
OFFICIAL PROGRAM

ABSTRACT BOOK

MAY 6 - 8TH 2022

21ST SYMPOSIUM

OF THE BELGIAN SOCIETY OF NUCLEAR MEDICINE

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Access the most recent program
and updates on www.belnuc22.be/info



WELCOME

Dear colleagues and friends,

The BELNUC symposium is going live again after three years of waiting. As president of BELNUC, it is with great pleasure that I welcome you to our '22 Symposium in Antwerp.

Aside from our desire to taste new scientific content, work on our professional development in a lifelong learning attitude, the social aspect and networking will deserve a prime place as well, at last.

We have kept the format as you know it, with general sessions on novel scientific and clinically highly relevant developments, lectures by national and international top experts, in depth and parallel break-out sessions for all Medical, Technologist, Physics and Radioharmacy tracks. The Young Nuclearist Challenge will again be one of the highlights where new talent will take the stage.

The future of nuclear medicine, both in diagnostics and therapeutics is brighter than ever, with many challenging opportunities for each of us. Based on scientific rigor and medical art, our multidisciplinary identity will ensure this future with the synergy that is so characteristic of our community.

On behalf of the BELNUC board, I wish you a successful conference. Let's make new plans and friends!



Prof. dr. Koen Van Laere
BELNUC President

PROGRAM OVERVIEW

FRIDAY, MAY 6, 2022

	MEDICAL	PHARMACY	PHYSICS	TECHNOLOGISTS	EXHIBITION	REGISTRATION	
	Green+Blue	Orange	Yellow	Red+Purple	Hall 4	Foyer	
18:00 19:00						Registration	18:00 19:00
19:00 21:00	„GE Satellite symposium: Precision imaging at the speed of tomorrow“					Registration	19:00 21:00
21:00 23:00					Opening reception	Registration	21:00 23:00

SATURDAY, MAY 7, 2022

7:30 8:30						Registration	7:30 8:30
8:30 8:45	Welcome address					Registration	8:30 8:45
9:00 10:30	Plenary opening session The role of PET in demen- tia: current clinical use and novel targets for the near future			Clinical update	Industry Exhibition	Registration	9:00 10:30
10:30 11:00					Coffee break	Registration	10:30 11:00
11:00 12:00	Proffered papers	GMP, quality and regula- tions Proffered papers	AI: from hype to medical physics?	Clinical management	Industry Exhibition	Registration	11:00 12:00

PROGRAM OVERVIEW

12:00 13:00					Lunch break	Posters	Registration	12:00 13:00
13:00 14:00	Reimbursement of ra- dionuclide therapies in Belgium				Industry Exhibition			13:00 14:00
SATURDAY, MAY 7, 2022								
14:00 15:30	Upcoming technologies	F-18 and C-11 chemistry Proffered papers	Applications of AI in nuclear medicine	Radionuclide therapy	Industry Exhibition	Registration	14:00 15:30	
15:30 16:00					Coffee break	Registration	15:30 16:00	
16:00 17:20	Young Nuclearist Chal- lenge	Theranostics + Proffered papers	Isotopes of the future + Proffered papers	FANC session + Proffered papers	Industry Exhibition	Registration	16:00 17:20	
17:30 18:30	Keynote lecture + BELNUC Awards					Registration	17:30 18:30	
19:00	Shuttle bus to social event							19:00
SUNDAY, MAY 8, 2022								
8:30 9:00						Registration	8:30 9:00	
9:00 10:00	Clinical state of PET/MR				Industry Exhibition	Registration	9:00 10:00	
10:00 10:30					Coffee break	Registration	10:00 10:30	
10:30 12:00	Are we ready for artificial intelligence?				Industry Exhibition	Registration	10:30 12:00	
12:00 12:10	Closing session						12:00 12:10	

THANK YOU TO OUR PARTNERS



VENUE



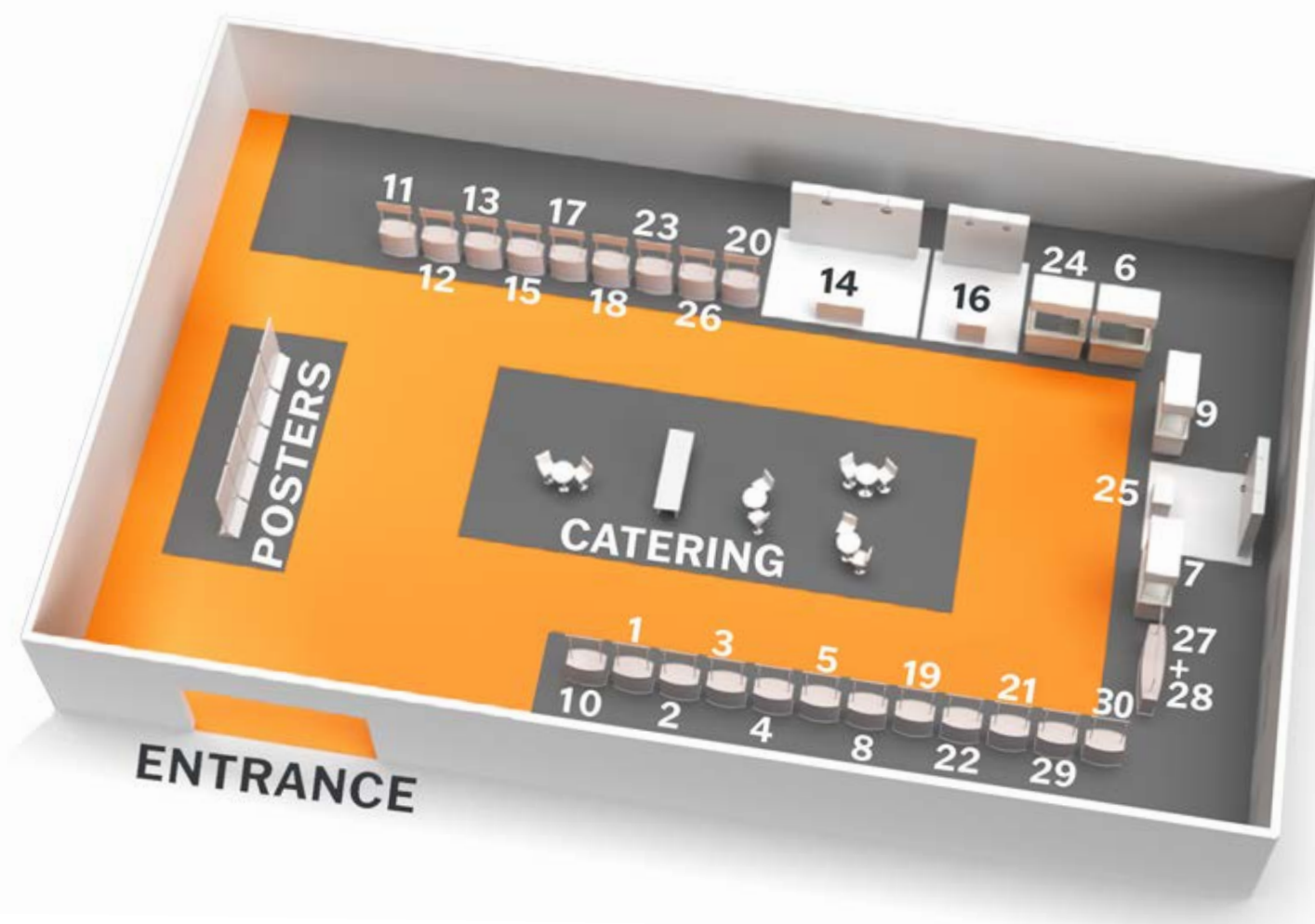
INDUSTRY EXHIBITION

01 - MIE Medical Imaging
Electronics GmbH

02 - ITM Medical isotopes GmbH

03 - Scannix

04 - IBA



05 - Hermes Medical Solutions

06 - MIM Software Inc

07 - Sirtex

08 - Trasis

09 - Siemens Healthcare SA/NV

10 - Mirion Technologies

11 - IRE-ELiT S.A.

12 - MILabs B.V.

13 - Elysia S.A.

14 - GE Healthcare

15 - IMA-X

16 - Curium Belgium B.V. & PI Medical
Diagnostic Equipment B.V.

17 - Comecer S.p.A.

18 - EANM (European Association of
Nuclear Medicine)

19 - OncoSil Medical

20 - Diagnostic Imaging Belgium srl

21 - Bayer

22 - Charles River Laboratories

23 - RQS Alexander Ruffani

24 - Advanced Accelerator
Applications Benelux,
a Novartis company

25 - Terumo Europe NV

26 - Mediso Medical Imaging Systems

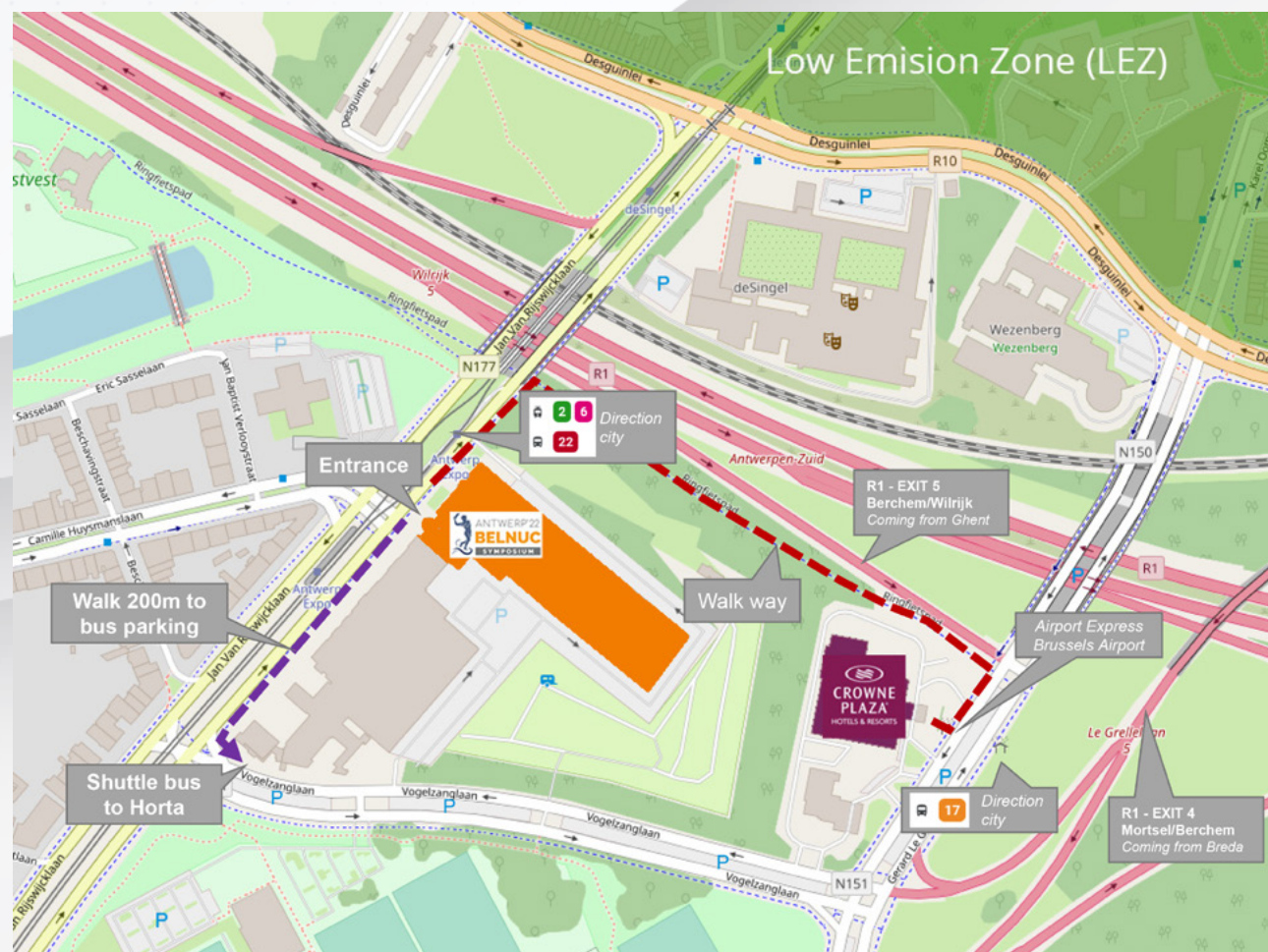
27 - Telix Innovations NV

28 - Telix Seneffe

29 - Van Overeem Nuclear

30 - Spectrum Dynamics Medical SA

AREA MAP



CLINICAL SYMPOSIUM

GE Healthcare @ BELNUC 2022 - Antwerp Expo

CLINICAL SYMPOSIUM - Friday May 6th • 19h15 - 21h00

Precision imaging at the
speed of tomorrow.

Building a world that works



FRIDAY MAY 6, 2022

18:00 - 19:00: Registration	Foyer
19:00 - 19:15: Welcome by BELNUC President	Green+Blue
19:15 - 21:00: GE satellite symposium	Green+Blue
21:00 - 23:00: Opening reception	Hall 4

SATURDAY MAY 7, 2022

08:30 - 08:45 Welcome address by BELNUC President	Green+Blue
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MEDICAL

9:00 - 10:30: The role of PET in dementia : current clinical use and novel targets for the near future	Green+Blue
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Moderators: Koen Van Laere and Thierry Vander Borght

09:00 - 09:40	Clinical PET in dementia : an update on FDG and amyloid Prof. Eric Salmon (BE)
09:40 - 10:10	Advances in tau imaging : ready for clinical use ? Prof. Alexander Drzezga (DE)
10:10 - 10:30	Synaptic density in dementia : a better marker than FDG ? Prof. Koen Van Laere (BE)

10:30 - 11:00: Coffee break	Hall 4
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11:00 - 12:00: Proffered papers	Green+BlueM
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Moderators: Géraldine Gebhart and Tim Van den Wyngaert

11:00 - 11:10 | [¹⁸F]AlF-NOTA-octreotide vs. [⁶⁸Ga]Ga-DOTA-somatostatin analogue PET in neuroendocrine tumour patients: interim results of a prospective multicentre trial.
Elin Pauwels (UZ Leuven, Leuven)

11:10 - 11:20 | Yttrium-90 radioembolization versus drug-eluting beads chemoembolization for unresectable hepatocellular carcinoma: results from the TRACE trial.
Bieke Lambert (UGent, Gent)

11:20 - 11:30 | Comparison between Peptide Receptor Radionuclide Therapy with ¹⁷⁷Lu-DOTATATE and external beam radiation therapy.
Wendy Delbart (Institut Jules Bordet, Anderlecht)

11:30 - 11:40 | 3p-C-NETA-TATE: A versatile somatostatin analogue for Al¹⁸F-labeled and therapeutic SSTR2 targeting radiopharmaceuticals.
Stephen Ahenkorah (SCK CEN, Mol)

11:40 - 11:50 | Disturbing the redox balance as a new radiosensitizing strategy for Peptide Receptor Radionuclide Therapy with ¹⁷⁷Lu-DOTATATE.
Wendy Delbart (Institut Jules Bordet, Anderlecht)

11:50 - 12:00 | Bone SPECT/CT for assessing persistent or recurrent pain post spondylodesis: a retrospective study and pattern analysis.
Bieke Lambert (AZ Maria Middelaes, Gent)

12:00 - 13:00: Lunch break	Hall 4
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12:00 - 14:00: Poster viewing	Hall 4
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13:00 – 14:00: Reimbursement of radionuclide therapies**Green+Blue**Moderators: Patrick Flamen and Christophe Deroose

- 13:00 - 13:30 **Actual status of reimbursement of RNT and need for revision**
Prof. Patrick Flamen (Institut Jules Bordet, Anderlecht)
- 13:30 - 14:00 **Proposal for upgrade of reimbursement of RNT (results of the meeting of the BELNUC WG Therapy)**
Prof. Christophe Deroose (UZ Leuven, Leuven)
- 13:30 - 14:00 **Interactive panel discussion**
Surf to sli.do and submit your question (event code #336573)

14:00 - 15:30: Upcoming technologies**Green+Blue**Moderators: Cédric Reichel and Nadia Withofs

- 14:00 - 14:45 **Is total body PET/CT here to stay? An investigation into clinical applications of a new imaging technique**
Prof. Stefaan Vandenberghe (BE)
- 14:45 - 15:30 **What to expect from annular SPECT/CT. A clinical center's opinion.**
Dr. Matthieu Bailly (FR)

15:30 - 16:00: Coffee break**Hall 4****16:00 - 17:20: Young nuclearist challenge****Green+Blue**Moderators: Félicie Sherer and Sander Jentjens

- 16:00 - 16:10 | **The nerve-racking case of [¹⁸F]PSMA-1007 PET/CT in a patient with continuous low back pain.**
Anne-Leen Deleu (UZ Leuven, Leuven)
- 16:10 - 16:20 | **Breaking the oculo-(para)neoplastic reflex on FDG-PET/CT: cerebellar hypermetabolism in a Hodgkin lymphoma leads to an unexpected diagnosis.**
Eef Vanerwegen (Imelda Hospital, Bonheiden)
- 16:20 - 16:30 | **"Looks like the raccoon sign..." "Baboon?" "No, RACCOON!!!"**
Lynn De Mey (UZ Brussel, Brussels)
- 16:30 - 16:40 | **Just a little RE(nal)SPECT.**
Geraldine Lens (UZ Leuven, Leuven)
- 16:40 - 16:50 | **Progestin-associated meningiomas: raising awareness about a causal oncological association.**
Amélie Castiaux (Institut Jules Bordet, Anderlecht)
- 16:50 - 17:00 | **Idiopathic SIADH: 4 years of diagnostic wandering.**
Omar Mzaiti (CHU Liège, Liège)
- 17:00 - 17:10 | **¹⁸F-FDG PET/CT unveils a cyst with a twist.**
Pieter Claes (Ziekenhuis Oost-Limburg, Genk)
- 17:10 - 17:20 | **Femoral osteonecrosis in the setting of myelodysplastic syndrome with blasts excess.**
Isaac Kargar Samani (CHU UCL Namur - Site Godinne, Yvoir)

17:30 - 18:30: Keynote lecture + BELNUC awardsModerators: Sophie Bourgeois and Géraldine Gebhart

- 17:30 - 18:15 **Keynote lecture: Cancer molecular imaging and immunotherapy**
Prof. Elisabeth de Vries (NL)
- 18:15 - 18:30 **BELNUC award ceremony**

PHARMACY**11:00 - 12:00: GMP, quality and regulations + proffered papers****Orange**Moderators: Filip De Vos and Dominique Vanderghinste

- 11:00 - 11:25 **Implementing the PIC/S guide in nuclear medicine: a practical guidance**
Prof. Filip De Vos (BE) and Apr. Caroline Vermeiren (BE)

Selected abstracts:

- 11:25 - 11:36 | **Development and evaluation of a trans-cyclooctene (TCO) probe for pretargeted PET imaging.**
Karuna Adhikari (University of Antwerp, Antwerp)
- 11:36 - 11:47 | **Site-specific conjugation of fluorescent dyes and chelators on antibody fragments via maleimide-thiol chemistry.**
Simon Leekens (Laboratory of Radiopharmaceutical Research KU Leuven, Leuven)
- 11:47 - 12:00 | **Development and in vitro evaluation of caspase-3-selective PET probes.**
Louis Lauwerys (University of Antwerp, Antwerp)

14:00 - 15:30: F-18 and C-11 chemistry + proffered papers**Orange**Moderators: Guy Bormans and Simon Lacroix

- 14:00 - 14:50 **Prosthetic group-based ¹⁸F labelling of peptides and proteins**
Dr. TERENCE Tshibangu Tshikindu Tshiamalu (BE)

Selected abstracts:

- 14:50 - 15:03 | **Preclinical validation of [¹⁸F]-FB-(Anti Human PD-L1) Nanobody for PET imaging.**
Herlinde Dierick (Vrije Universiteit Brussel (VUB), Brussels)
- 15:03 - 15:16 | **Development and preclinical evaluation of [¹¹C]HSP990 as an Hsp90 PET brain probe and potential biomarker for diagnosis and follow up of CNS disease progression.**
Romy Cools (Laboratory for Radiopharmaceutical Research KU Leuven, Leuven)
- 15:16 - 15:30 | **Second generation Al¹⁸F-labeled D-amino acid based peptide for CXCR4 targeted molecular imaging.**
Spahn Muriel (KU Leuven, Leuven)

16:00 - 17:20: Theranostics + proffered papers

Orange

Moderators: Vicky Caveliers and Zena Wimana

16:00 - 16:30	Theranostic radiopharmaceuticals: where are we now? Prof. Rudolf Werner (DE)
16:30 - 17:00	Recent advances in chelators for alpha emitters Dr. Sophie Poty (FR)

Selected abstracts:

- 17:00 - 17:10 | **RANKL immunoPET using ⁶⁴Cu radiolabeled antibody Fab fragments to improve imaging characteristics.** Jonatan Dewulf (University of Antwerp, Antwerp)
- 17:10 - 17:20 | **Using the site-specific radiolabeling of a PD-L1 nanobody via maleimide-cysteine chemistry to develop a PET-tracer as screening tool for personalized oncology treatment.**
Dora Mugoli Chigoho (Vrije Universiteit Brussel, Brussels)

PHYSICS

11:00 - 12:00: AI: from hype to medical physics?

