the presence and the functionality of SSTR and differences in radiosensitivity parameters in all cell lines. Although all these characteristics are likely to affect response to radionuclide therapy, high antioxidant defenses was associated with a higher survival after ¹⁷⁷Lu-DOTATATE treatment. Therefore and in this context of metabolic radiotherapy, oxidative stress must be considered along with DNA damage assessment.
Development and evaluation of selective PET probes for imaging of caspase-3 activity.

Lucas Beroske1,2, Cheima Amrouch1,2, Angelo Solania1, Pieter Van der Veken1, Sigrid Stroobants1,2, Dennis W. Wolan3, Leonie Wyffels1,2, Filipe Elvas1,2,4

Authors affiliation:
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2. Department of Nuclear Medicine, Antwerp University Hospital, Antwerp, Belgium;
3. Departments of Molecular and Experimental Medicine and Chemical Physiology, The Scripps Research Institute, La Jolla, California, USA;
4. Laboratory of Medicinal Chemistry, University of Antwerp, Antwerp, Belgium.

Abstract body:
Despite rapid advancements in oncology with revolutionary treatments such as immunotherapy, tumor progression and treatment response are still evaluated by monitoring tumor morphology. Since changes in tumor size can take weeks to months to be visible, patients may experience unnecessary side effects, especially in the case of non-responders. Therefore, the development of an efficient and non-invasive method for the objective and accurate evaluation of tumor response to therapy is of the utmost importance. A multitude of anti-cancer therapies rely on targeted induction of apoptosis to exert their therapeutic effect. Caspase-3 is the main executor of apoptosis, making it an attractive target for cell death imaging. Recently, fluorescent activity-based probes (ABPs) containing unnatural amino acids in their peptide structure have shown good selectivity for caspase-3 over other caspases. When fitted with a warhead, the probe affinity and selectivity for caspase-3 was improved. However, not much is known about cell permeability of these probes. Our aim was to compare the kinetic properties and uptake of MICA-304 and MICA-309 (non-methylated and methylated probes, respectively).

The ABP precursors contain a terminal alkyne for click radiolabeling. [18F]FEA was reacted with the alkyne precursors to obtain the radiotracers. They were purified by HPLC and formulated for in vitro experiments. HeLa cells were pre-incubated with MICA-309 or the pancaspase inhibitor Z-VAD-FMK before treatment with the pro-apoptotic molecule staurosporine. Caspase activity of the cell lysates was quantified by a fluorogenic assay. The same experimental setting will be used with MICA-304. Moreover, the IC50 of the tracers will be determined by incubating them with a panel of caspases along with their fluorescent substrates.

Click radiolabelling gave the [18F]-labeled ABPs in 20.8 ± 11.5% (n=6, decay-corrected) and 8.3 ± 3.4% (n=5, decay-corrected) isolated radiochemical yield for [18F]MICA-304 and [18F]MICA-309, respectively. Lipophilicity of the methylated probe [18F]MICA-309 (logD = 1.81 ± 0.13) was higher than [18F]MICA-304 (logD = -1.78 ± 0.002). MICA-309 was able to penetrate the cell and inhibit caspase activity. After 1h, slight inhibition was observed whereas partial caspase inhibition was observed after 5h. These results may indicate low cell penetration or slow cleavage of the ester to obtain the active tracer.

The caspase-3 ABPs developed here showed promising results for cell death imaging by targeting caspase-3. Future plans include in vivo studies to investigate biodistribution and tumor uptake following apoptosis-inducing therapy.

Acknowledgments
Financed by DOCPRO (36838), University of Antwerp and a FWO post-doctoral grant (12T8818N).
Abstract category
☒ Radiochemistry & radiopharmacy

Title:
Comparison of \([\text{^{68}}\Gamma\text{Ga}]\text{PSMA-11} \) and \([\text{^{18}}\Gamma\text{F}]\text{PSMA-11} \) for in vivo PET/CT imaging of prostate cancer

Authors (name and surname) and affiliation number (presenter author underlined):
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Abstract body:
Prostate specific membrane antigen (PSMA) is highly overexpressed in prostate cancer (PCa). In recent years, many PSMA targeting tracers have been developed, including \([\text{^{68}}\Gamma\text{Ga}]\text{PSMA-11} \) and more recently \([\text{^{18}}\Gamma\text{F}]\text{PSMA-11} \) which has superior imaging characteristics such as a longer half-life and lower positron energy. Therefore, \([\text{^{18}}\Gamma\text{F}]\text{PSMA-11} \) is expected to visualize smaller lesions, provide a more precise delineated tumour border and higher SUV values compared to \([\text{^{68}}\Gamma\text{Ga}]\text{PSMA-11} \).