Yellow

Moderators: Stefaan Vandenberghe

11:00 - 11:30	AI in medical imaging Prof. Erik Ranschaert (BE)
11:30 - 12:00	AI in nuclear medicine Prof. Dimitris Visvikis (FR)

14:00 - 15:30: Applications of AI in nuclear medicine

Yellow

Moderators: Michel Koole and Stijn De Schepper

14:00 - 14:30	Starting an AI project Zelda Paquier (BE)
14:30 - 15:00	Image reconstruction Dr. Georg Schramm (BE)
15:00 - 15:30	Radiomics Dr. Fanny Orlhac (FR)

16:00 - 17:20: Isotopes of the future + proffered papers

Yellow

Moderators: Claire Bernard and Bruno Vanderlinden

16:00 - 16:30	Isotopes of the future Prof. Thomas Elias Cocolios (BE)
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Selected abstracts:

- 16:30 - 16:40 | **Dosimetric model for patients with renal failure undergoing dialysis during I-131 therapy for thyroid cancer.**
Victor Nuttens (OLV Aalst, Aalst)
- 16:40 - 16:50 | **Development of an anthropomorphic phantom for mandibular condyle imaging.**
Stijn De Schepper (UZA, Antwerpen)
- 16:50 - 17:00 | **Feasibility of lesion dosimetry assuming constant pharmacokinetics over cycles in patients treated with ¹⁷⁷Lu-DOTATATE.**
Rachele Danieli (Institut Jules Bordet, Anderlecht)
- 17:00 - 17:10 | **Radiation dose optimization of CT acquisitions in SPECT/CT examinations.**
Lauren Podevyn (UGent, Ghent)
- 17:10 - 17:20 | **StarGuide Tc-99m imaging reconstruction parameters optimization.**
Jirair Karabet (Institut Jules Bordet, Anderlecht)

TECHNOLOGIST

9:00 - 10:30: Clinical update

Red+Purple

Moderators: Sara Vieira and Kim Van Hullebusch

09:00 - 09:45	Cardiac PET: patient preparation, acquisition, and clinical applications Prof. Véronique Roelants (BE)
09:45 - 10:30	Nuclear medicine in endocrinology: an update Dr. Duran Derijckere (BE)

11:00 - 12:00: Clinical management

Red+Purple

Moderators: Christelle Terwinghe and Geraldine Vandermeiren

11:00 - 11:30	Paediatric Patient care - Technologist practice improvement Mrs. Andrea Santos (PT)
11:30 - 12:00	Patient communication Mrs. Hanne Kindermans (BE)

14:00 - 15:30: Radionuclide therapy**Red+Purple**Moderators: Nele Eecloo and Wouter Daenen

14:00 - 14:45	Calibration of non-imaging instrumentation Prof. Kristof Baete (BE)
14:45 - 15:30	Apha emitters: current and future applications Dr. Maarten Ooms (BE)

16:00 - 17:20: FANC session + Proffered papers**Red+Purple**Moderators: Jean-Paul Thys and Filip Lavent

16:00 - 16:30	Radionuclide therapy waste management Mrs. Jolien Berlamont (BE)
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Selected abstracts:

- 16:30 - 16:42 | **Logistical analysis of the individual “whole body” dosimetry of personnel professionally exposed to ionizing radiation in Belgium, over the last 10 years.** Ana Mafalda Pereira Gomes (Vinçotte S.A, Vilvoorde)
- 16:42 - 16:54 | **Design of an integrated Radiopharmaceutical Supply Chain (SC) to enhance its overall Supply Chain Performance Methodology.** Haingo, Rabarijaona (Université Libre de Bruxelles, Brussels)
- 16:54 - 17:06 | **Can a third party software vendor (MIMVista) match the image quality of native software vendor?** Nele Eecloo (AZ Jan Palfijn Gent, Ghent)
- 17:06 - 17:20 | **Implementing Lutetium-177 PSMA ligand therapy: practical aspects concerning radioprotection and dosimetry.** Nico Dhondt (AZ Maria Middelaes, Ghent)

SUNDAY MAY 8, 2022**9:00 - 10:00: Clinical state of PET/MR****Green+Blue**Moderators: Koen Van Laere and Vanessa Schelfhout

09:00 - 09:30	PET/MRI in brain imaging Prof. Ian Law (DK)
09:30 - 10:00	PET/MRI in oncology Prof. Irene Burger (CH)

10:00 - 10:30: Coffee break**Hall 4****10:30 - 12:15: Are we ready for artificial intelligence?****Green+Blue**Moderators: Patrick Flamen and Anne Delcourt

10:30 - 10:55	The technical and methodological aspects of AI Prof. Irene Buvat (FR)
10:55 - 11:20	Medical applications of AI with focus on (nuclear) imaging Prof. Henry Woodruff (NL)
11:20 - 12:00	The ethical and legal aspects of AI in healthcare Prof. Tom Goffin (BE)

ABSTRACTS

MEDICAL TRACK ORAL PRESENTATIONS

OP-MED01

[¹⁸F]AIF-NOTA-octreotide vs. [⁶⁸Ga]Ga-DOTA-somatostatin analogue PET in neuroendocrine tumour patients: interim results of a prospective multicentre trial

Elin Pauwels¹, Frederik Cleeren², Terence Tshibangu³, Michel Koole⁴, Kim Serdons⁵, Lennert Boeckxstaens⁵, Jeroen De-kervel⁵, Timon Vandamme⁶, Willem Lybaert⁷, Bliede Van den Broeck⁸, Paul Clement⁵, Karen Geboes⁹, Eric van Cutsem¹⁰, Sigrid Stroobants¹¹, Chris Verslype⁵, Guy Bormans¹², Christophe M. Deroose¹;

¹ Uz Leuven - Ku Leuven; Gasthuisberg; Nuclear Medicine, ² Laboratory for Radiopharmaceutical Research; University of Leuven; Department of Pharmacy and Pharmacology, ³ Kuleuven, ⁴ Kuleuven; Uz Gasthuisberg; Nuclear Medicine and Molecular Imaging, ⁵ Uz Leuven, ⁶ Antwerp University Hospital, ⁷ Netwerk Antwerpen-Waasland Coe, ⁸ Uz Gent; Uz Gent, ⁹ Ghent University Hospital, ¹⁰ Uz Leuven; Head of the Digestive Oncology Unit, University Hospital Gasthuisberg, ¹¹ University Hospital Antwerp; University of Antwerp; Department of Nuclear Medicine, ¹² K.U. Leuven; University of Leuven; Lab Radiopharmacy, ¹³ Uz Leuven; Campus Gasthuisberg; Nuclear Medicine

Aim: Although gallium-68-labelled somatostatin analogue (SSA) PET is the current gold standard for somatostatin receptor imaging, its widespread implementation is restricted by practical, regulatory and financial challenges associated with the use of [⁶⁸Ga]/[⁶⁸Ge]-generators. These challenges could largely be overcome by a fluorine-18-labelled alternative. Recently, [¹⁸F]AIF-NOTA-octreotide ([¹⁸F]AIF-OC) has been identified as a promising candidate [1,2], but a thorough comparison with [⁶⁸Ga]Ga-DOTA-SSA in large patient groups is needed.

This prospective multicentre trial (clinicaltrials.gov:NCT04552847) aims to demonstrate non-inferiority of [¹⁸F]AIF-OC compared with [⁶⁸Ga]Ga-DOTA-SSA PET in neuroendocrine tumour (NET) patients. Here, results from the first 60 patients scanned with PET/CT are reported. Analysis of the final 15 patients is ongoing.

Methods: Patients with histologically confirmed NET and a routine clinical [⁶⁸Ga]Ga-DOTA-SSA PET, performed according to the EANM guidelines [3], within a 3-month interval prior to or after the study scan, were prospectively included. Patients (39M/21F; age 37-84y) underwent a whole-body PET with low-dose CT two hours after IV administration of 4 MBq/kg [¹⁸F]AIF-OC. The median interval between the study scan and the routine [⁶⁸Ga]Ga-DOTATATE (n=45) or [⁶⁸Ga]Ga-DOTANOC (n=15) PET, was 7 days (range: -30 to +32 days). A randomized, blinded consensus read was performed by two experienced readers to count tumour lesions. Following unblinding, the detection ratio (DR) was determined for each scan, i.e. the fraction of lesions detected using the union of lesions detected by both tracers ([⁶⁸Ga]Ga-DOTATATE/NOC and [¹⁸F]AIF-OC) in a patient as reference. The differential detection ratio (DDR; difference in DR between [¹⁸F]AIF-OC and [⁶⁸Ga]Ga-DOTATATE/NOC) per patient was calculated. Finally, tracer uptake was evaluated by comparing SUV_{max} and tumour-to-background ratios (TBRs) in concordant lesions.

Results: In total, 3481 different tumour lesions were counted, 2467 with [⁶⁸Ga]Ga-DOTATATE/NOC and 3279 with [¹⁸F]AIF-OC. In only 12 patients, [¹⁸F]AIF-OC detected less lesions than [⁶⁸Ga]Ga-DOTATATE/NOC and in 9 patients the same amount of lesions was observed by both tracers. The mean DR with [¹⁸F]AIF-OC was significantly higher than with [⁶⁸Ga]Ga-DOTATATE/NOC (93.2% vs. 75.8%; p<10⁻⁵). The resulting mean DDR was 17.4% (95% confidence interval: 10.9%–23.9%). No significant differences were observed in mean SUV_{max} (19.9±13.6 for [¹⁸F]AIF-OC vs. 22.8±16.3 for [⁶⁸Ga]Ga-DOTATATE/NOC; p=0.058), but mean TBR was significantly higher for [¹⁸F]AIF-OC (30.3±33.3 vs. 25.4±34.8; p=0.017).

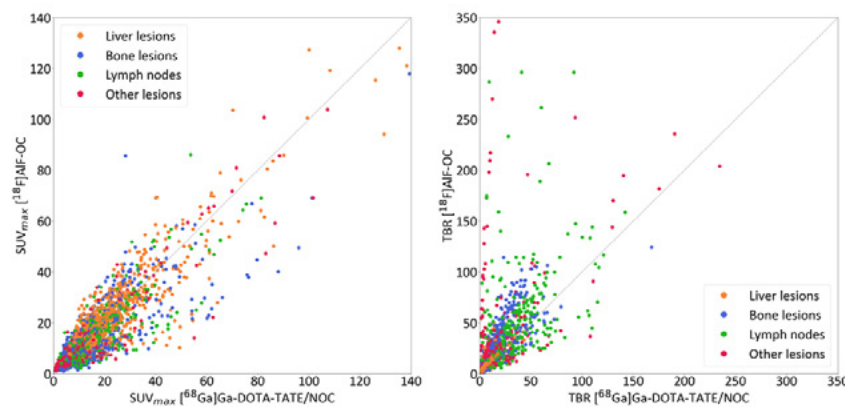
Conclusions: [¹⁸F]AIF-OC demonstrates an excellent diagnostic performance, meeting our pre-specified criterion for non-inferiority, even showing superiority compared with [⁶⁸Ga]Ga-DOTA-SSA in NET patients according to these interim findings. These data suggest that [¹⁸F]AIF-OC is an emerging tracer for clinical practice.

[1]Long.*Clin.Nucl.Med.*2019;44:452-8

[2]Pauwels.*Eur.J.Nucl.Med.Mol.Imaging.*2020;47:3033-46

[3]Bozkurt.*Eur.J.Nucl.Med.Mol.Imaging.*2017;44:1588-1601

Comparison of tracer uptake in concordant lesions (n = 2193)



OP-MED02

Yttrium-90 radioembolization versus drug-eluting beads chemoembolization for unresectable hepatocellular carcinoma: results from the TRACE trial.

Bieke Lambert¹, Elisabeth Dhondt², Laurens Hermie², Lynn Huyck², Xavier Verhelst², Hans Van Vlierberghe², Peter Vanlangenhove², Anja Geerts², Aude Vanlander², Frederik Berrevoet², Roberto Troisi³, Luc Defreyne²;

¹ Maria Middelaers Hospital and Ghent University, ² Uz Gent, ³ Ugent, Gent, Belgium.

Aims: Transarterial chemoembolization (TACE) is recommended for intermediate HCC in the Barcelona Clinic Liver Cancer (BCLC) guidelines. Prospective uncontrolled studies suggest that Yttrium-90 (Y90) transarterial radioembolization (TARE) is a safe and effective treatment option. We aimed to compare the efficacy and safety of Yttrium-90 TARE to TACE for unresectable HCC.

Methods: The TRACE trial is a single center **randomized controlled trial**. We enrolled intermediate stage HCC patients, extended to Eastern Cooperative Oncology Group performance status 1 and/or subsegmental portal vein thrombosis, and early-stage HCC patients not eligible for surgery or thermoablation. Patients were randomized to receive Y90 glass TARE or TACE with doxorubicin loaded drug-eluting beads (DEB-TACE). The primary endpoint was time to progression (TTP_{overall}). Analyses were performed on the intention-to-treat (ITT) and per protocol (PP) population.

Results :Ad interim analysis, 38 patients (median age 67 years (IQR 63;72); 33 men) were randomized to the TARE arm and 34 (median age 68 years (IQR 63;73); 30 men) to the DEB-TACE arm. **Median TTP_{overall} was 17.1 months in the TARE arm versus 9.5 months in the DEB-TACE arm** (in the ITT cohort HR 0.36; 95% CI 0.18-0.70; $p = 0.002$) (in the PP cohort: HR 0.29; 0.14-0.60; $p < 0.001$). Median overall survival (OS) in the ITT population was 30.2 months in the TARE group and 15.6 months in the DEB-TACE group (HR 0.48; 0.28-0.82; $p = 0.006$).). Downstaging led to transplantation in 10 patients in the TARE group and 4 patients in the DEB-TACE group. Median OS with censoring for liver transplantation was 27.6 months in the TARE group and 15.6 months in the DEB-TACE group (HR 0.49; 0.28-0.87; $p = 0.012$). Four patients in the TARE group developed extra-hepatic metastases during the 2 years follow up period, compared to 7 in the DEB-TACE group ($p=0.329$). Adverse events of Common Terminology Criteria for Adverse Events grade ≥ 3 ($p=0.47$) and 30-day mortality ($p=0.24$) were similar in the safety cohorts. Ad interim the HR for the primary endpoint TTP_{overall} was <0.39 , indicative to halt the study.

Conclusions: With the same safety profile, Y90 glass TARE conferred superior tumor control and survival compared to DEB-TACE in the selected early and intermediate HCC patients.

OP-MED03

Comparison between Peptide Receptor Radionuclide Therapy with ¹⁷⁷Lu-DOTATATE and external beam radiation therapy

Wendy Delbart¹, Gwennaëlle Marin¹, Jirair Karabet¹, Ghanem Ghanem¹, Patrick Flamen¹, Zéna Wimana¹;

¹Institut Jules Bordet.

Aims Despite the differences in terms of dose-rate and -distribution over time, radiobiological principles of targeted radionuclide therapy (TRT) tend to be extrapolated from external beam radiation therapy (EBRT) studies. In this *in vitro* study we aimed at comparing the biological responses, over time, induced by EBRT and ¹⁷⁷Lu-DOTATATE targeting somatostatin receptor (SSTR)-positive neuroendocrine tumours.

Methods SSTR-positive human cancer cell lines selected for their different intrinsic radiosensitivities; HBL and MM162 (melanoma;radioresistant), COLO-677 and EJM (multiple myeloma;radiosensitive), MIA-PACA-2 and HT-29 (pancreatic and colon carcinoma;intermediate radioresistance); were exposed to comparable absorbed doses (2Gy) of EBRT or ¹⁷⁷Lu-DOTATATE (5MBq during 4hours). Cells were assessed over time for cell survival by crystal violet, cell cycle, cell death mode (apoptosis and autophagy), DNA damage (γ -H2AX) and oxidative stress by flow cytometry. In order to investigate radiation-induced non-targeted effects, at 3 and 10 days post-irradiation, the secretome of irradiated cells was analyzed for IL-8, TNF- α and TGF β by ELISA, and H₂O₂ by a spectrophotometric assay.

Results At day 10, cell survival was significantly decreased in all cell lines, except HT-29, by ¹⁷⁷Lu-DOTATATE (COLO -33 $\pm$ 2%; HBL -25 $\pm$ 3%; EJM -23 $\pm$ 1%; MIA-PACA-2 -15 $\pm$ 3%; MM162 -14 $\pm$ 3%) and EBRT (COLO -58 $\pm$ 2%; EJM -56 $\pm$ 2%; MIA-PACA-2 -46 $\pm$ 2%; HBL -39 $\pm$ 2%; MM162 -34 $\pm$ 3%; HT-29 -12 $\pm$ 3%). Surviving cells at day 10 were equally distributed across the cell cycle compared to the non-treated counterpart, suggesting a cytotoxic rather than a cytostatic effect of both treatments. EBRT and ¹⁷⁷Lu-DOTATATE induced apoptosis and autophagy, independent of the tumour type or radiosensitivity status, with a more important induction following EBRT. Furthermore, in all cell lines, DNA damage repair was initiated early following EBRT with an immediate H2AX phosphorylation peak, while no such peak was observed after ¹⁷⁷Lu-DOTATATE at any time over a period of 10days. Similarly, EBRT induced an immediate significant ROS increase (+16% to +46%), while this was only increased in COLO-677 after ¹⁷⁷Lu-DOTATATE (+17 $\pm$ 4%). In the secretome, no TNF α was found of any cell lines, while IL-8 was produced only by MIA-PACA-2 and HT-29, being greater after EBRT compared to ¹⁷⁷Lu-DOTATATE. H₂O₂ was produced only by HT-29, with a higher increase at day 3 after EBRT compared to ¹⁷⁷Lu-DOTATATE.

Conclusions By investigating fundamental radiation-induced biological mechanisms, our results showed that EBRT radiobiology is not directly transposable to TRT with ¹⁷⁷Lu-DOTATATE, especially regarding the induction of the DNA damage response. This warrants a specific radiobiology approach for TRT. Furthermore, it may have implication when designing new combination therapy strategies.

OP-MED04

3p-C-NETA-TATE: A versatile somatostatin analogue for Al¹⁸F-labeled and therapeutic SSTR2 targeting radiopharmaceuticals

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Aims: Somatostatin-based radiopharmaceuticals (e.g. [⁶⁸Ga]Ga-DOTATATE and [¹⁷⁷Lu]Lu-DOTATATE) have been used to diagnose, monitor, and treat neuroendocrine tumor patients with great success. [¹⁸F]AIF-NOTA-octreotide, a promising ¹⁸F-labeled somatostatin analogue and potential alternative for ⁶⁸Ga-DOTA-peptides, is under clinical evaluation. However, ideally, the same precursor (combination of chelator-linker-vector) can be used for production of both diagnostic and therapeutic radioprobes with very similar (e.g. Al¹⁸F/²¹³Bi/¹⁷⁷Lu) or identical (e.g. complementary Tb-radionuclides) pharmacokinetic properties, which is possible with the promising chelator 3p-C-NETA, allowing accurate personalised dosimetry estimation, and radionuclide therapy of NET patients. In this study we evaluated 3p-C-NETA-TATE as therapeutic precursor, and present first results of the preclinical evaluation of the diagnostic compound [¹⁸F]AIF-3p-C-NETA-TATE.

Methods: 3p-C-NETA-TATE was synthesized using standard solid/liquid-phase peptide synthesis and purified using HPLC. [¹⁸F]AIF-3p-C-NETA-TATE was synthesized in an automated AllinOne® synthesis module and the *in vitro* stability of [¹⁸F]AIF-3p-C-NETA-TATE was evaluated in formulation buffer, PBS and human serum at 37 °C using radioHPLC. *In vitro* cell binding and internalization was performed with [¹⁸F]AIF-3p-C-NETA-TATE using SSTR2 expressing cells (QGP1.SSTR2) and the pharmacokinetics were evaluated in healthy rats and in xenograft (QGP1.SSTR2) bearing mice using μ PET/MRI and μ PET/CT, respectively. [¹⁸F]AIF-NOTA-Octreotide was used as a benchmark.

Results: [¹⁸F]AIF 3p-C-NETA-TATE was obtained in good RCY (56 ± 10%) and >98% radiochemical purity. [¹⁸F]AIF-3p-C-NETA-TATE displayed excellent *in vitro* stability with >95% intact tracer after 4 hours in all tested conditions. High SSTR2 specific cell binding and internalization (18.4 ± 2.1 % of which 78.3 ± 2.1 % is internalized) was observed after 60 min incubation. Finally, [¹⁸F]AIF-3p-C-NETA-TATE showed excellent pharmacokinetic properties (rats and mice) and tumor accumulation (SUV_{mean} 60 min: 2.7 ± 1.1), which was comparable to [¹⁸F]AIF-NOTA-Octreotide in the same model system (SUV_{mean} 60 min: 3.2 ± 0.76). We were also able to block uptake in SSTR2 expressing organs and in tumors (>90%) by coinjecting [¹⁸F]AIF 3p-C-NETA-TATE with 2.5 mg/kg octreotide acetate, indicating SSTR2 specific uptake (Figure 1).

Conclusions: [¹⁸F]AIF-3p-C-NETA-TATE has demonstrated to be a promising diagnostic tracer for SSTR2 expressing tumors. [²¹³Bi]Bi-3p-C-NETA-TATE and [¹⁷⁷Lu]Lu-3p-C-NETA-TATE will be evaluated as potential therapeutic partners in QGP1.SSTR2 expressing tumor mice.

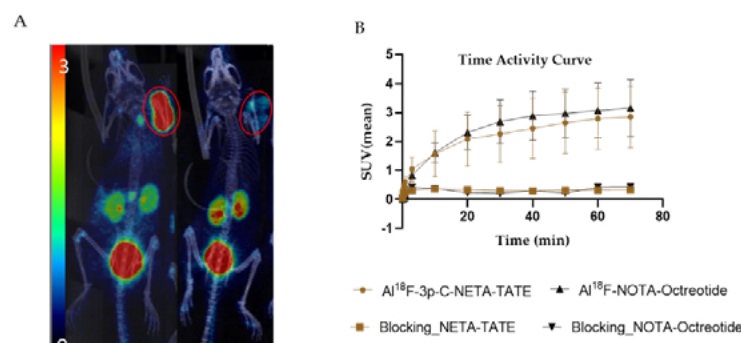


Figure 1: A) μ PET/CT (60-75 min) MIPs images of [¹⁸F]AIF-3p-C-NETA-TATE in QGP1.SSTR2 tumor bearing mice without (left) or with (right) coinjection of 2.5 mg/kg octreotide acetate; and (B) Time activity curves indicating [¹⁸F]AIF-3p-C-NETA-TATE SSTR2 specific tumor uptake in function of time with [¹⁸F]-NOTA-Octreotide as reference.

OP-MED05

Disturbing the redox balance as a new radiosensitizing strategy for Peptide Receptor Radionuclide Therapy with ¹⁷⁷Lu-DOTATATE

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Aims: The biological effects of ¹⁷⁷Lu-DOTATATE, targeting somatostatin receptors (SSTR) and characterized by low LET radiation, rely mostly on indirect effects via reactive oxygen species (ROS) production. Hence oxidative damage to DNA and other macromolecules occur if ROS can exceed the cell antioxidant defenses. We have evaluated *in vitro* and *in vivo* the radiosensitizing potential of decreasing antioxidant defenses in combination with ¹⁷⁷Lu-DOTATATE, using buthionine sulfoximine (BSO), an inhibitor of glutathione (GSH) synthesis.

Methods: Six human cancer cell lines expressing SSTR were exposed to 5MBq ¹⁷⁷Lu-DOTATATE during 4 hours. In the combination experiments, BSO (10⁻⁷M) was added 24h prior to the former and maintained during the entire experiment (10days). Cell survival was assessed using crystal violet. A multiple myeloma xenograft mouse model received 10mM BSO via drinking water for 3 weeks, starting the day before a single intravenous injection of 30MBq ¹⁷⁷Lu-DOTATATE. GSH was assessed in tumor, liver and kidneys using a commercial kit. Safety assessments comprised *ex vivo* biodistribution of ¹⁷⁷Lu-DOTATATE and the combination (24h, 72h and 168h post-injection (PI)) as well as bone marrow (BM) toxicity (apoptosis). Efficacy was assessed by measuring tumor volume by caliper and on CT.

Results: BSO showed encouraging radiosensitizing properties *in vitro* on 4 cell lines out of 6 treated with ¹⁷⁷Lu-DOTATATE. *In vivo*, tumor GSH levels were efficiently depleted by a 48h BSO exposure (-79±7%, p < 0.001). Besides, liver (-25±5%, p=0.03) and kidneys (-49±17%, p=0.01) had lower GSH levels as well. However, kidneys GSH normalized to baseline levels within 8days. Regarding BM toxicity (4-5 weeks PI), the percentage of apoptotic cells in the BM was not increased in the BSO combination group compared to ¹⁷⁷Lu-DOTATATE alone or the control group. Furthermore, BSO did not influence ¹⁷⁷Lu-DOTATATE organ distribution. In terms of efficacy, tumor growth slowed down with an increased doubling time induced by ¹⁷⁷Lu-DOTATATE alone (18.5days) and further enhanced in combination with BSO (23days) compared to the control (13days) or BSO alone (13.5days). Moreover, the tumor volume was decreased compared to control (control 1257±218%; BSO 1095±262%, p=0.67; ¹⁷⁷Lu-DOTATATE 1018±247%, p=0.52; ¹⁷⁷Lu-DOTATATE+BSO 640±130%, p=0.03).

Conclusions: Our results showed that disturbing the cell redox balance using a GSH synthesis inhibitor had a radiosensitizing effect *in vitro* and *in vivo* when given in combination with ¹⁷⁷Lu-DOTATATE. This combination did not result in disturbed organ distribution or toxicity. Targeting the antioxidant defense system opens new safe treatment combination opportunities with ¹⁷⁷Lu-DOTATATE.

OP-MED06

Bone SPECT/CT for assessing persistent or recurrent pain post spondylodesis: a retrospective study and pattern analysis

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¹AZ Maria Middelaers Hospital and Ghent University; ²AZ Jan Palfijn, Ghent; ³Universiteit Antwerpen, Belgium

Aims: We investigated the role of bone scintigraphy in the post-operative spine. We documented the impact of SPECT/CT on the clinical management of patients with persistent or recurrent pain. Secondly, we explored the clinical significance of various SPECT/CT patterns observed at the fusion level.

Methods: We designed a retrospective study to investigate the impact of bone SPECT/CT performed 6m-2y post-spondylodesis. Structured reporting was done with assessment of axial and non-axial pain generators. When addressing the potential axial pain generators, we separately comment on the fusion level and the adjacent levels. In case of absent fusion, the non-union is subclassified with versus without features suggestive of instability. Instability scoring is done by reviewing the bone remodelling at screw and facet joint level. In a first dataset we scored patients who were all operated by the same neurosurgeon. We confronted our SPECT/CT findings with the final clinical diagnosis, established by the neurosurgeon. A second retrospective analysis of patients referred by a single orthopedic surgeon, was performed to validate our conclusions from the first dataset. In a subsequent analysis we explored the spontaneous evolution of the various patterns (non-union with and without instability features) observed on SPECT/CT.

Results: A total of 77 SPECT/CT-scans were included in the first dataset. SPECT/CT did not yield any positive finding in 9, of which 4 also remained clinically without diagnosis. At the fusion levels SPECT/CT showed a sensitivity of 98% and a specificity of 73%. For pain generators identified outside the fusion level, sensitivity and specificity of SPECT/CT were 97% and 94%. The positive SPECT/CT findings impacted the clinical management in 55/77 cases. SPECT/CT-scan guided the treatment strategy at least partially in 80% of patients. In the second dataset, 35 patients were analyzed. In 30/35 patients (86%) the SPECT/CT report clearly impacted the clinical management. In a subsequent analysis we explored whether the observed patterns of non-union were persistent over time in patients who were managed conservatively. We observed a trend towards persistence of non-union in the patients presenting with features of instability. We did not detect a trend towards instability features in patients who were initially categorized as a cold non-union without instability features.

Conclusins: A systematic reanalysis of bone SPECT/CT studies in homogeneous group of patients after spinal fusion surgery showed a good accuracy for identifying the main pain generator. SPECT/CT affected clinical management in at least 80% of patients.

POSTER PRESENTATIONS

PP-MED01

The investigations of the deep lymphatic system of the lower limbs: spect-ct is mandatory!

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Aims: The lymphoscintigraphic investigations (LLySc) of the deep lymphatic system (DLyS) are now part of the management of lower limb edemas (LLE) and the visualisation of the popliteal lymph nodes (PopLN) is expected in these cases. However, these PopLN may be of deep and/or superficial lymphatic drainage. The aim of the study was to review the clinical situations when these LLLySc of the DLyS were performed (after one deep injection of radiocolloids in the retro-achillear space), to analyze their results and to compare the contributions of the planar imagings and of the SPECT-CT imagings.

Methods: retrospective monocentric review of 135 LLLySc performed according to our standardized 3 phase protocol from 01/2021 to 1/02/2022

Results: among 26 patients (3 men and 23 women: mean age = 52.3 years: cases with Dermal BackFlow were excluded from the analysis) who had undergone one (bilateral) LLLySc of the DLyS, PopLN were seen at the level of 40 limbs (20

left and 20 right). On dynamic planar imaging performed with exercise (15 minutes long), PopLN could be related for the right limbs to medially and vertically running LV in 18 cases suggesting the presence of one deep lymphatic drainage (associated in 10 cases to internal saphenous LV) but only to the visualisation of one internal saphenous LV in 7. For the left limbs, the corresponding numbers were 17 (12) and/but 5. However, SPECT-CT could confirm the presence of one deep LV in the calf in only 19 cases and showed that in other cases these PopLN received their colloidal lymphatic activity from posterior superficial LV.

Conclusions: when the deep lymphatic system is investigated, spect-ct acquisition should be systematically carried in order to define whether deep and/or superficial lymphatic drainages are present, which determines the management of these patients

PP-MED02

The popliteal lymph nodes and the investigations of the superficial lymphatic system of the lower limbs: spect-ct is recommended!

Pierre Bourgeois¹, Gary Callebaut¹;

¹HIS-IZZ Hospitals, Brussels, Belgium.

Aims: The visualisation of the popliteal lymph nodes (PopLN) in the framework of the lymphoscintigraphic investigations (LLySc) of the lower limb edemas (LLE) is common. However, these PopLN may be of deep and/or superficial lymphatic drainage. The aim of the study was to analyze and to compare the contributions of the planar imagings and of the SPECT-CT imagings

Methods: retrospective monocentric review of 135 LLLySc performed according to our standardized 3 phase protocol from 01/2021 to 1/02/2022

Results: 18 patients (4 men and 14 women: mean age = 62 years: cases with Dermal BackFlow were excluded from the analysis) had 23 PopLN (bilateral in 5: right-sided in 8 and left-sided in 5) seen on the planar LLLySc (in one patient, the PopLN were faintly visualised on planar LLLySc and could only be confirmed on SPECT-CT). In four cases, the presence of sural LN intercalated at the level of the calf could confirm that these PopLN were related to deep lympho-vascular drainage. In all but 3, normal internal saphenous Lymphatic vessel (LV) was seen and in 18 cases, the presence of one medially and vertically running LV suggested the presence of one deep lymphatic drainage. However, SPECT-CT could confirm the presence of one deep LV in the calf in only 11 cases and showed that these PopLN received their colloidal lymphatic activity from posterior superficial LV.

Conclusions: 1. Popliteal LN could be definitely related to true deep lymphatic drainage in only half of the cases

2. when popliteal LN are seen on planar imagings of LLE, the realisation of spect-ct acquisition is recommended in order to define whether they are of deep and/or superficial lymphatic drainages, which determines the management of these patients

PP-MED03

“Natural History” of Dermal BackFlows? Insights from lymphoscintigraphic investigations and practical recommendationsPierre Bourgeois¹, Gary Callebaut¹;¹HIS-IZZ Hospitals, Brussels, Belgium.

Aims: Vascular lymphatic reflux (VLR), also called Dermal Backflows (DBF), are frequently seen in patients with Lower Limb Lymphatic Edema (LLE) in the framework of the lymphoscintigraphic investigations (LLLySc) of these situations. However, the localisation and extent of these VLR and DBF are variable and raise the questions of their origin and natural evolution. The aim of the study was to review the LLLySc with VLR and DBF and to try to define their origin and natural evolution.

Methods: retrospective monocentric review of 135 LLLySc performed according to our standardized 3 phase protocol from 01/2021 to 1/02/2022. **Results:** 24 patients had DBF (distal progression-DBF limited to the foot excluded: mean age = 62; range = 12-86: 7 men and 17 women: 5 had 2 exams: 6 had one history of previous cancer treatment-s and 9 of osteo-articular problem: BMI was higher than 30 in 14). 29 VLR-DBF were seen (at the level of the two limbs in 4, only right sided in 16 and only left sided in 5: most frequently at the level of the calf and/o the ankle) on WBS obtained after one hour of walking and their extent varied from very limited to extended from the foot to the inguinal area. The starting level was seen in 9 cases on the WBS after the 30 minutes in resting conditions, in 10 on the WBS after the tip-toeing (not done in 9 patients) and only after walking in 10.

Conclusions:

- 1.in order to determine the starting point of one DBF, a dynamic and sequential approach should be performed
- 2.most of the DBF are rooted in (begin by) limited lympho-vascular lesions which raises the question of surgically correcting them and/or to limit manually their extension
- 3.these DBF are 2 times more frequent at the level of the right LL than at the level of the left

PP-MED04

“Retex” from lymphoscintigraphic investigations in the management of lower limb edemas in BelgiumPierre Bourgeois¹;¹HIS-IZZ Hospitals, Brussels, Belgium.

Aims: for the physicians in charge of the patients with lower limb edema(s), the 3 phases lymphoscintigraphic imaging (LLLySc) represents the “gold standard” with diagnostic and therapeutic implications. However, the methodology has to be respected and the images-results have to be correctly understood and interpreted. The aim of the study was to review the practices and results of LLLySc from various services of Nuclear Medicine

Methods: retrospective review of LLLySc performed for patients seen in the framework of lymphological consultations

Results: from this limited survey, it appears that the protocol is rarely and completely respected and that errors in the analysis of the morphologic images and/or functional parameters are very frequent.

Conclusions: it appears mandatory that specialists in nuclear medicine who are performing these exams should be well-trained in their realisation and interpretation.

PP-MED05

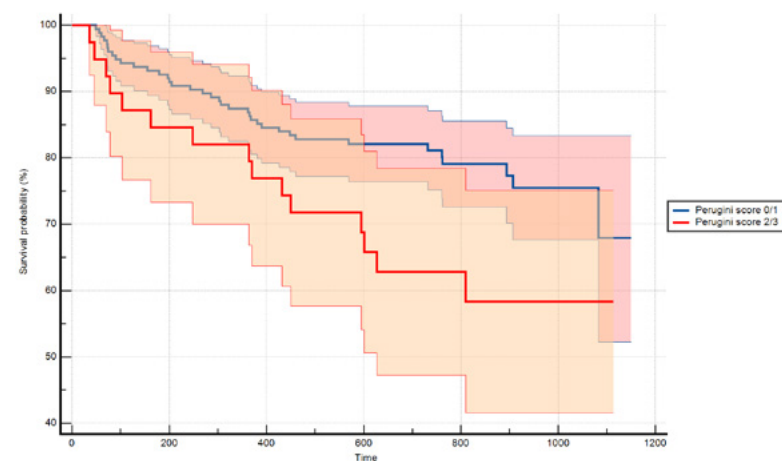
Does the semiquantitative assessment of cardiac uptake of ^{99m}Tc-HDP predicts survival in patients with suspected transthyretin cardiac amyloidosis?Pieter De Bondt¹, Victor Nuttens¹, Sim Vermeulen², Dirk Ooms¹, Olivier De Winter¹, Marc Vanderheyden¹, Nicole Dorny¹;¹ Oly Ziekenhuis Aalst Asse Ninove; Department of Nuclear Medicine, Aalst, Belgium, ²University Hospital Brussels, Belgium

Aims: ^{99m}Tc-HDP imaging has emerged as an important non-invasive method to diagnose transthyretin cardiac amyloidosis (ATTR-CA). The aim of this study was to examine the association between Tc-HDP uptake and overall mortality in a group of patients with suspected ATTR-CA referred for ^{99m}Tc-HDP imaging.

Methods: ^{99m}Tc-HDP scans from 214 patients with a clinical suspicion of ATTR-CA were retrospectively analyzed. In all patients a whole body and SPECT/CT of the thorax was obtained two hours following injection with ^{99m}Tc-HDP. Retention of the ^{99m}Tc-HDP in the heart was assessed and scored in line with the semiquantitative Perugini grading system: 0: no uptake; 1: uptake less than rib; 2: uptake equal or more than rib; 3: uptake greater than rib uptake with lower bone uptake. Patient files were reviewed and all-cause mortality was retrieved from the electronic health record.

Results: 175 patients (82%) (group A) had a score < 2, 39 patients (18%) had a score >1 (group B) and were classified as having ATTR-CA. The Kaplan-Meier survival curves (Figure) showed a significant higher overall mortality in group B patients (p=0.02) with a mean survival in group A of 961 days, and of 801 days in group B.

Conclusions: Irrespective of the underlying treatment, this study demonstrates a significant difference in survival between patients with a negative vs those with a positive ^{99m}Tc-HDP Scans for ATTR-CA. Although preliminary we speculate that further refinement of patient selection and optimization of the extent of the disease by ^{99m}Tc-HDP imaging might be helpful in better discriminating patients at risk.



PP-MED06

Are the values from different myocardial perfusion quantification programs interchangeable?

Pieter De Bondt¹, Victor Nuttens¹, Sim Vermeulen², Dirk Ooms¹, Olivier De Winter¹;

¹ Olv Ziekenhuis Aalst Asse Ninove, Aalst, Belgium, ²ASZ Hopital, Aalst, Belgium.