Male athymic mice were inoculated with \(5 \times 10^5 \) LNCaP cells (PSMA positive) or \(5 \times 10^5 \) PC3 cells (PSMA negative) suspended in \(100 \mu\text{L} \) FBS free medium and \(100 \mu\text{L} \) Matrigel\(^\text{TM} \). 5-6 weeks after inoculation, all mice received 2 dynamic PET/CT scans of 2.5h after IV injection of 3.7 MBq \([\text{^{68}}\Gamma\text{Ga}]\text{PSMA-11} \) or 3.7 MBq \([\text{^{18}}\Gamma\text{F}]\text{PSMA-11} \). For tumour confirmation of PSMA negative PC3 tumours, static \([\text{^{18}}\Gamma\text{F}]\text{FDG} \) PET/CT scans were performed. After the last scan, mice were sacrificed and tumours were removed for immunohistochemical evaluation.

In PSMA positive LNCaP tumours, SUV values 60 min post injection for \([\text{^{68}}\Gamma\text{Ga}]\text{PSMA-11} \) (0.89 ± 0.11) and \([\text{^{18}}\Gamma\text{F}]\text{PSMA-11} \) (1.71 ± 0.37) were significantly different (p-value = 0.0294). The optimal time point for scanning was determined at 20 min post injection for \([\text{^{68}}\Gamma\text{Ga}]\text{PSMA-11} \) and 60 min post injection for \([\text{^{18}}\Gamma\text{F}]\text{PSMA-11} \). In the PSMA negative control group, no significant difference in uptake was seen between the two PSMA tracers (p-value = 0.342), but tumour visualization was possible with \([\text{^{18}}\Gamma\text{F}]\text{FDG} \) (SUV 0.79 ± 0.20). Immunohistochemical staining confirmed PSMA expression on LNCaP tissue and its absence on PC3 tissue.

\([\text{^{18}}\Gamma\text{F}]\text{PSMA-11} \) is possibly a superior radiotracer for imaging of small PSMA positive PCa lesions. Further investigation in a phase 3 clinical trial will be conducted.
Abstract category
 Radiochemistry & radiopharmacy

Title:

Authors (name and surname) and affiliation number (presenter author underlined):
Jeroen Verhoeven1, Glenn Pauwelyn1, Tristan Baguet1, Sarah Piron1, Valerie De Meulenaere2, Sam Donche3, Ken Kersemaens3, Benedicte Descamps4, Christian Vanhove4, Ingeborg Goethals3, Filip De Vos1.

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Abstract body:
The differentiation between brain tumor recurrence and radiation necrosis remains a diagnostic challenge because they share a similar appearance on conventional magnetic resonance imaging (MRI). Metabolic imaging, such as positron emission tomography (PET), may provide additional functional and biochemical information. In this study, the potential of [18F] FDG, [18F]FET and 2-[18F]FELP PET in discriminating glioblastoma from radionecrosis in rat was investigated.

Induction of radionecrosis was achieved by irradiating the left frontal region by means of the small animal radiation research platform with 60 Gy by using three arcs with a beam aperture of 3 x 3 mm². When radionecrosis was visible on MRI, F98 glioblastoma cells were inoculated in the contralateral hemisphere of the animal. Dynamic PET imaging with [18F]FDG, [18F]FET, and 2-[18F]FELP, as well as [18F]FDG PET at a delayed time interval (240 min postinjection), were performed on three consecutive days.

On the [18F]FDG PET images, the SUVmax and maximum lesion-to-normal ratio (LNRmax) were significantly higher in GB compared to RN. The difference SUVmean, SUVmax, LNRmean and LNRmax were all significantly different between GB and RN on the late [18F]FDG PET scans. No differences were found for [18F]FET PET between GB and RN, while only the SUVmax and TBRmax were significantly different based on the 2-[18F]FELP images. Our results suggest that using semi-quantitative parameters like SUV and LNR can be used for the distinction of RN and GB with (late) [18F]FDG and 2-[18F]FELP PET, while this was not possible with [18F]FET.
Title:
PET quantification of [18F]MPPF in the canine brain using blood input and reference tissue modelling.