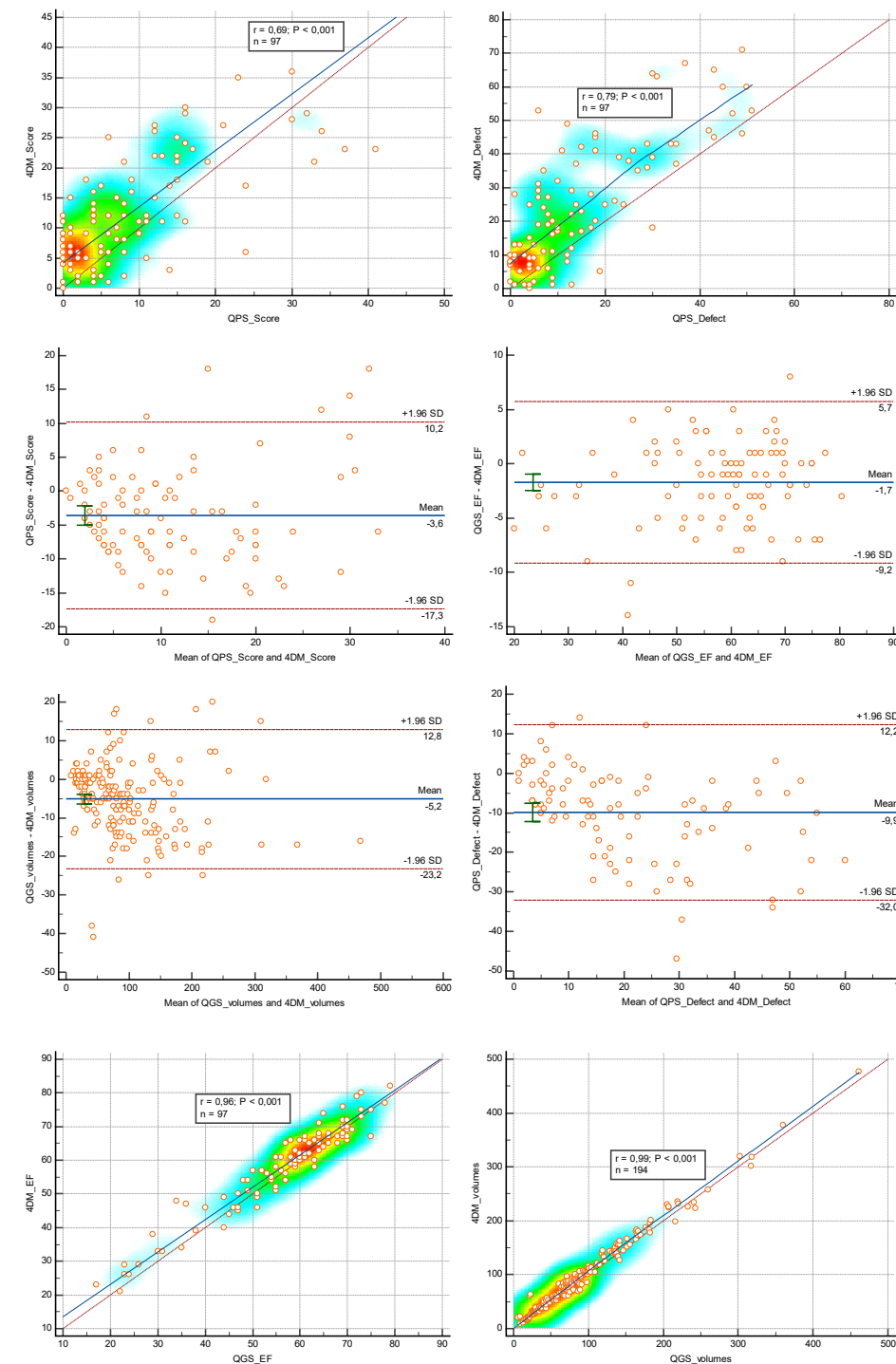
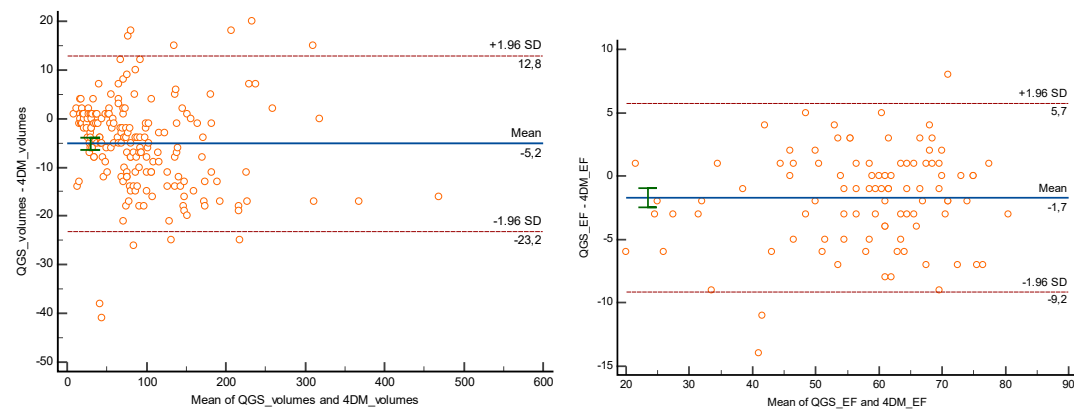
¹ Univesity Hospital Brussels,, Belgium.

Aims: Different software packages are validated and used to calculate functional parameters from myocardial perfusion scintigraphies. We compared perfusion defect (PD, %), perfusion score (PS, summes stress and summes rest score), left ventricular volumes (LVV, ml) and left ventricular ejection fraction (LVEF, %) from Autoquant 7 (Cedars-Sinai, LA, USA) with those calculated from Corridor4DM (Invia, USA).

Methods: 97 myocardial perfusion scans, post stress and rest, where analysed with Autoquant and Corridor4DM, and automatic calculated values of PD, PS, LVV and LVEF were compared.

Results: Correlaton for PD, SS, LVV and LVEF was resp : 0.79, 0.69, 0.99 and 0.96, all significant (p<0.01). Whereas volumes and LVEF from these two myocardial perfusion quantification programs were interchangeable, this is not the case for PD and PS. Especially the defect size is calculated higher, sometimes double, with Corridor4DM compared to Autoquant. When Bland-Altman plots were analyzed, a mean difference of almost 10% was found for PD and almost 4 for PS in favor of Corridor4DM.

Conclusions: Caution has to be taken when comparing or shifting from one myocardial perfusion quantification program to another, and especially perfusion defect and perfusion score can substantially differ.



YOUNG NUCLEARIST CHALLENGE

ORAL PRESENTATIONS

OP-YNC01

The nerve-racking case of [¹⁸F]PSMA-1007 PET/CT in a patient with continuous low back pain

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An 83-year-old patient with a prostate adenocarcinoma in the left lobe was treated curatively with radiation therapy and hormone therapy in 2015. Despite the detection of biochemical recurrence since a few months, no suspicious lesions were seen on ultrasound, abdominal CT and bone scintigraphy. However, the patient reported continuous pain in the lower back as well as in the hypogastric region. Given the further rising PSA to 4.5 ng/ml, the patient was referred by his treating urologist for a [¹⁸F]PSMA-1007 PET/CT scan.

The [¹⁸F]PSMA-1007 PET/CT revealed an intense intradural tracer uptake on the level of the second sacral vertebra, extending through the sacral foramina distally towards the S2/S3 nerves, the sciatic nerve and the autonomic nerves innervating the prostate, as well as proximally towards the hypogastric plexus (Figure 1). This increased tracer uptake was strongly suspicious of malignant nerve invasion, as seen in neoplastic lumbosacral plexopathy (nLSP). These findings were confirmed on a pelvic magnetic resonance imaging (MRI) scan performed five days later.

Local perineural involvement (PNI) is observed in as many as 75% of resected prostate cancer specimens and is a distinct and underrecognized route of tumor spread that can be seen in the absence of lymphatic or vascular invasion [1]. The nerve sheaths of the rich autonomic innervation of the posterior aspect of the prostate act as a low-resistance and early route of extraprostatic tumor spread, resulting in an emerging explanation for nLSP as an underestimated source of patient morbidity and mortality [2,3]. The most common initial symptom is pain followed by weakness and sensory disturbances, often misdiagnosed as radiculopathy or radiation induced nerve injury. PNI is difficult to recognize on MRI, especially after pelvic radiation therapy which was the case in this patient [3,4] these patients are often times a clinical conundrum—to diagnose and to treat. Building on previous results in modeling glioblastoma multiforme (GBM). Given the findings on [¹⁸F]PSMA-1007 PET/CT, the patient is now planned to receive metastasis-directed radiation therapy for the purpose of symptom relief and further disease control.

To our knowledge, this is the first case in which prostate cancer involvement in the lumbosacral plexus is extensively visualised by [¹⁸F]PSMA-1007 PET/CT. The risk of developing nLSP should be kept in mind for every patient with prostate carcinoma, stressing the importance of the knowledge of the pelvic neuroanatomy. This case illustrates that [¹⁸F]PSMA-1007 PET/CT could be an early and sensitive tool in detecting this common though often more subtle spread of prostate cancer, with disabling consequences for the patient if undetected and thus left untreated.

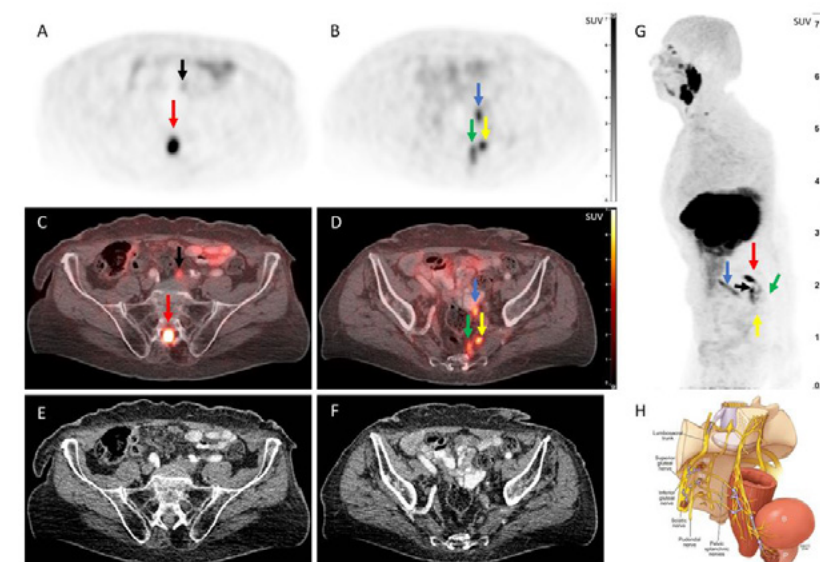


Figure 1 Axial reconstruction of attenuation-corrected (AC) [¹⁸F]PSMA-1007 PET images (A, B) and of fused [¹⁸F]PSMA-1007 PET/CT images (C, D) showing an intradural metastasis (red arrow) as well as perineural spread of the prostate carcinoma to the sacral nerves S2/S3 (green arrow), the sciatic nerve (yellow arrow), the hypogastric plexus (black arrow) and the autonomic nerve plexus innervating the prostate (blue arrow). These lesions were difficult to delineate by an experienced radiologist on the corresponding CT images (E, F). Maximum intensity projection (MIP) image of the patient (G) showing the linear PSMA expression along the lumbosacral plexus. H: Illustration of the proposed mechanism of perineural spread of prostate cancer with B = bladder; P = prostate (Source: Mayo Foundation for Medical Education and Research. All rights reserved.)

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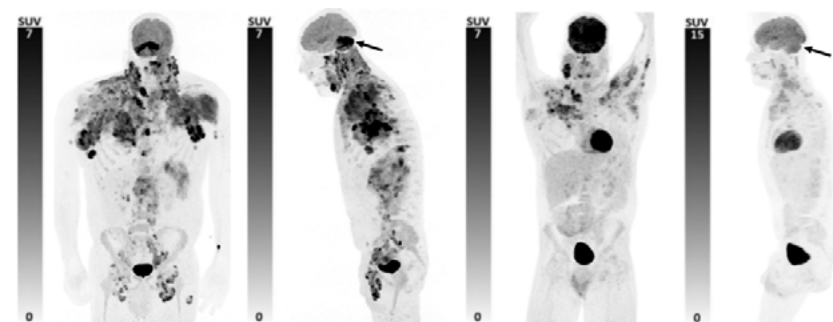
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OP-YNC02

Breaking the oculo-(para)neoplastic reflex on FDG-PET/CT: cerebellar hypermetabolism in a Hodgkin lymphoma leads to an unexpected diagnosis.

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Figure

Left panels: MIP images of [¹⁸F]FDG-PET/CT during staging. **Right panels:** MIP images of [¹⁸F]FDG-PET/CT after two cycles of ABVD.

A 33-year old male presented with general malaise, fever and palpable lymph nodes in neck and armpits for three years. Initial investigation further displayed generalized lymphadenopathy, anemia and an important inflammatory syndrome. Histopathological examination after supraclavicular lymphadenectomy revealed a nodular sclerosis Hodgkin lymphoma. [¹⁸F]FDG-PET/CT (left panels) showed hypermetabolic supra- and infradiaphragmatic lymphadenopathy and disseminated involvement of extralymphatic organs, compatible with Ann Arbor stage IVB, in conjunction with a diffuse, intense cerebellar relative hypermetabolism (arrow). The latter finding was unexpected, since the patient experienced mere episodic retro-ocular headache - no meningism or neurological deficits. To differentiate between central nervous system (CNS) infiltration and immune-mediated paraneoplastic subacute cerebellar degeneration, subsequent investigation with MR and lumbar puncture was carried out. MR showed discrete leptomeningeal enhancement along the cerebellar folia and cerebellar edema, but malignant CNS infiltration remained undetected at repeated lumbar punctures. In addition, liquor screening for antineuronal antibodies was negative. On the contrary, liquor analysis unexpectedly unveiled substantial pleocytosis with increased lactate/protein and decreased glucose, establishing the diagnosis of a meningitis; the culprit was *Cryptococcus neoformans* (titer >1/2560). Blood cultures and serum antigen testing for *Cryptococcus* remained negative. The patient underwent prompt treatment with liposomal amphotericin B and flucytosine. Due to this concomitant *Cryptococcus* meningitis, chemotherapy was shifted from eBEACOPP towards the less toxic ABVD regimen and the first cycle postponed. The patient responded well to the antifungal therapy with gradual antigen titer decline on liquor analysis; causal treatment began the morning after completion of the antifungal induction therapy. After two cycles of ABVD, [¹⁸F]FDG-PET/CT (right panels) showed a modest metabolic response with normalization of the cerebellar metabolism (arrow). The patient is currently treated with pembrolizumab monotherapy and fluconazole, displaying an excellent metabolic response.

Although paraneoplastic subacute cerebellar degeneration could have coexisted, this was less likely due to i) the absence of liquor antineuronal antibodies ii) the absence of a cerebellar clinical phenotype despite a three-year history of multiple lymphadenopathies, whilst the disease course generally evolves to limited activities of daily living within three months.

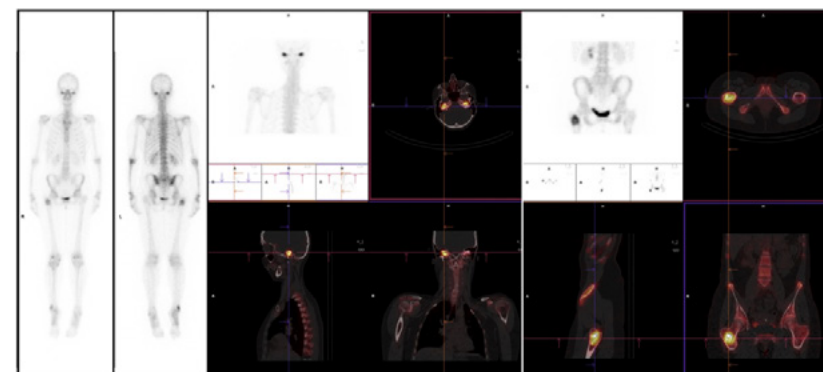
This case highlights the possibility of pauci-symptomatic CNS infections as differential diagnosis in lymphoma-associated cerebellar hypermetabolism in addition to paraneoplastic cerebellar degeneration and neurolymphomatosis, enabling opportunities to detect opportunistic infections in lymphoma patients during staging and intervene before – and thus prevent- infectious dissemination during chemotherapy.

OP-YNC03

“Looks like the raccoon sign...” “Baboon?” “No, RACCOON!!!”

Lynn De Mey¹, Kristoff Muylle², Sophie Bourgeois¹, Jeroen de Filette¹, Odrade Gondry¹, Amelientje Bracke¹, Lode Goethals¹, Hendrik Everaert¹, Tony Lahoutte¹;

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Case Presentation

A 41-year-old woman with osteogenesis imperfecta was referred to the Nuclear Medicine department for a ^{99m}Tc-HDP-bone scintigraphy, because she suffered from neck pain and dizziness. The bone scan showed two unexpected findings: 1) osteoblastic activity in the right femur, confirmed to be an enchondroma, and 2) strong osteoblastic activity at the level of the ossicles (of the middle ear). The findings at the level of the ossicles were further investigated in the ENT (Ear-Nose-Throat) department, as the patient was also known with hearing loss. In the context of osteogenesis imperfecta, these imaging findings are highly suggestive for bilateral otosclerosis, which was confirmed in the ENT department. However, the dizziness could not be attributed to this. A follow-up at the neurology department was planned for further investigation.

Discussion

Osteogenesis imperfecta comprises a heterogeneous group of conditions with estimated incidence of about 1-2/20.000. The disease is an inherited form of skeletal dysplasia. Bone fragility and skeletal deformations are typical (1). The disease is a known risk factor for otosclerosis (2,3). Otosclerosis is one of the most common causes of progressive hearing loss in young adults, and is caused by disturbed resorption and formation of bone at the level of the ossicles (2,3). The disease has a prevalence of 0.3–0.4% in the Caucasian population (2). Hearing loss is the main symptom (3,4). Half of the patients report tinnitus, while only 10% suffer from vertigo (4). The diagnosis of otosclerosis can be made by histological examination after stapedectomy or stapedotomy. Usually, however, the diagnosis is made based on clinical history and examination, audiogram, and CT of the temporal bone (3). As demonstrated in this case, the diagnosis can also be made by SPECT-CT (5). A study by Berrettini et al. shows that SPECT detects otosclerosis with a sensitivity of 95,2% and a specificity of 96,7%. This is a higher sensitivity than that of HR-CT, which is only 58%. In addition, they demonstrated a significant relationship between the morphological findings of bone demineralization on HR-CT and a high uptake index on SPECT (6). SPECT-CT is particularly useful in otosclerosis that is difficult to detect, as well as in the follow-up of otosclerosis under drug treatment (5). Care should be taken not to miss this diagnosis on a bone scan performed for other reasons, as otosclerosis is a known and treatable cause of hearing loss.

OP-YN04

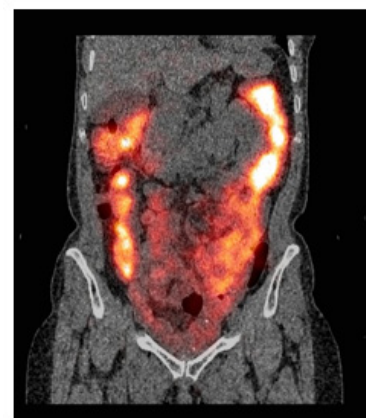
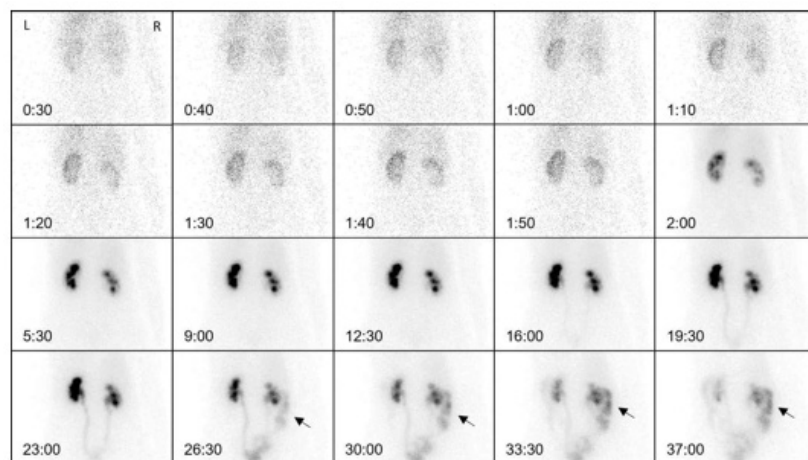
Just a little RE(nal)SPECT

Geraldine Lens¹, Raf Verscuren¹, Koenraad Van Laere¹, Frank Van der Aa¹, Karolien Goffin¹;

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We report the case of a 56 year old female patient with a history of an adenocarcinoma of the cervix more than ten years ago, for which she was treated with concomitant radiochemotherapy and which was complicated by the development of radiation cystitis. As a result of the latter, she developed a right distal ureteral stenosis and secondary hydroureteronephrosis. For this she was consecutively treated with a nephrostomy, placement of a double J stent and eventually a reimplantation of the right ureter, bladder augmentation and suturing of a piece of preterminal ileum to a bladder defect. Several weeks after the surgery, she started to complain of uncontrollable watery stool, not improving with loperamide. Because of these symptoms, she was referred to the gastroenterology department where a Clostridium infection and celiac disease were ruled out. An additional colonoscopy showed no abnormalities and also a trial therapy with Colestyramine did not improve her symptoms. Postoperative ultrasound 3 months after the surgery, showed a persistent hydroureteronephrosis and ureteral stenosis on the right, with now also development of the same pathology on the left side. To evaluate functional ramifications of this ureteral stenosis, the patient was referred for a ^{99m}Tc-MAG3 renal scintigraphy. The scan showed timely perfusion of both kidneys with slightly reduced perfusion on the right (40%) and early efflux of urine to the bladder bilaterally. Remarkably, shortly after bladder filling became visible, also blurred tracer activity started to appear laterally to the right of the bladder, extending to the right flank and then perireally on the right (figure 1). An additional SPECT/CT of the abdomen and pelvis was performed (figure 2), showing tracer activity at the level of the right and left colon as well as at the level of the small intestine. Thus, the presence of a vesico-enteric or vesico-colic fistula was suspected. A subsequently performed RX cystography (figure 3) confirmed the presence of a vesico-enteric fistula to the preterminal ileum. Hereafter the patient underwent a second operation to resect the fistula, which provided resolution of the gastrointestinal symptoms.

This case is a great example of how a long-standing nuclear medicine examination, although unexpected, contributed significantly to the clinical diagnosis. It is also a good reminder that when reviewing a ^{99m}Tc-MAG3 scintigraphy, the dynamic images should always be evaluated carefully as well, as they may provide additional information.



OP-YN05

Progesterin-associated meningiomas: raising awareness about a causal oncological association.

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A 50-year-old woman presents with palpitations/sinus tachycardia, occasionally associated with chest pain and dyspnea and symptom onset the last 6 months prior to presentation. These episodes occur most often in the morning. Cardiological assessment with electrocardiogram, ultrasound and maximal stress test demonstrated sinus tachycardia, with no evidence of underlying heart disease. Laboratory tests (particularly hemoglobin, D-dimers, TSH and troponin) were normal. The personal medical history included endometriosis [since 2013, treated with norgestrel acetate (Lutonyl®) continuously since 2014], common migraine for twenty years and active smoking. An assessment for a suspicion of pheochromocytoma is carried out with normal plasma cortisol (08h00) and normal 24-hour urinary catecholamines and 5HIAA. Chromogranin A was slightly increased but the patient is on a proton pump inhibitor. To completely rule out this diagnosis, a Ga-68-DOTA-TATE PET/CT was performed demonstrating no evidence of pheochromocytoma, but the presence of numerous intracranial lesions with high somatostatin receptor (SSTRs) expression (Figure 1), corresponding to multiple meningiomas. Subsequent cerebral magnetic resonance imaging (MRI) confirmed the diagnosis, while a previously performed cerebral MRI in 2012 (for vertigo symptoms) was completely normal without any sign of meningioma.

Meningiomas constitute the most common non-glial intra-cranial tumor in adults and are most frequently benign (1) the most common primary brain tumor, has refined contemporary management of these tumors. Problematic, however, is the paucity of prospective clinical trials that provide an evidence-based algorithm for managing meningioma. This review summarizes the published literature regarding the treatment of newly diagnosed and recurrent meningioma, with an emphasis on outcomes stratified by WHO tumor grade. Specifically, this review focuses on patient outcomes following treatment (either adjuvant or at recurrence). The majority of meningiomas express hormonal receptors including progesterone receptors, and for many years, progesterin drug have been suspected to play a role in the development of meningiomas, especially if patients were treated for a long duration and/or with high doses (2,3)outcome and management.\nMATERIAL AND METHODS: We included 53 patients operated on and/or followed in the department for meningioma with progesterin intake longer than one year and with recent drug discontinuation.\nRESULTS: Cyproterone acetate (CPA). Progesterin-associated meningiomas (PAM) constitute a rare adverse event (4), are mostly multiple and are mainly located in the anterior or in the medial skull base (2)outcome and management.\nMATERIAL AND METHODS: We included 53 patients operated on and/or followed in the department for meningioma with progesterin intake longer than one year and with recent drug discontinuation.\nRESULTS: Cyproterone acetate (CPA). They are generally less aggressive, associated with a good prognosis, and the majority of meningiomas regress or stabilise upon treatment discontinuation. The most commonly involved progesterin drug is cyproterone acetate, however PAMs are also described with norgestrel acetate (2,3,5)outcome and management.\nMATERIAL AND METHODS: We included 53 patients operated on and/or followed in the department for meningioma with progesterin intake longer than one year and with recent drug discontinuation.\nRESULTS: Cyproterone acetate (CPA). Our patient has been treated with norgestrel acetate continuously for about 8 years, which may have led to the development of multiple meningiomas (appeared since her normal brain MRI in 2012).

In conclusion, this case highlights a rare adverse event associated with the chronic use of progesterins which can be visible with SSTRs PET. Raising awareness about this causal association is important given the prevalence of endometriosis.

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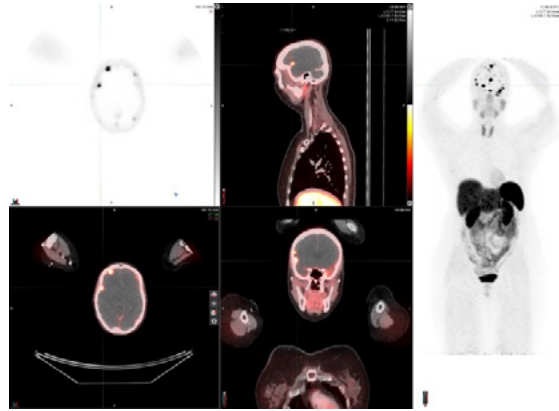


Figure: Ga-68-DOTA-TATE PET/CT showing multiple intracranial lesions with high somatostatin receptors (SSTRs) expression. No other lesions detected, especially extracranial.

OP-YNC06

Idiopathic SIADH: 4 years of diagnostic wandering

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We report the case of a 39-year-old woman who was initially admitted to the emergency room in 2016 for neurological symptomatology in context of hyponatremia (ideomotor slowing, headache, and cervical contracture) with no suspicious lesions on conventional imaging, biologic infectious signs, or CSF abnormalities. Tumor markers, chromogranin A and colonoscopy were normal.

Three 18FDG PET/CT scans (2017, 2018, and 2019) didn't find any suspicious hypermetabolic lesions.

A close follow-up was necessary because of the persistence of SIADH, qualified as idiopathic.

Eventually, a neuroendocrine tumor was suspected and 68Ga-DOTA-NOC PET/CT was performed in October 2020. It showed an ethmoidal lesion with overexpression of somatostatin receptors.

Consequently, it was resected on 11/02/21 and corresponded to a low grade olfactory neuroblastoma (aesthesioneuroblastoma).

In retrospect, this lesion was already visible on previous 18-FDG-PET/CT. Its localization made it difficult to notice because of the activity of the brain and the ocular muscles.

Adjuvant radiotherapy was not performed due to the limited nature of the disease.

The natraemia remains within normal range since surgery and the august 2021 68Ga-DOTA-NOC PET/CT shows no evidence of recurrence.

Aesthesioneuroblastoma is a rare tumor of the neuro-olfactory epithelium of the nasal cavities (less than 2000 cases in the literature) and of difficult diagnosis.

It usually presents with ENT symptoms and signs (epistaxis, rhinorrhea, otitis...), sometimes ophthalmological (ocular pain, exophthalmos...). It preferentially affects men between 30 and 70 years old. The first-line treatment is surgical. Adjuvant radiotherapy is an option in case of significant extension of the lesion or involvement of local lymph nodes. The role of chemotherapy has not yet been established.

SIADH resulting in hyponatremia is a paraneoplastic syndrome encountered in various tumors, notably pharyngeal, SCLC, pancreatic and neuroendocrine. It is very rare in the setting of an aesthesioneuroblastoma (a few dozen cases reported).

This patient's history illustrates the value of 68Ga-DOTA-NOC PET/CT in the development of unexplained SIADH by searching for a neuroendocrine tumor.

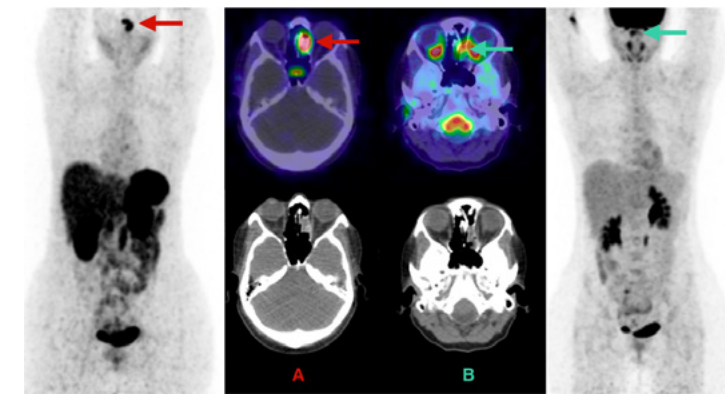


Figure : A - ⁶⁸Ga-DOTA-NOC PET/CT 21/10/2020 B - ¹⁸F-FDG-PET/CT 10/04/2020 (arrows indicate the lesion)

OP-YNC07

¹⁸F-FDG PET/CT unveils a cyst with a twist

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¹ Ku Leuven; ² Nucleair Medicine; ³ Ziekenhuis Oost-Limburg, ³ University Hospitals Leuven, Belgium

Following a biopsy proven recurrent breast carcinoma, a 59-year-old woman underwent an 18F-FDG PET/CT as a routine staging procedure. This revealed two malignant lesions in the left breast, but also increased FDG-uptake anterior in the bladder dome, suspicious of malignancy. An additional cystoscopy was performed with no abnormal findings; biopsies were not taken at that time. Subsequent CT-Urography showed a focal thickening of the anterosuperior part of the bladder wall with a small endoluminal polypoid expansion from the caudal part of the wall thickening, suspicious for a malignant lesion, compatible with either a transitional cell carcinoma or, less likely, an urachal remnant malignancy.

Given the confirmation of a possibly malignant lesion anterior in the roof of the bladder a robot assisted partial cystectomy was performed. Pathologic findings of the resection specimen showed on gross examination a cyst measuring approximately 1,1 x 1,6 cm with mucoid content and tumour-free resection margins. Immunohistochemical stains showed that the epithelial lining of the cyst was positive for CK20 and CDX2, while negative for CK7 (intestinal immunophenotype). The cyst was classified as an urachal mucinous cystic tumour of low malignant potential.

The urachus is a fibrous tube extending from the umbilicus to the anterosuperior bladder dome as part of the sagittal division of the cloaca into the urogenital sinus, including bladder and sex organs, anteriorly and the forming rectum dorsally. This connection is supposed to obliterate at week 12 of gestation becoming the median umbilical ligament. When this obliteration is incomplete in foetal development urachal pathology can occur, resulting in the formation of a patent urachus, urachal sinus, urachal diverticulum or urachal cysts. Urachal cysts, arising from the lower part of the urachus, are the most common of these abnormalities and are frequently asymptomatic and an incidental find. Malignant transformation of an urachal remnant can occur; however, it is rare. In case of malignant transformation most patients present with advanced disease due to the asymptomatic course until secondary infiltration of the bladder dome, which causes mainly haematuria, pain, irritative complaints and mucinuria.

This case accentuates the value of 18F-FDG PET/CT, despite of the urinary excretion of FDG, in visualization of possible urachal malignancies not visible on cystoscopy and could be helpful in follow-up of these lesions.

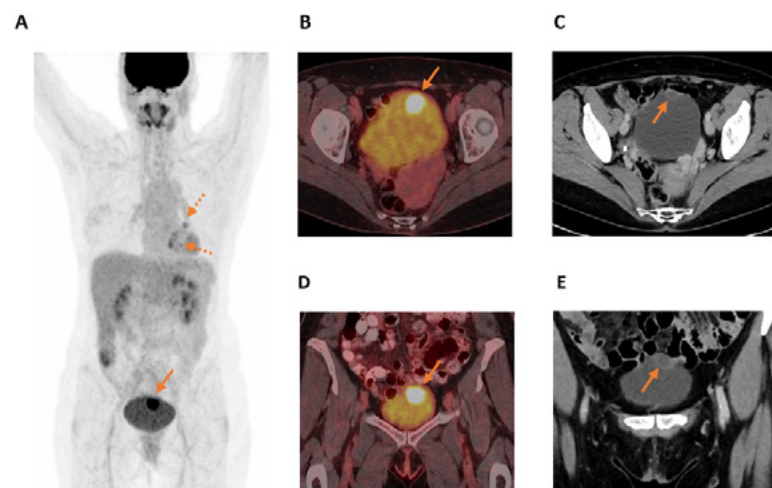


Figure Legend:

A: Maximum intensity projection of the ^{18}F -FDG PET performed for staging of the recurrent breast cancer showing two malignant breast lesions (dotted arrows) and the focal FDG-avid mass in de bladder dome (full arrow).

B/D: Axial and coronal ^{18}F -FDG PET/CT performed for staging of the recurrent breast cancer showing the FDG-avid mass in de bladder dome (full arrow).

C/E: Axial and coronal CT-Urography performed after the negative cystoscopy showing the focal thickening of the anterosuperior part of the bladder wall with a small endoluminal polypoid expansion from the caudal part of the wall thickening (full arrow).

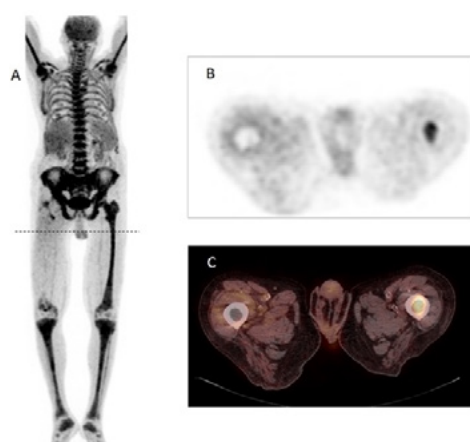
OP-YNCO8

Femoral osteonecrosis in the setting of myelodysplastic syndrome with blasts excess

Isaac Kargar Samani,¹ Yassin Akachar,² Anne Sonet,² Elodie Collinge,² Carlos Graux,² Thierry Vander Borght,¹ Bruno Krug

¹ Chu Ucl Namur; Site Godinne; Médecine Nucléaire, ² Chu Ucl Namur; Site Godinne; Hématologie, Yvoir, Belgium

A 76-year-old male patient suffering from myelodysplastic syndrome was made 5 months before the start of chemotherapy which was eventually begun because of worsening of cytopenias and increase in the rate of blasts. Two weeks after the start of the treatment, biology showed a macrophage activation syndrome and the patient developed an intense pain in the right femur.



The maximal intensity projection image (A) and the corresponding PET (B) and CT (C) axial slices, show an absent of FDG uptake nearly in the entire femur.

Magnetic resonance imaging centered on the right femur showed medullary replacement with T2-weighted high signal patches surrounded by T1-weighted high signal borders without any enhancement after gadolinium injection. The differential diagnosis in decreasing order of probability was osteonecrosis or transient osteoporosis. Arthritis is unlikely given the absence of acetabular involvement but could not be formally excluded. To confirm one of these diagnoses and to exclude any occult source of infection, F-18 fluorodeox-

ylucose positron emitting tomography/computed tomography (FDG PET/CT) was performed and showed an intense hypermetabolism of the axial and appendicular skeleton without any uptake in the right femur. Femoral biopsy confirmed the diagnosis of femoral osteonecrosis. After exhaustive literature review, this appears to be the first reported case of femoral osteonecrosis visualized on FDG PET/CT, moreover in a context of myelodysplastic syndrome.

POSTER PRESENTATION

PP-YNCO1

18-FDG PET/CT of Takayasu arteritis in a 13-year-old girl.

Eman Sirfouq¹, Hendrik Everaert¹, Sophie Bourgeois¹, Lode Goethals¹, Tony Lahoutte¹;

¹UZ Brussel, Belgium,

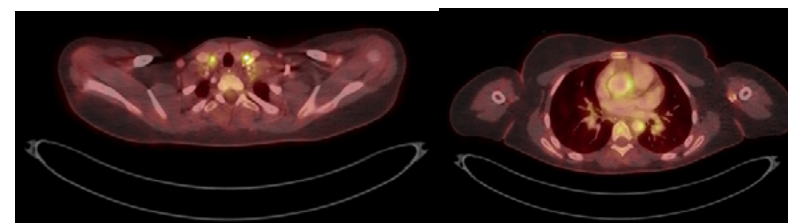
Case Presentation

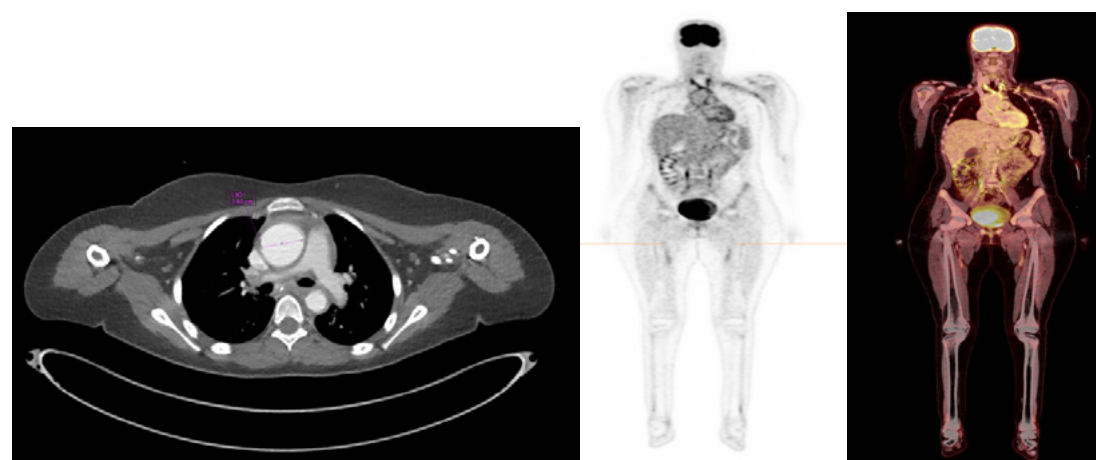
A 13-year-old girl was presented with fatigue, nausea, vomiting, anorexia, weight loss, abdominal pain and arthralgia since two weeks. Clinical examination revealed a fever and a punctiform rash on her legs. Laboratory tests showed elevated serum levels of inflammatory markers. Urine test demonstrated increased levels of proteins, ketones and leukocytes. IV antibiotic therapy was started without improvement of the symptoms. Chest X-ray showed a mild bronchitis but no infiltrates. Abdominal X-ray, MRI of the brain, ultrasound of the abdomen and the ankle joint were also negative. The first echocardiogram demonstrated a mild aortic valve insufficiency. PET/CT (fig. 1) revealed an increased uptake of ^{18}F -FDG in the wall of the ascending aorta, the aortic arch and proximal trajectory of the common carotid arteries. On CT an increased aortic wall thickness was seen. Transverse CT shows the dilation of the ascending aorta up to 63 mm (mean diameter for a child of 12-13 years old is 22.40 mm). The second echocardiogram confirmed the dilation of the ascending aorta. MRI angiography of the brain showed no abnormalities of the cerebral arteries. Based on these PET/CT findings and the constitutional symptoms, the diagnosis of Takayasu arteritis was made. High dose corticosteroid therapy was started, with resolution of the symptoms.

Discussion section

Takayasu arteritis is a rare disease typically occurring women in their twenties to thirties. This type of vasculitis mainly affects large vessels such as the aorta and its major branches. This disease has a variety of presenting complaints. In children, hypertension and systemic symptoms like headache, fever, and weight loss are the most common symptoms. Because of the non-specific nature of its presenting complaints and lack of appropriate biomarkers, delay in diagnosis of this illness can come with complications. The clinical features and elevated inflammatory markers can indicate the diagnosis but imaging plays a crucial role. Conventional angiography and Doppler ultrasound are widely used modalities when a vasculitic syndrome is suspected. However, these imaging methods only show changes in vascular morphology which appear later in the disease course. ^{18}F -FDG PET/CT is the latest addition which can provide more information about the inflammatory activity. Our case highlights the value of PET/CT imaging in the diagnosis of Takayasu arteritis in pediatric patient.

Figure 1: ^{18}F -FDG PET/CT image of a pediatric patient with Takayasu arteritis. A. Coronal PET. B. Coronal fused. C-D. Transverse fused. E. Transverse CT.





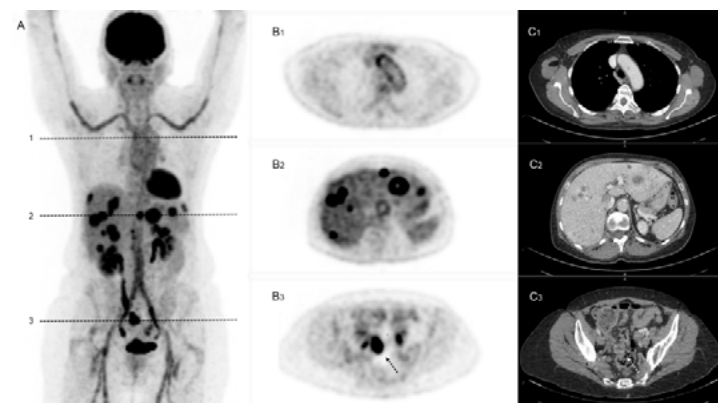
PP-YNC02

Concomitant finding of a large vessel vasculitis and a colorectal neoplasia on FDG PET/CT

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A 64-year-old female patient underwent an F-18 fluorodeoxyglucose positron emitting tomography/computed tomography (FDG PET/CT) for evaluation of inflammation not responding to steroid therapy in the setting of suspected polymyalgia rheumatica. A hypermetabolic mass was found at the rectosigmoid junction associated with hypermetabolic hepatic hypodense lesions as well as a hypermetabolic thickening of large vessels' wall (aorta, carotids, subclavian arteries, axillary arteries, iliac arteries and femoral arteries).