Authors (name and surname) and affiliation number:
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Abstract body:

Introduction and aim:
Numerous studies have shown that the serotonin1A (5-HT1A) receptor is implicated in the pathophysiology and treatment of several psychiatric and neurological disorders. Furthermore, functional imaging studies in a variety of species have demonstrated that 4-(2’-Methoxyphenyl)-1-[2’-(N-2’-pyridinyl)-p-[18F]fluorobenzamidoethylpiperazine ([18F]MPPF) is a valid and useful PET tracer to visualize the 5HT1A receptor. However, to our knowledge, [18F]MPPF has never been demonstrated in the canine brain. The ability to image the 5HT1A receptor with PET in dogs could improve diagnosis and therapy in both canine and human behavioural and neuropsychiatric disorders.

Materials and methods:
To examine the potential use of [18F]MPPF in dogs, five healthy adult laboratory beagles underwent a 60-minutes dynamic PET scan with [18F]MPPF while arterial blood samples were taken. For each region of interest, total distribution volume (VT) and corresponding binding potential (BPND) were calculated using the 1-tissue compartment model (1-TC), 2-Tissue compartment model (2-TC) and Logan plot. The preferred model was chosen based on the goodness-of-fit, calculated with the Akaike information criterium (AIC). Subsequently, the BPND values of the preferred compartment model were compared with the estimated BPND values using three reference tissue models (RTMs): the 2-step simplified reference tissue model (SRTM2), the 2-parameter multilinear reference tissue model (MRTM2) and the Logan reference tissue model.

Results and conclusions:
After a bolus injection of [18F]MPPF, high radioactive uptake was found in all brain regions of interest followed by a rapid washout. The pattern of [18F]MPPF uptake into the brain corresponded well to the known distribution of the 5HT1A receptor observed in human, rodent and cat studies. In accordance to the clinical study of Costes et al., a rapid metabolism of [18F]MPPF to polar metabolites was observed; 21 ± 4 % of unmodified [18F]MPPF was found after ten minutes and declined to 7 ± 2 % at 40 minutes. According to the lower AIC values of the 2-TC model compared to the 1-TC in all ROIs, the 2-TC model showed a better fit. Calculating BPND using reference tissue modelling demonstrated high correlation with the BPND obtained by metabolite corrected plasma input 2-TC. Based on the highest correlation values (R²=0.999) with the 2-TC model, the Logan reference model and MRTM2 model would be the models of choice, but a small enlargement correlating to the BPND levels should be mentioned for both models. An excellent alternative would be the SRTM2 model, which doesn't have this dependency and showed also a very good correlation (R²=0.982) with the 2-TC model.

Conclusion:
This study indicates the results of a bolus injection with [18F]MPPF in dogs are consistent with the observations presented in the literature for other animal species and humans. The kinetics of [18F]MPPF in the canine brain could be best described by a 2-TC model. Furthermore, for future experiments, compartmental modelling using invasive blood sampling could be replaced by RTMs, using the cerebellum as reference region. This could be of great value for future experiments analysing the function of the 5HT1A receptor, improving both diagnosis and therapy in canine and human behavioural and neuropsychiatric disorders.
Fig 1A-1E. Method comparisons. Graphical comparison of each kinetic model to the 2-TC model presented as a regression analysis (column 1) and a Bland and Altman plot were differences are presented as percentage (bold line: mean, dotted line: ± SD) (column 2). 4A: 1-TC model vs 2-TC model; 4B: 2-TC model vs Logan Plot; 4C: 2-TC model vs Logan reference model; 4D: 2-TC model vs SRTM2 model; 4E: 2-TC model vs MRTM2.
**BELNUC LIEGE 2019 SYMPOSIUM: TECH 01**

**Abstract category**
- Technologist

**Title:**
Patient experience and information, quality partners

**Authors (name and surname) and affiliation number (presenter author underlined):**
Vandermeiren Géraldine Belnuc id: 1031

**Authors affiliation:**
Division of Nuclear Medicine and Oncological Imaging, Department of Medical Physics, CHU of Liege, Liege, Belgium

**Abstract body:**
Presentation of the results of a statistical study carried out at the University Hospital of Liège in 2018 by a nurse in advanced practices in nursing.
This study wanted to determine what information could impact the patient experience when performing a myocardial perfusion scintigraphy.

**BELNUC LIEGE 2019 SYMPOSIUM: TECH 02**

**Abstract category**
- Technologist

**Title:**
After having determined the most irradiant moment in a TEP-SCAN, is the ring dosimeter show an interest for the technologists?