The maximal intensity projection image (A) and the corresponding PET (B) and contrast enhanced CT (C) axial slices, at levels 1, 2 and 3, show hypermetabolic thickening of large vessels' wall, like the aortic arch (B₁ and C₁) as well as liver metastases (B₂ and C₂) and the pelvic colonic tumor (dotted arrows on B₃ and C₃).

In this setting, we suspected the vasculitis to be paraneoplastic. Paraneoplastic vasculitis is a rare condition that has not been frequently described mainly because of the difficulty to establish a causal relationship between cancer and vasculitis. They account for 2 to 5% of all vasculitides. They predominantly affect small and medium vessels, the most common vasculitis being leukocytoclastic vasculitis, and seem to be more often related to hematologic neoplasms with a proven association between hairy cell leukemia and polyarteritis nodosa. Nonetheless, there have been a few articles reporting associations between large vessels vasculitis and hematologic cancers such as chronic myeloid leukemia, chronic myelomonocytic leukemia and myelodysplastic syndrome and there was one case report of an aortitis as a paraneoplastic syndrome of a colon adenocarcinoma. Response to treatment appears to be very inconsistent with some patients showing a rapid response to steroid therapy and others relapsing, some never showing any improvement in the first place and needing specific treatment of the underlying malignancy. In our case, the patient was not showing much response to steroid therapy either, but after initiating chemotherapy, C-reactive protein started declining, going from 102 mg/L to 19 mg/L in a month and dwindling to 5.8 mg/L the following month, which gave weight to the diagnosis of paraneoplastic vasculitis

Consent:

Consent was obtained from the patient.

PP-YNC03

Rare transformation of hairy cell leukemia to high-grade lymphoma: a case report.

Paulien Moyaert¹, Hendrik Everaert¹, Lode Goethals¹, Udunda Anazodo², Eric Achten³, Sophie Bourgeois⁴;

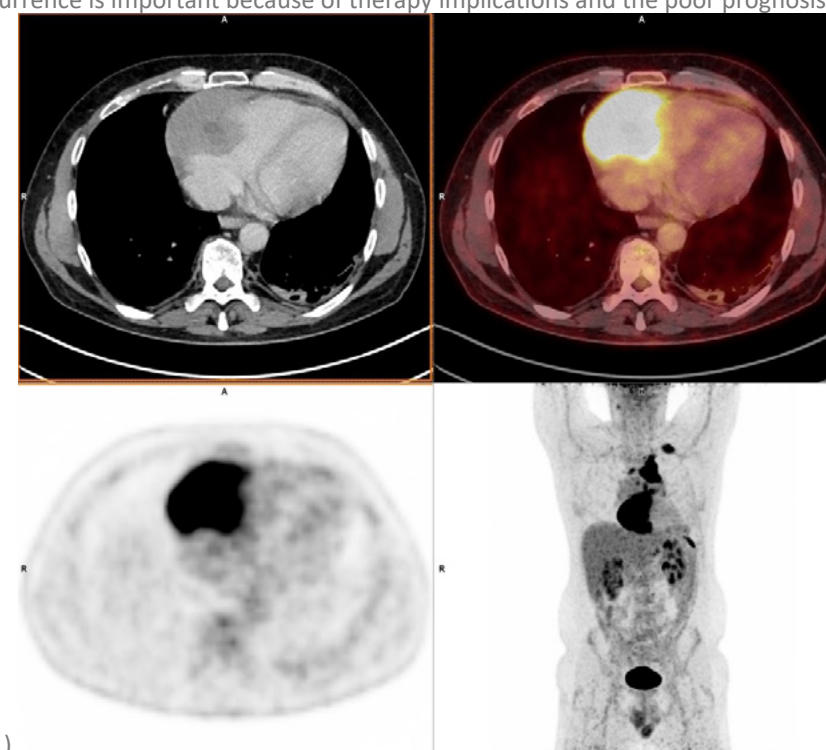
¹UZ Brussel, Brussels, Belgium, ²McGill University, Canada ³UZ Gent, Gent, Belgium

Case presentation: In December 2021, a 51-year-old man presented to the emergency department with shortness of breath. He was diagnosed with hairy cell leukemia (HCL) in 2017 and was treated with Rituximab, Litak, Mabthera, and R-bendamustine. Complete remission was achieved in June 2020.

Bedside echocardiogram showed a pericardial effusion for which a drain was placed. Flow cytometric analysis of the pericardial fluid revealed a monoclonal cell population. This could - at that point - also have been a monoclonal B-lymphocytosis of uncertain origin (MLUS). However, cardiac MRI on January 18th, 2022, showed an infiltrating mass encasing the right coronary artery, and several spinal metastases, suggestive of malignancy. These lesions, together with several lymph nodes, were hypermetabolic on ¹⁸F-FDG-PET (figure 1), further raising the suspicion of malignancy. Biopsy revealed high grade immunoblastic diffuse large B-cell lymphoma (DLBCL) (CD20+, CD22+, CD30-, Ki67 90%, P53 gene mutated). In the light of the patient's history of HCL, this DLBCL is most likely a transformed lymphoma. The patient will be treated with R-CODOX-IVAC.

Discussion: HCL is a slowly progressive lymphoproliferative disorder. Transformation to DLBCL is extremely rare. To date, only a handful of cases have been reported. The suggestion of blastic transformation is based on the fact that the blasts share the same surface immunoglobulin light chain and immunophenotype (CD20+, CD22+, CD30-) with HCL cells. Furthermore, the marked increase in Ki-67 expression indicates transformation of a low-grade lymphoid leukemia to a high-grade lymphoma. Lastly, p53 overexpression is often demonstrated in hematologic malignancies transforming to high-grade neoplasms. ¹⁸F-FDG-PET played an important role in this case. It was used to aid in the diagnosis of HCL in 2017, then to assess remission in 2020, and finally to detect disease recurrence in 2022. ¹⁸F-FDG-PET will continue to play an important role in the assessment of chemosensitivity and treatment response.

In conclusion, we report a rare case of transformation of HCL into high-grade lymphoma. The patient will be treated with R-CODOX-IVAC and followed up with ¹⁸F-FDG-PET. Although this transformation is uncommon, awareness of its occurrence is important because of therapy implications and the poor prognosis (5-year survival rate 41,3% vs. 87% for



HCL).

Figure 1. Axial ¹⁸F-FDG-PET images (with myocardial suppression) showed an intensely ¹⁸F-FDG-avid right atrial and ventricular mass extending into the mediastinum. In addition, there was uptake in lymph nodes at the level of the mediastinum, the internal thoracic artery, the left retroclavicular and the right parajugular area.

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PP-YNC04

Infection or inflammation? That's the question. A fracture-related infection detected by FDG PET/CT.

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Case presentation: A 66 year old man, suffered a right pertrochanteric femoral fracture after a trauma last year, for which a proximal femur nail was placed. Initially, his recovery went well without wound healing issues. However, after a few months the patient visited the hospital with fatigue, pain in the right hip region, and he told he had a period of fever two months ago. Except for an elevated ESR (37 mm/h), there are no clinical signs of infection. A (dynamic) FDG-PET/CT scan was performed on a total body PET/CT system (Biograph Vision Quadra) with iMAR (Iterative Metal Artifact Reduction) reconstruction. This scan showed an increased heterogeneous uptake around the pen, which also persisted on the non-attenuation corrected (NAC) images. Increased uptake was also visible in the soft tissue surrounding the proximal femur nail and inguinal lymph nodes. Based on these imaging result and clinical suspicion, the nail was surgically removed. The prosthesis itself, along with several biopsies and a puncture (which was cloudy), was sent to microbiology for analysis. We are still awaiting the results.

Discussion: Based on the FDG PET/CT, it is often difficult to properly differentiate between an infection and reactive inflammation due to foreign body material or recent surgery (e.g. due to soft tissue and bone healing processes). FDG uptake can be present even years after placement of a prosthesis. However, in this case, the heterogeneous uptake and its persistence on the NAC images were indicative of an ongoing infection. Additionally, multiple positive inguinal lymph nodes may also be an indicator of infection. In the left femur, a proximal femur nail was placed four years ago, which allowed us to make a comparison between the two prostheses. No increased FDG uptake was visible around the left prosthesis.

Regarding the total body PET/CT system, a great advantage is the significantly reduced scan time due to the large field of view (106 cm, up to an acquisition time of 3 minutes). Moreover, it is expected that smaller infectious foci can be detected. The CT-image reconstruction with iMAR also is of added value for the surgeon, since it clearly showed that the fracture is consolidated enough to surgically remove the proximal femur nail. Concerning the dynamic scan performed, these dynamic images will be evaluated at a later stage (including more patients) to see if uptake curves in time can help us to properly differentiate between inflammation and infection.

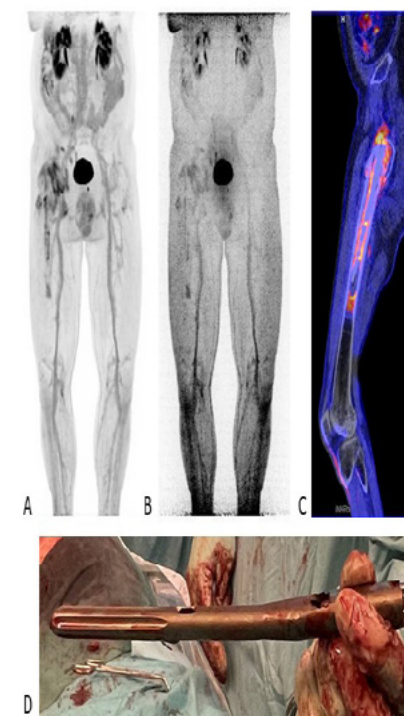


Figure 1: A) The maximum intensity projection (MIP) showing heterogeneous FDG-activity in the right hip. It is even possible to recognize the outlines of the proximal femur nail. B) The non-attenuation corrected (NAC) MIP imaging showing persistent FDG-uptake along the proximal femur nail, especially at the tip. C) Sagittal view of the heterogeneous activity along the nail, reconstructed with iMAR. D) Proximal femoral nail after surgical removal, which was sent to the microbiology department for analysis.

PP-YNC05

Bilateral hot caudate nuclei, what diagnosis to be raised?

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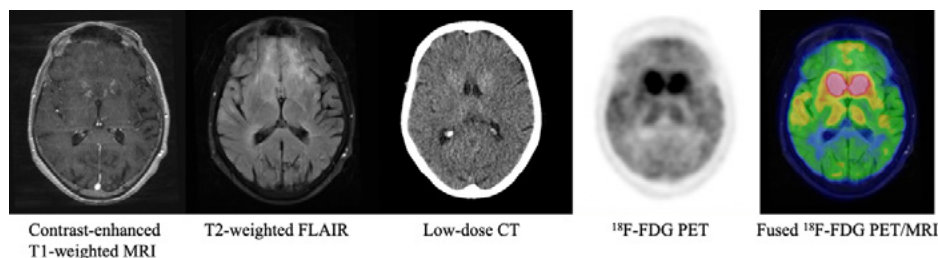
A 75-year-old patient with no known medical history was admitted for desaturation and acute neurological deficits (right facial hemiparesis, cognitive disorders and hallucinations). The biology shows an elevated CRP attributed to bronchopneumonia.

MRI showed hyperintense lesions (T2-weighted FLAIR) in the bilateral fronto-orbital areas and the caudate nuclei, the internal capsules and the internal pale globes, with contrast enhancement after injection of Gadolinium (T1-weighted MRI). Among the multiple diagnoses for bilateral abnormalities of the basal ganglia¹, three hypotheses were retained by the radiologist: encephalitis, neurosarcoidosis or primary central nervous system (CNS) lymphoma. Cerebrospinal fluid (CSF) analysis showed lymphocytosis.

The whole-body ¹⁸F-FDG PET/CT showed no extra-cerebral lesions. In the brain, intense symmetric bilateral intense ¹⁸F-FDG uptake in the caudate nuclei (SUVmax: 19.7) was visualized and associated with diffuse cortical hypometabolism (Fig). The diagnosis of encephalitis was raised as similar cases have been reported in anti-VGKC (voltage gated kalium channels) and anti-NMDAr (N-methyl-D-aspartate receptor) encephalitis with lymphocytosis in the CSF.² Another possible diagnosis was neurosarcoidosis which is a very rare disease, less likely in the absence of coexisting systemic manifestations and the absence of increased serum or CSF angiotensin-converting enzyme.^{3,4}

The stereotactic biopsy guided by ¹⁸F-FDG PET/CT and MRI led to the final diagnosis of primary diffuse Large B-cell lymphoma (DLBCL) of the CNS. The flow cytometric results revealed the presence of a monoclonal B-cell population in the CSF. The patient was treated with corticosteroids followed by Rituximab-Methotrexate; he died after a few weeks.

Even if ¹⁸F-FDG PET/CT cannot make the differential diagnosis of brain lesions with certainty, it has an added value in the diagnostic work-up. In this case, highly ¹⁸F-FDG avid lesions associated with spontaneous caudate nuclei hyperdensity in CT images, attributed to high cellularity, might have directed towards the diagnosis of DLBCL.^{1,5}



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PP-YNC06

When phagocytosis goes wrong

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We report the case of a 26-year old woman who presented herself to the emergency department for severe bilateral visual loss, headache, and nausea, associated with left hemiface and upper limb paresthesia since one month. A brain MRI was performed and demonstrated a meningeal thickening, expanding from the cranium basis to the cervical canal, with no related brain lesions. Cervico-dorsal MRI confirmed the extension of this thickening to the spine. Whole body ¹⁸F-FDG PET/CT highlighted intense hypermetabolic infiltration along the brain stem and medullary cervical canal with only one isolated cervical lymph node. No primitive neoplasia was detected.

Those investigations led us to the differential diagnosis of neurosarcoidosis, lymphomatous disease, neoplastic meningeal carcinomatosis, histiocytosis, IgG4 related-disease or infectious disease like syphilis,...

Exhaustive biological tests were realized but all the infectious, inflammatory, auto-immune and neoplastic markers were negative, leading to a diagnosis of neurosarcoidosis in first hypothesis. A treatment with high-dosed corticoids, anti-TNF and Ledertrexate was introduced although imaging control obviously demonstrated an increase of the cerebrospinal lesion.

A meningeal biopsy was therefore performed and histologic analysis confirmed the diagnosis of Rosai-Dorfman-Destombes histiocytosis, which is a rare and idiopathic non neoplastic-disease, often characterized by painless cervical lymphadenopathy and general symptoms. Extranodal sites have also been reported but neurological complications are very unusual.

This case highlights the interest of whole body ¹⁸F-FDG PET/CT in this type of disorder to exclude more aggressive diseases as lymphoma, but also to detect extranodal involvement, including neurological lesions. Furthermore, ¹⁸F-FDG uptake of the lesions allows rapid response assessment of standard treatments, and could lead to earlier implementation of novel therapies to improve patient outcomes.

PP-YNC07

Progressively worsening back pain in a 16 year old patient

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Case presentation:

A 16-year-old male, without any relevant medical history, presented with progressively worsening back pain, especially when using the M. trapezius and Mm. rhomboidei. Clinical examination showed a scoliosis of the dorsal spine. An MRI (magnetic resonance imaging) of the cervical spine and the upper part of the dorsal spine was performed and followed by a CT (Computed Tomography) of the spine. These exams excluded herniated discs. Due to suspicion of an osteoblastoma the patient was referred to our centre for more specialized follow-up. The MRI was repeated; now with Gadolinium contrast enhanced images. These images showed multiple bone lesions in the corpora of T6, T7, T8, T10 and the 8th rib and perilesional edema, suggestive for an osteoblastoma. An [¹⁸F]FDG-PET/CT (Fluorodeoxyglucose-positron emission tomography/computed tomography) was performed and showed enhanced metabolic activity in the arcus and left processus articularis of T8 but no significantly elevated metabolic activity in the surrounding tissues.

The [¹⁸F]FDG-PET/CT allowed a better distinction between the osteoblastoma and the extensive reactive perilesional edema.

The patient is treated in a centre of expertise for osteoblastoma.

Discussion:

Osteoblastoma is a benign tumour that due to its local aggressiveness can cause much pain and harm. It is quite rare and accounts for only 1 % of the benign primary bone tumours (1). The spine and the tubular bones are the most frequent locations of occurrence (2). It is typically seen in men (twice as often as in female) in their second or third decade (3).

Although the best way to confirm the diagnosis remains through anatomopathological examination, imaging plays an important role in assessing the tumour. Due to the low incidence of osteoblastoma, there is not much information about which imaging modality is best to use. An overestimation of the lesions on MRI is a known problem (4,5). This might be due to the "flare phenomenon"; inflammatory edema together with loose fibrous tissue, hypervascularisation and the presence of mature lymphocytes, and plasma cells. Since osteoblastoma is a metabolically very active tumour and no uptake is seen in the flare [¹⁸F]FDG-PET/CT can be used to differentiate between the flare and the osteoblastoma itself. Huang et al. conclude in their recent retrospective study that the combination of MRI and PET/CT is very interesting as this might make up for the shortcomings of MRI (6,7).

PP-YNC08

Inflammation PET: don't forget the head.

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Case presentation

A 68-year-old woman presented at the outpatient general internal medicine specialist clinic with complaints of neck pain with irradiation to both ears, shoulder pain and temporal headache since two months. A previous CT scan of the cervical spine only showed mild degenerative changes. Upon further questioning she also reported night sweats, loss of weight and jaw claudication. She did not report vision loss. Blood testing revealed strongly elevated sedimentation rate and C-reactive protein. Clinical examination showed a prominent and painful temporal artery upon palpation on both sides with a purple-colored swelling of the overlying skin. Movement of the shoulders was painful but the range of motion was preserved.

¹⁸F-FDG PET-CT was performed because of high suspicion of giant cell arteritis (GCA), and showed intense FDG accumulation (more than liver) in the vertebral artery and also high FDG uptake in other cranial arteries such as the temporal artery, maxillary artery and the occipital artery. Other medium and large-sized arteries showed no pathological FDG uptake. Besides active vasculitis, ¹⁸F-FDG PET-CT also showed mild signs suggestive of associated polymyalgia rheumatica (PMR). A biopsy of the temporal artery was performed which confirmed the diagnosis of temporal arteritis with diffuse infiltration of eosinophils, lymphocytes and aggregates of multi-nucleated giant cells in the vascular wall. Treatment with high dose oral corticosteroids was commenced and clearly improved symptoms three weeks later.

Discussion

This case demonstrates the use of ¹⁸F-FDG PET-CT in GCA, even when only cranial arteries are involved. ¹⁸F-FDG PET-CT is currently not recommended for the assessment of inflammation in cranial arteries in GCA and the use of ¹⁸F-FDG PET-CT is currently limited to detect extracranial vascular involvement. With the use of newer generation PET-CT scan-

ners and new reconstruction methods resulting in improved signal-to-noise and spatial resolution, detecting cranial artery involvement in GCA becomes more specific and reliable. Because of generally low uptake and complex anatomical locations of the involved arteries, specific assessment of the cranial arteries can improve sensitivity and specificity.

This case demonstrates the anatomical locations on ^{18}F -FDG PET-CT of the most important cranial arteries: temporal artery, vertebral artery, maxillary artery and occipital artery. When GCA is suspected, one should always systematically observe these anatomical sites.

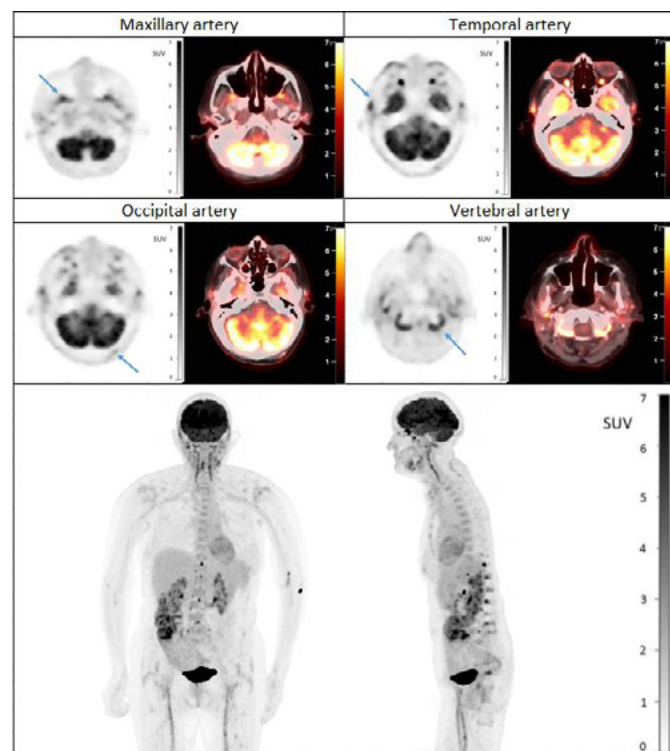


Figure 1: ^{18}F -FDG PET-CT of biopsy-proven GCA, with high FDG uptake in the cranial arteries (vertebral artery, temporal artery, maxillary artery and occipital artery) but without extracranial vascular involvement.