**Authors (name and surname) and affiliation number (presenter author underlined):**
Gomez Louis\(^1\), Greffe Jean-Louis\(^1\), Costalonga Vésio\(^1\)

**Authors affiliation:**
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**Abstract body:**
A statistical analysis of the whole body and ring dosimetric results in 2017 of the TEP-scan team of Gilly has been done. This study shows that the injection work station is more irradiating that the console work station and the most irradiant step is the patient installation at the console work station. In comparison with the national standard, the limite of 20 mSv whole body isn't exceeded by technologists just like those of 500mSv for the extremities. The raised dose at the fingers extremities is lower than this limit. Hence, we can conclude that the radiation protection in TEP-scan is sufficiently optimized to work without using dosimeter ring.
BELNUC LIEGE 2019 SYMPOSIUM: TECH 03

Abstract category
□ Technologist

Title:
Analysing routine working procedures in hot labs in three European countries

Authors (name and surname) and affiliation number (presenter author underlined):

Authors affiliation:
1. Odisee vzw
2. Tampereen Ammattikorkeakoulou Oy
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Abstract Body:

Background
Previous research showed that doses to the hands and fingers of technologists preparing radiopharmaceuticals can be quite high, exceeding the annual dose limits. Recommendations to reduce radiation exposure for standard nuclear medicine procedures were developed. Despite these efforts, differences in preparing and administering radiopharmaceuticals still exist.

Aim
An inventory of daily routine in nuclear medicine hot labs in three European countries (Slovenia, Finland, Belgium) is made, focusing on working procedures, and finger dose.

Materials and methods
Ten departments of nuclear medicine were selected to participate in the project. In every department, between one and three trained technologists were selected to participate. All nuclear medicine departments were invited to participate from their national professional bodies, 15 technologists participated in the study.
The participating technologists were asked to film the different manipulations during their daily routine, while preparing radiopharmaceuticals. These films were analyzed using a checklist based on the human health campus of the IAEA, with a focus on sterility and radiation protection. A score was given on 56 items during the different stages. All technologists were wearing finger dosimeters over a period of two weeks to see if a correlation can be found between the procedures used and the dose to the fingers.

Results and discussion
In the three countries 57% scores were positive, in Belgium this score was 47%. This means that in the three countries 43% of the manipulations in the hot lab did not comply with the checklist. For some items nearly none of the participants complied with the checklist. When only the manipulations related to radiation safety are considered 51% of all participants and 38% of the Belgian technologists comply with the checklist. Regarding the manipulations related to sterility 46% of all technologists and 32% of the Belgian technologists complied to the checklist. These last figures ask for some attention, since there is a strong urge for sterility.

Conclusions and work in progress
The results of this inventory show there is reason to evaluate daily routine in the hot lab in the participating countries. The results show that the checklist, based on the human health campus of the IAEA, possibly could take an update. An online refresher course on daily routine in the hot lab is presented to the participating technologists. We expect to have data on the impact of this course on daily routine at the participating departments in autumn 2019.
**Title:**
Following the FDG PET/CT guidelines: a critical review of 6 consecutive days in our new PET/CT department.

**Authors (name and surname) and affiliation number (presenter author underlined):**
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**Abstract body:**

**Aim**
We checked FDG activity administration, waiting time between injection and imaging and SUVmax (standardized uptake value) in normal liver and lungs in 85 consecutive patients who were sent to our department for a whole body FDG PET/CT image. We wanted to see if the planned activity and waiting time were feasible and determine the SUVmax in liver and lung VOI’s (volume of interest) in regions without known lung or liver disease.

**Methods**
FDG activity was calculated using the formula within the FDG PET/CT EANM procedure guidelines version 2.0 (https://www.eanm.org/publications/guidelines/2015_GL_PET_CT_TumorImaging_V2.pdf). Waiting time was supposed to be 60 minutes and was calculated from the difference between injection time and scan time, both recorded in the electronic patient file and PACS. VOI’s of minimal 20 ml were drawn on the right liver lobe and right lung in the software package syngo.via® version 2016 and PET/CT was performed on a Siemens Biograph mCT Flow 40, installed March 2018.

**Results:**
The activities administered ranged from 91 MBq to 417 MBq and were plotted against the patient weight (Fig 1), the relation was exponential, as expected from the guidelines formula. SUVmax mean ± standard deviation calculated from liver and lung was 3.91 ± 0.67 and 0.93 ± 0.29 respectively, Box and whisker plots with quartiles are in Fig 2 and 3. 50% of the patients were scanned between 59 and 61 minutes and over 90% of the patients were scanned between 55 and 65 minutes, blue bars proportions and red cumulative percentage curve in Fig 4.

**Conclusion**
Activities were exponential for higher weighted patients, SUVmax in normal liver and lung were around 4 and 1 respectively and patient waiting time was acceptable, but could be further approved by better time registration and automatic injection device.
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