PP-YNC09

A mysterious case of a persistent hypermetabolism in the bone marrow

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A 69-year-old Armenian male patient presented with fever, pain and tingling of the feet, fatigue and anorexia (15 kg weight loss in one year). Clinical examination revealed an erythema nodosum in the lower extremities. Biochemical examination showed a pronounced pancytopenia, furthermore also an inflammatory tableau with reactively disturbed protein electrophoresis without arguments for monoclonal gammopathy. Chest radiography was normal. Ultrasound of the abdomen showed splenomegaly. ^{18}F -FDG PET/CT was performed and showed multiple hypermetabolic adenopathies in the cervical region on both sides, as well as a diffuse homogeneous hypermetabolism of the bone marrow, without noticeable hypermetabolism in the enlarged spleen. Bone biopsy was performed and showed a hypercellular bone marrow with dysplastic features in the 3 marrow series and hemophagocytosis. Skin biopsy of the lower extremities showed a vasculopathy with subendothelial complement deposition. Based on the ^{18}F -FDG PET/CT, a lymph node biopsy was performed of a left cervical gland, which showed an important presence of plasma cells, sinus histiocytosis and hemophagocytosis. The preferred diagnosis was an idiopathic multicentric Castleman disease, plasma cell variant. Therapy with corticosteroids and rituximab was initiated. Despite this therapy, there was further deterioration of the patient's condition with development of deep anemia and episcleritis of the right eye. A new ^{18}F -FDG PET/CT was performed and showed a strong hypermetabolic lymph node in the left axilla, as well as a persistent diffuse hypermetabolism in the bone marrow. Additional excisional biopsy of the left axillary gland showed a parenchymal and sinusoidal histiocytic expansion, without granuloma formation, furthermore presence of foam macrophages and some Touton-like multinucleated giant cells. Genetic analysis showed no pathogenic mutations on the axillary lymph node. The differential diagnosis consisted of a histiocytic systemic disease, type Rosai-Dorfman, Erdheim-Chester or disseminated adult xanthogranuloma. Sirolimus was associated to the therapy, resulting in a decrease in all known disease sites, with exception of the bone marrow. Additional bone marrow Sanger sequencing however revealed a somatic

UBA1 mutation consistent with VEXAS syndrome. Therapy with Siltuximab was initiated. VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome is a newly-described adult-onset inflammatory syndrome characterized by vacuoles in myeloid and erythroid precursor cells and somatic mutations affecting methionine-41 (p.Met41) in UBA1. In this case, bone marrow hypermetabolism was a consistent finding independent of the patient's clinical condition and may be related to the underlying myelodysplasia in VEXAS syndrome. This is the first illustration of VEXAS syndrome on PET.

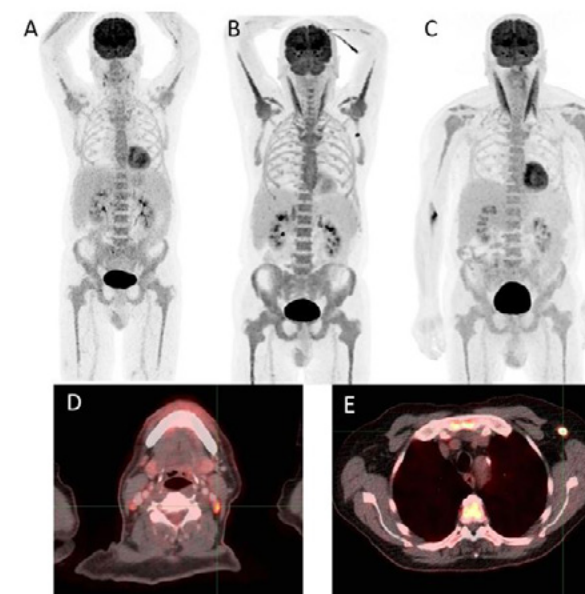


Figure legend:

A: MIP of the initial ^{18}F -FDG PET/CT showing multiple hypermetabolic adenopathies in the cervical region on both sides, as well as a diffuse homogenous hypermetabolism of the bone marrow.

B: MIP of the follow up ^{18}F -FDG PET/CT showing a strong hypermetabolic lymph node in the left axilla, as well as a persistent diffuse hypermetabolism in the bone marrow.

C: MIP of the follow up ^{18}F -FDG PET/CT after association of Sirolimus showing a persistent diffuse hypermetabolism in the bone marrow and resolution of the other disease localizations.

D: Fused axial illustration of the initial ^{18}F -FDG PET/CT showing a hypermetabolic lymph node in the left cervical region.

E: Fused axial illustration of the follow up ^{18}F -FDG PET/CT showing a hypermetabolic lymph node in the left axillary region.

PHARMACY TRACK ORAL PRESENTATIONS

OP-PHARM1

Development and evaluation of a trans-cyclooctene (TCO) probe for pretargeted PET imaging

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Aims: Bioorthogonal pretargeting employing a radiolabelled 1,2,4,5-tetrazine (Tz) and a monoclonal antibody (mAb) conjugated *trans-cyclooctene* (TCO) is an extensively studied approach to increase the target-to-background ratios while circumventing the radiation burden to healthy tissues. However, the liability of the TCO to isomerize to its less reactive cis-form and the internalization of the mAb conjugates over time has hampered its way towards clinical trial as a powerful diagnostic tool. Given this we envisaged to develop and more stable ^{18}F -labelled d-TCO-probes to investigate their utility in pretargeted immuno-positron emission tomography (PET) imaging using a tetrazine-modified antibody.

Methods: A small library of fluorinated (^{19}F) d-TCOs was synthesized and a pretargeted blocking *in vivo* study was performed to assess their capability to target and react with pretargeted tetrazine-tagged CC49 antibody (anti-TAG-72) in tumor bearing mice. TAG-72-expressing human colorectal cancer LS174T cells (5×10^6) were subcutaneously inoculated in the right hind leg of BalbC nude mice. CC49-Tz (100 $\mu\text{g}/100 \mu\text{L}$) or CC49 alone (100 $\mu\text{g}/100 \mu\text{L}$; negative control) were intravenously administered 72h before fluorinated (^{19}F) dTCO. After 1h TCO-Cy5 was administered followed by *in vivo* and *ex vivo* fluorescence imaging using an IVIS scanner after 24h.

From this study, selected d-TCO compound was used for radiolabeling with ¹⁸F. Briefly, the tosylated d-TCO precursor (5mg) in dry ACN was reacted with [¹⁸F]F⁻ for 10 min at 70°C, to afford [¹⁸F]MICA-214. Purification was performed using semi-preparative HPLC. Radiochemical purity was determined by analytical HPLC.

LogD was determined using the shake flask method. Stability of radiotracer was evaluated in PBS and mouse plasma at 37°C.

Results: A novel d-TCO derivative showed an excellent blocking efficiency (91%) against TCO-Cy5 in a pretargeted blocking study, confirming good *in vivo* ligation with the Tz-conjugated antibody (Figure1). The radiolabeling of d-TCO with ¹⁸F resulted in a RCY of 11±0,4% (decay-corrected to EOB) and >98% radiochemical purity. The tracer showed moderate lipophilicity with a logD value of 1.25 ± 0.11. The tracer showed no isomerization to cis-form after incubation in PBS for up to 2h, and up to 96% intact tracer was found in mouse plasma after 2h.

Conclusions: A novel fluorinated d-TCO-probe was synthesized, and demonstrated high *in vivo* IEDDA reactivity in tumor-bearing mice, as shown by the blocking effect. A new [¹⁸F]-d-TCO tracer was successfully radiolabelled in good RCY and good *in vitro* stability. Further *in vivo* evaluation of this radiotracer will determine its future use towards in pretargeted imaging approaches.

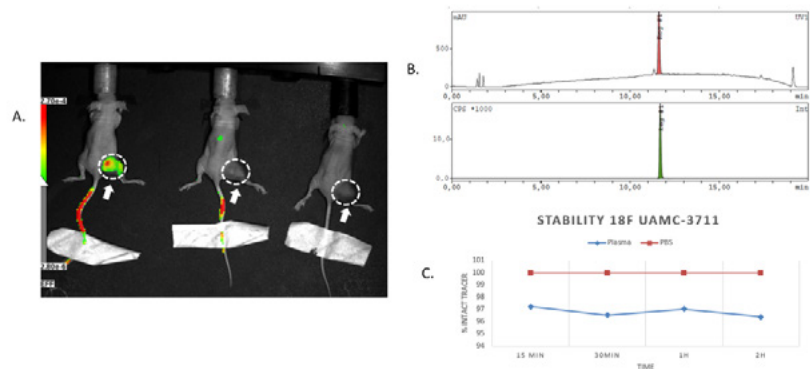


Figure 1: A) From left to right, tumor uptake of TCO-Cy5 in positive control, negative control and blocked group (UAMC-3711). B) HPLC radiochromatogram of the isolated tracer co-injected with cold-reference. Stability of tracer in PBS and in mouse plasma at 37°C

OP-PHARM2

Site-specific conjugation of fluorescent dyes and chelators on antibody fragments via maleimide-thiol chemistry.

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Aims: Radioimmunoconjugates (RICs) rely on the conjugation of a radionuclide to a biological vector molecule for therapeutic or diagnostic applications. Antibody fragments are excellent vectors with high selectivity and affinity. Furthermore, optimal target-to-background ratios can be obtained at early time points p.i. (i.e., 1-2 hours) which is not the case for standard mAbs. The radioactive payload on RICs can be attached by either random or site-specific radio-labeling methods. With site-specific labeling, it is possible to preserve the antigen-binding site and control the payload-to-vector ratio, producing homogeneous end-products. Here, we describe an optimized protocol for site-specific conjugation of fluorescent dyes and chelators using maleimide-thiol chemistry.

Method: The antibody fragment (1 eq) containing a C-terminal free cysteine was reduced in 10 mM DTT (dithiothreitol) D-PBS buffer (pH 7.4) for two hours at room temperature (RT). Next, a buffer exchange (PD-10) was performed to 0.1 mM TCEP (tris(2-carboxyethyl)phosphine) in D-PBS buffer (pH 7.4). Subsequently, the fluorescent dye (Alexa Fluor™ 647 C₂ Maleimide) or DFO*-maleimide was added dropwise (2 eq., 10 mM in DMSO) and incubated for two hours at RT. After concentrating the sample (Amicon® Ultra-15), another buffer exchange (PD-10) was performed to a non-reducing DPBS (pH 7.4) buffer, separating the conjugated vector from the excess of dye or chelator. A subsequent overnight incubation at 4 °C facilitated the oxidation of unconjugated thiols to form dimers. To ensure no reactive cysteines would be present in the final sample, N-maleoyl-β-alanine (0.2 eq., 20 mM in DMSO) was added, and size-exclusion (SE) chromatography (Superdex®75 10/300 GL) was used as the final purification step. The sample was analyzed by SE-HPLC, SDS-PAGE, and LCMS, ensuring a monodisperse sample.

Results: As TCEP is not a stable reducing agent in phosphate buffers, an initial incubation period with DTT was necessary. The subsequent use of TCEP was essential to prevent dimerization of the vector during conjugation and thus in-

creased labeling efficiency. Optimal conjugation conditions were achieved with a 50 μM vector concentration and two equivalents of maleimide construct, resulting in a coupling yield of 85 %. The overall recovery of the vector was 60 %.

Conclusion: We described a selective and robust maleimide conjugation protocol for site-specific labeling of biological vectors. The fluorescent-labeled and DFO*-derivatized antibody fragments will be used for *in vitro* binding studies and zirconium-89 PET imaging studies, respectively.



Fig. 1. Schematic illustration of site-specific conjugation of an antibody fragment with a maleimide-based construct (fluorescent tag or chelator)

OP-PHARM3

Development and *in vitro* evaluation of caspase-3-selective PET probes

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Aims: Many cancer treatments exert their therapeutic effect by inducing apoptosis in the tumours. The use of positron emission tomography (PET) radiotracers that selectively target apoptosis could allow for non-invasive assessment of response to therapy, allowing transition to second-line therapy and avoiding adverse effects. Caspase-3 is well known for its role as the main executor of apoptosis. Moreover, caspase-3 activation is an early event of the apoptosis cascade, representing an undisputable biomarker for apoptosis. Therefore, our goal was to develop PET radiotracers for selective caspase-3 imaging, and to investigate their value for evaluation of responses to cancer therapy.

Methods: The highly selective caspase-3 inhibitor, ATS-010-KE, was N-terminally extended with different azide-bearing linkers and were radiolabelled with [¹⁸F]fluoropentyne to form [¹⁸F]MICA-314 to -318. The affinity and selectivity of the activity-based probes (ABPs) for different caspases was measured. After radiosynthesis, the stability of the radiotracers was examined in the final formulation and in mouse plasma. Lipophilicity of the ABPs was assessed using the shake-flask method and expressed as LogD. Cell uptake of [¹⁸F]MICA-315 was assessed in HeLa cells incubated with the apoptosis inducer staurosporine (STS) or DMSO as control for 4h at 37°C. The pharmacokinetic profile of [¹⁸F]MICA-314 and [¹⁸F]MICA-315 was assessed in CD1 nude mice using μPET-CT imaging, static imaging at 2h post-injection and post-mortem ex-vivo biodistribution.

Results: The non-radiolabelled probes showed higher selectivity for caspase-3 over other caspases. The ABPs were synthesized in moderate radiochemical yields and remained stable up until 2 hours after formulation (Table 1). However, both [¹⁸F]MICA-314 and [¹⁸F]MICA-315 showed a fast degradation in mouse plasma with approximately 20% of the tracer remaining at 60 min post injection. The cell uptake of [¹⁸F]MICA-315 increased twofold in STS-treated HeLa-cells, compared to the DMSO-treated HeLa-cells. *In vivo*, both [¹⁸F]MICA-314 and [¹⁸F]MICA-315 displayed a high accumulation in the small intestine and liver.

Tracer	Caspase-3 K _i /K _{inact} (x10 ⁴ s ⁻¹ M ⁻¹)	LogD	Decay-corrected radiochemical yield (%)	Radiochemical purity (%)
MICA-314	86.34	-1.78 ± 0.002	25.0	99.39
MICA-315	124.91	-1.73 ± 0.40	24.7	95.21
MICA-316	85.09	N.A.	34.9	75.37
MICA-317	162.11	-1.83 ± 0.04	3.7	87.85
MICA-318	54.87	-1.15 ± 0.07	7.4	93.50

Table 1
K_i/Kinact, radiochemical yield, radiochemical purity and LogD of the developed ABPs.

Conclusion: The caspase-3-selective ABPs show promising results for cell-death imaging. Future work includes further *in vitro* and *in vivo* characterisation.

Acknowledgments: This research was funded by DOCPRO (46060), University of Antwerp and a FWO post-doctoral grant (12T8821N).

OP-PHARM4

Preclinical validation of [¹⁸F]-FB-(Anti Human PD-L1) Nanobody for PET imaging

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Aims: Tumor cells use immune checkpoints, such as Programmed Death Ligand-1 (PD-L1), to escape the anti-tumor immune response by limiting the T-cell activity. Cancer immunotherapy and more specifically Programmed Death-1 (PD-1): PD-L1 checkpoint blockade therapy has proven to be effective against multiple types of cancer. The expression of PD-L1 in the tumor microenvironment has proven to be a positive indicator for the responsiveness to therapy but its assessment is limited by the inherent limitations of immunohistochemistry assays. Non-invasive imaging techniques, such as Positron Emission Tomography (PET)-imaging could overcome these limitations as they depict the whole picture of PD-L1 expression within the body. This study aims to develop a radiofluorinated Nanobody (Nb)-based tracer targeting human PD-L1 (hPD-L1) for PET-imaging.

Methods: The anti-hPD-L1 Nb was labelled with N-succinimidyl-4-[¹⁸F]fluorobenzoate ([¹⁸F]-SFB) prosthetic group. [¹⁸F]-SFB is produced using disposable cassettes on an AllinOne[®] synthesizer module (Trasis) in a 3-step, 1-pot reaction. Radiochemical purity (RCP) was assessed by reverse phase chromatography (RPC). The dried [¹⁸F]SFB was incubated with the anti-hPD-L1 Nb (4.34 mg/mL) for 30 min at room temperature in 0.2 M phosphate buffer pH 8.5-8.7 containing 20% V/V ethanol. The radiolabeled Nb was purified using a disposable PD-10 size exclusion column (SEC). RCP was assessed by SEC and RPC. The affinity and specificity towards PD-L1 were assessed on PD-L1-positive (pos.) or -negative (neg.) 624-MEL cells as control and biodistribution was evaluated in female C57BL/6 mice (N = 3, 6 weeks old). The biodistribution study was compared to previously obtained data from [⁶⁸Ga]-Ga-NOTA-(hPD-L1) Nb.

Results: [¹⁸F]-SFB was obtained after the automated production of 48 minutes with RCP > 95% and decay corrected radiochemical yield of 31 ± 4 % (N = 8). [¹⁸F]-FB-(hPD-L1) Nb was obtained with > 95% RCP. In vitro characterization showed that the radiofluorinated Nb retained its affinity (K_d = 2.5 nM) (figure 1a) and specificity (2.37 ± 0.01% of total well activity on pos. cells vs. 0.32 ± 0.00% on neg cells, p<0.001) (figure 1b). The biodistribution study showed no unspecific organ accumulation and excretion via the kidneys (7.11 ± 0.95%). Kidney retention is 2.7 times lower compared to the [⁶⁸Ga]-Ga-NOTA-(hPD-L1) Nb (figure 1c).

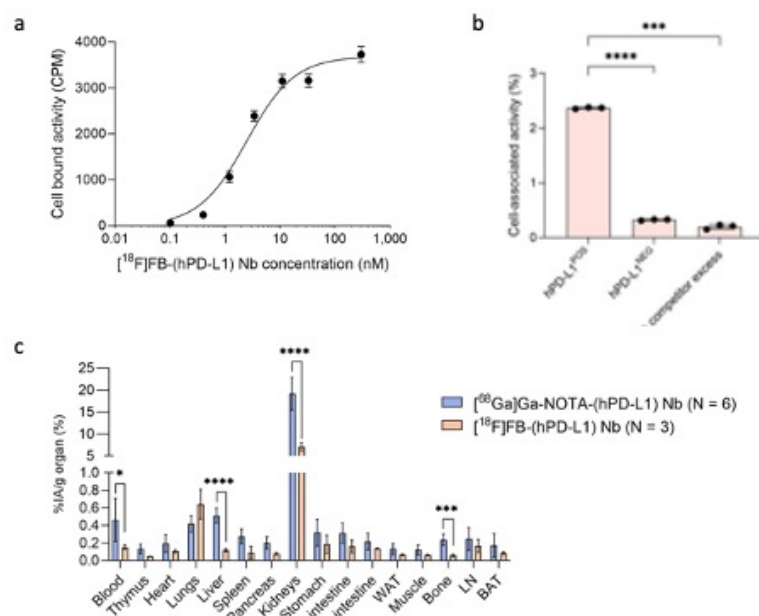


Figure 1: a. Radioligand binding study on hPD-L1 pos. 624-MEL cells. Cell bound activity in counts per minutes (CPM) expressed as a function of the Nb concentration (nM). b. Relative amount of cell-associated activity of the [¹⁸F]FB-(hPD-L1) Nb on hPD-L1 pos. cells at 3 nM Nb concentration, or on hPD-L1 neg. cells, or in presence of an excess of unlabelled Nb as control groups. (****, p<0,0001; ***, p<0,001). c. Comparison of ex vivo biodistribution of [¹⁸F]FB-(hPD-L1) Nb and [⁶⁸Ga]Ga-NOTA-(hPD-L1) Nbs in C57BL/6 healthy mice (liver: ****, p<0,0001; kidneys: ****, p<0,0001; bone: ***, p<0,001); Small intestine (S. intestine), Large intestine (L. intestine), White adipose tissue (WAT), lymph nodes (LN), brown adipose tissue (BAT)

Conclusions The anti-hPD-L1 Nb was successfully labelled with ¹⁸F and shows a favorable biodistribution pattern which, together with its in vitro characteristics, is attractive for further characterization as a new tracer for imaging PD-L1 overexpression in tumors.

OP-PHARM5

Development and preclinical evaluation of [¹¹C]HSP990 as an Hsp90 PET brain probe and potential biomarker for diagnosis and follow up of CNS disease progression

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Aims: Hsp90 is a key player in the protein quality control system to maintain protein homeostasis upon stress conditions. An aberrant role of Hsp90 has been attributed to several neurodegenerative disorders, including Alzheimer's disease (AD). The development of a suitable Hsp90 PET probe can provide *in vivo* quantification of the expression levels of Hsp90 as a biomarker for diagnosis and follow-up of CNS disease progression. In this respect, the radiosynthesis of [¹¹C]HSP990 was developed and the tracer was evaluated as an Hsp90 PET brain probe.

Methods: *In vitro* binding of [¹¹C]HSP990 to rodent brain tissue was evaluated using autoradiography. *Ex vivo* biodistribution and metabolization of [¹¹C]HSP990 was assessed in healthy rodents at baseline conditions and after pre-treatment with HSP990 and SNX-0723. *Ex vivo* brain region biodistribution was compared in healthy young, aged and APP^{NL-G-F} mice. *In vivo* brain uptake was assessed by dynamic μ PET studies in healthy rats after combined pre-treatment with Onalespib and HSP990 or SNX-0723. Full body dynamic μ PET scans were performed on healthy young, aged and APP^{NL-G-F} mice. Dynamic μ PET brain scans with arterial blood sampling were acquired in a rhesus monkey.

Results: *In vitro* [¹¹C]HSP990 binding to brain slices was deemed Hsp90 specific by competition studies with Hsp90 inhibitors. *Ex vivo* biodistribution studies indicated saturable Hsp90 binding in brain, bone marrow, blood cells and blood-rich organs in healthy rodents. In combined pre-treatment and displacement μ PET studies, reversible and Hsp90-specific binding of [¹¹C]HSP990 was demonstrated in healthy rat brain. Reduced [¹¹C]HSP990 brain uptake, especially in hippocampus and cortex, was observed in AD mice compared to age-matched controls and in aged mice compared to young controls. Dynamic μ PET brain scans in a rhesus monkey demonstrated high and sustained [¹¹C]HSP990 uptake in cortical brain regions. Arterial blood sampling confirmed the presence of a saturable Hsp90 binding pool in the blood cell fraction of a rhesus monkey. The fraction of radio-metabolites accounted for only 10% of total plasma activity at 60 min post tracer injection.

Conclusions: This study shows that despite the ubiquitous expression of Hsp90, saturable pools of Hsp90 inhibitor binding are present in blood cells, bone marrow and brain in healthy animals. PET with [¹¹C]HSP990 demonstrated a reduced amount of saturable Hsp90 in brain of AD mice compared to healthy controls, confirming the putative role of Hsp90 in this CNS disorder. Clinical evaluation of [¹¹C]HSP990 Hsp90 PET is warranted to investigate whether our results translate to man.

OP-PHARM6

Second generation Al¹⁸F-labeled D-amino acid based peptide for CXCR4 targeted molecular imaging

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Aims: This project focuses on targeting the chemokine receptor 4 (CXCR4) using fluorine-18 labeled D-amino acid viral macrophage inflammatory protein II derivatives, [18F]AIF-NOTA-DV1-k-(DV3) and the second generation [18F]AIF-NOTA 2xDV1(c11sc12s). The advantage of using fluorine-18 lies in the higher PET resolution and its capability of being produced at high-scale, which would render these ligands superior over the already clinically used [68Ga]Pentixafor.

Methods: Al18F-labeling was performed on a fully automated Trasis AllinOne® synthesis module and quality control was performed using radio-HPLC. The in vitro affinity towards human CXCR4 (hCXCR4) was determined via IC50 measurements in a competitive binding assay with fluorescently labelled CXCL12 and cell binding assays using u87.hCXCR4 cells with or without adding the CXCR4 antagonist AMD3100 were conducted. Finally, the in vivo profile was assessed in u87.hCXCR4 xenografted mice via µPET/CT scans and ex vivo biodistribution study at 75 min. p.i..

Results: The labeling of [18F]AIF-NOTA-DV1-k-(DV3) resulted in a RCY of 26±6%, a RCP of 98% and an apparent molecular activity of 11.5±2.5 MBq/nmol (n=3). [18F]AIF-NOTA-(2x)DV1(c11sc12s) was obtained with a RCY of 16±3%, a RCP of 98% and an apparent molecular activity of 12.4±3.9 MBq/nmol (n=11). IC50 values of 5.3±0.9 nM, 1.3±0.2 nM and 8.6±1.1nM were obtained for AIF-NOTA-DV1-k-(DV3), AIF-NOTA-(2x)DV1(c11sc12s) and [natGa]Pentixafor, respectively.

These affinities were mirrored in the cell binding assays, where the total-bound fraction of [18F]AIF-NOTA-(2x)DV1(c11sc12s) was the highest with 12.2±0.5%, compared to [68Ga]PentixaFor (8.9 ± 0.3%) and [18F]AIF-NOTA-DV1-k-(DV3) (6.0 ± 0.1%). Interestingly, the uptake of both Al18F-tracers was not completely blocked with AMD3100 (92%) in u87.hCXCR4 cells, in contrast to self-block (100%). In vivo, both Al18F-tracers demonstrated high accumulation in the liver, spleen and bone marrow, but moderate tumor uptake. This effect was even more pronounced in the high affine construct [18F]AIF-NOTA-(2x)DV1(c11sc12s). Injecting AMD3100 in vivo fully blocked the uptake in these organs, including the u87.hCXCR4 tumor. The presence of CXCR4, CCR5 and CXCR7 in the liver was confirmed via Western Blot.

Conclusions: [18F]AIF-NOTA-2xDV1(c11sc12s) displayed a lower IC50 value than DV1-k-(DV3) and Pentixafor, which is reflected in vitro and in vivo. However, the in vitro uptake is not fully blocked by AMD3100, which requires further investigation by analyzing the impact of the minor or major groove of CXCR4 on the ligand binding [1]. The binding profile and CXCR4 specificity will be further assessed by including u87.CD4.CCR5 and u87.CD4.CXCR7 cell lines, as AMD3100 has been reported to bind to CXCR4 heterodimers as well [2].

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[2]Kalatskaya”AMD3100isaCXCR7ligandwithallostericagonistproperties,”doi:10.1124/mol.108.053389

OP-PHARM7

RANKL immunoPET using ⁶⁴Cu radiolabeled antibody Fab fragments to improve imaging characteristics.

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Aims:Receptor activator of nuclear factor kappa B ligand (RANKL) expression in the tumor microenvironment (TME) is associated with carcinogenesis and formation of metastases. Recently, RANKL treatment has been shown to convert a tumor from a hostile to immune-mediated therapies to an immune-susceptible environment. To facilitate patient selection we developed [⁸⁹Zr]Zr-DFO-denosumab. However, in order to mitigate the unfavorable pharmacokinetics commonly associated with antibody based immuno-PET, here we aim to develop radiolabeled ⁶⁴Cu-Fab fragments with improved pharmacokinetics and imaging quality.

Methods:[⁶⁴Cu]Cu-NOTA-Fab was radiolabeled in high radiochemical yield and purity, showing favorable stability and intact immunoreactivity. Xenografts were developed via injection of huRANKL transduced ME-180 or native ME-180 (cervical cancer) cells (8x10⁶) in the right hind leg of female CD-1 nude mice. In tumor-bearing mice, [⁶⁴Cu]Cu-NOTA-Fab (~33µg; ~26MBq; n=4) was injected and PET-MRI scans were performed 1h, 5h and 24h post radiotracer injection. A blocking study was performed to confirm the binding specificity of [⁶⁴Cu]Cu-NOTA-Fab, by injecting an excess dose (4mg) of native denosumab, two days prior to radiotracer injection.

Results: [⁶⁴Cu]Cu-NOTA-Fab PET demonstrated a mean radiotracer uptake of 2.14 ± 0.21 % ID/mL at 1 h and a peak uptake at 5 h (2.72 ± 0.61 % ID/mL) post injection in RANKL-ME-180 xenografts. The specificity was confirmed in a blocking study with a significant lower uptake at 1 h (0.94 ± 0.44 % ID/mL, p = 0.0033) and at 5 h (0.87 ± 0.40 % ID/mL, p = 0.0014) post injection. Additionally, in negative ME-180 xenografts [⁶⁴Cu]Cu-NOTA-Fab showed a significant lower uptake at 1 h (1.22 ± 0.24 % ID/mL, p = 0.0095) and 5 h (0.96 ± 0.29 % ID/mL, p = 0.0012) post injection. A near-complete clearance was observed at 24 h post radiotracer injection. Good tumor/background ratios with high imaging contrast were seen (Figure 1).

Conclusions: huRANKL could be specifically imaged using [⁶⁴Cu]Cu-NOTA-Fab and shows improved tumor/background ratios compared to antibody imaging radiotracer.

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Supported by BELNUC 2021 travel award.

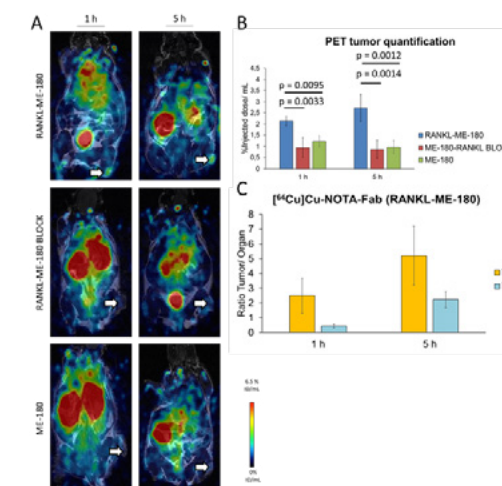


Figure 1 A) [⁶⁴Cu]Cu-NOTA-Fab PET images of RANKL-ME-180 (top), RANKL-ME-180 BLOCK (middle) and ME-180 (bottom) xenografts at 1h and 5h post radiotracer injection. B) PET analysis of [⁶⁴Cu]Cu-NOTA-Fab tumor uptake. C) [⁶⁴Cu]Cu-NOTA-Fab tumor/background ratios in RANKL-ME-180 xenografts. (ID/mL: injected dose/mL; data graph: mean +/- 1 standard deviation; white arrow: tumor, T/M: tumor/ muscle, T/H: tumor/ heart).

OP-PHARM8

Using the site-specific radiolabeling of a PD-L1 nanobody via maleimide–cysteine chemistry to develop a PET-tracer as screening tool for personalized oncology treatment

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Aims: Immune checkpoints inhibitors of programmed cell death-1 (PD-1) and its ligand PD-L1 have proven to successfully treat cancer in a subset of patients. Typically, from all the patients with various cancer types, 20% have a positive response. Cancer cells expressing PD-L1 are more likely to be responsive to the treatment. Therefore, distinguishing oncology patients that do express PD-1/PD-L1 from patients that do not allows a more personalized and efficient treatment. PD-1 and PD-L1 expression in cancer cells is often assessed through immunohistochemical detection in a tumor lesion biopsy. Besides being invasive, taking a tumor biopsy to assess PD-1/PD-L1 expression does not take into account the heterogeneity of cancer cells in a tumor lesion. We aim to develop a nanobody (Nb)-based radio-immunotracer for PET-imaging targeting human PD-L1 to efficiently screen oncology patients in a non-invasive manner for a more personalized treatment.

Methods: Maleimide (mal)-cysteine chemistry was used to site-specifically conjugate the cysteine-tagged Nb with a mal-NOTA chelator. The radiolabeling of the conjugated Nb with gallium-68 (68Ga) was tested at different Nb concentrations and temperatures. Affinity and specificity were assayed by surface plasmon resonance and on hPD-L1POS or hPD-L1NEG 624-MEL cells. Xenografted athymic nude mice bearing 624-MEL PD-L1POS or PD-L1NEG tumors were injected with the tracer and imaging was acquired 1 h post-injection (p.i.). Ex vivo biodistribution studies were performed 1 h 20 min p.i.

Results: Ideal 68Ga-labeling conditions were found at 50 °C for 15 min and at a concentration of 3.6 µM of NOTA-mal-hPD-L1 Nb. [68Ga]Ga-NOTA-mal-hPD-L1 Nb was obtained in 80 ± 5% DC-RCY with a RCP > 99%, and was stable in injection buffer and human serum up to 3 h. The in vitro characterization confirmed the affinity and selectivity of [68Ga]Ga-NOTA-mal-hPD-L1 Nb for hPD-L1POS cells. 1 h p.i. PET-imaging allowed the visualization of the tumor lesions with PD-L1 expressing cells. Ex vivo biodistribution revealed a tracer uptake of 1.86 ± 0.67% IA/g in the positive tumors compared with 0.42 ± 0.04% IA/g in the negative tumors. Low background uptake was measured in the other organs and tissues, except for the kidneys and bladder, due to the expected excretion route of Nbs.

Conclusions: The data obtained show that ⁶⁸Ga-labeled NOTA-mal-hPD-L1 Nb is a promising PET-tracer targeting tumor lesions with PD-L1 expressing cells. Thanks to its ease of production, stability, and specificity for PD-L1, the developed tracer could routinely be used for non-invasive screening of oncology patient.

PHYSICS TRACK

ORAL PRESENTATIONS

OP-PHYS1

Dosimetric model for patients with renal failure undergoing dialysis during I-131 therapy for thyroid cancer

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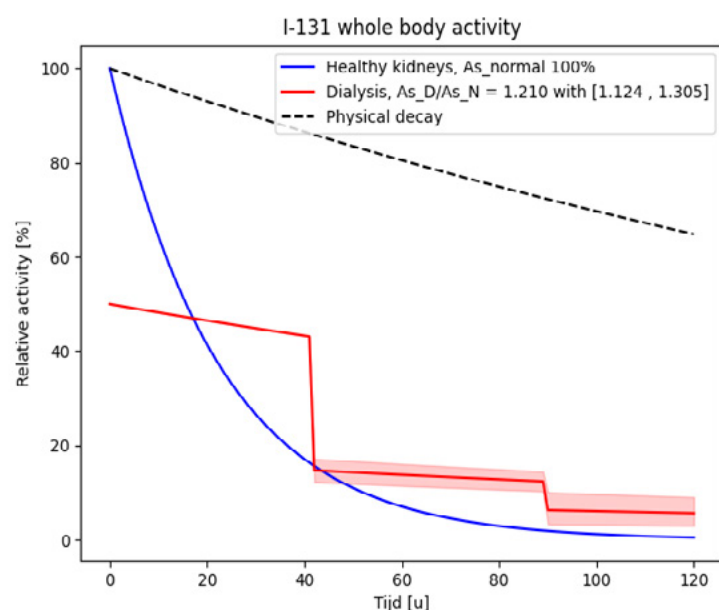
Aims: To create an easy-to-use dosimetric model that can estimate the administered activity to a patient for I-131 therapy who has almost to no renal clearance.

Methods: Based on literature values [1][2] renal clearance estimates were used to determine time activity curves as seen in Figure 1. Dialysis in this simulation takes place 42h and 90h after administration of the I-131 capsule. The time-integrated activity (TIA)-ratio is defined as and gives a measurement of the dose for the patient with dialysis compared to a patient with healthy kidneys [3] with recombinant human thyroid-stimulating hormone stimulation or thyroid hormone withdrawal.

Results: A 50% reduction of administered activity corresponds to a TIA-ratio of 1.2 [1.124, 1.305]. 100% of the activity for normal patients results in a TIA-ratio of 2.4 [2.248, 2.611].

Conclusions: The dosimetric model can compare the radiation dose for a hemodialysis patient to a normal patient. Furthermore, it can be seen that careful consideration of the administered activity and dialysis scheme is needed when considering I-131 therapy for patients with almost to no renal clearance; the blood pool activity stays high for a longer time and can therefore result in a high dose to the bone marrow. Further work will include validation of the model with blood sample and whole body dose rate measurements.

Code available: <https://github.com/vnuttens/i131dose>



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OP-PHYS02

Development of an anthropomorphic phantom for mandibular condyle imaging

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Aims: Bone SPECT/CT is part of the assessment of mandibular growth of patients with unilateral mandibular condyle hyperplasia. Relative difference in tracer uptake in the left and right mandibular condyle larger than 10% is considered a marker for unilateral hyperplasia. The irregular, small geometry and high density of the bone structures are likely to influence the absolute quantification. An anthropomorphic phantom was developed to investigate the absolute quantification of the tracer uptake in the mandibular condyles.

Methods: The mandibular condyles and skull base were segmented on a patient CT. A phantom was constructed using CAD software and spherical compartments of diameter 8 mm were added to represent the mandibular condyles. The phantom was printed in parts using a resin printer and post-treated by washing and curing before assembly. The absolute activity concentration was measured with a target-to-background ratio of 6:1 (background 50kBq/mL and spheres 300 kBq/mL). The higher density of bone compared to surrounding soft-tissue was simulated using a 60wt% solution of HK₂O₄P, matching the Hounsfield density of bone. The geometry of the phantom was compared with the original CT using MIM 7.1.4. The recovery coefficient (RC) for 2D ROIs and 3D VOIs were determined at 80% of the sphere diameter for both.

Results: Visual comparison of phantom geometry with the original CT showed good agreement and quantitative comparison showed a Dice coefficient of 0.863. The structural integrity of the phantom was sufficient to use the phantom for multiple experiments. For the first experiment, the phantom background volume and spheres were filled with water with ^{99m}Tc-concentration of 45.8 kBq/mL and 287.1 kBq/mL, respectively. For the second experiment, the background volume was filled with a bone-equivalent solution by adding HK₂O₄P. The average HU of the bone structures on the original CT was 531 HU, and that of the bone-equivalent solution 605 HU in the same VOI. The activity concentration in the background volume was 46.6 kBq/mL and in the spheres 284.1 kBq/mL. For the first experiment, the RC of the spheres were 25.6% (2D) and 26.0% (3D). The second experiment resulted in RC of the spheres of 29.6% (2D) and 30.0% (3D).

Conclusions: We developed a fillable, anthropomorphic phantom of the mandibular condyles and skull base. The geometry of the phantom showed excellent similarity with the CT upon which it was based. The structural integrity of the phantom was sufficient to allow reusability and two experiments were performed.



OP-PHYS03

Feasibility of lesion dosimetry assuming constant pharmacokinetics over cycles in patients treated with ¹⁷⁷Lu-DOTATATE

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Aims Dosimetry-driven treatment planning in Peptide-Receptor Radionuclide Therapy is one of the major challenges in the framework of personalized medicine. Individualised dosimetry requires multi-Time Point (TP) imaging after each cycle, which is resource consuming for the clinic and burdensome for the patients. The implementation of dosimetry protocols using a reduced number of TPs is therefore essential. This study aims to evaluate the accuracy of simplified protocols for lesion dosimetry after ¹⁷⁷Lu-DOTATATE therapy.

Methods 26 patients with advanced gastroenteropancreatic neuroendocrine were included. For each patient, two SPECT/CTs were acquired at 24 and 168 hours post-injection. 56 lesions were segmented on the ⁶⁸Ga-DOTATATE PET/CT performed 1-3 weeks prior to each ¹⁷⁷Lu-DOTATATE cycle. The same lesions were segmented on the ¹⁷⁷Lu-DOTATATE SPECT/CT in order to reach the same volume. The quantified activity was time-integrated using a mono-exponential fit and then converted into absorbed dose (AD) using the OLINDA\EXM sphere model.

Two simplified protocols were selected based on preliminary analysis:

- Protocol-A: 2TP dosimetry in C1/C3 and no imaging in C2/C4 (i.e. assuming the same AD per injected activity as in the preceding cycle)
- Protocol-B: 2TP dosimetry in C1 and a 1TP dosimetry (imaging at 24 h post injection) in subsequent cycles (i.e. assuming the same pharmacokinetics in subsequent cycles)

The one-way ANOVA analysis was used to compare the cumulative AD obtained with Protocol-A/B to the reference. The % differences between the cumulative AD and the AD after C2, C3 and C4 were also assessed.

Results Lesions received a mean cumulative AD of 108 Gy (SD=52 Gy), 114 Gy (SD=58 Gy) and 108 Gy (SD=52 Gy) according to the reference protocol, Protocol-A and Protocol-B, respectively.

The one-way ANOVA analysis showed a statistically significant difference between Protocol-A and the reference ($p \leq 0.0001$). No statistically significant difference was found comparing Protocol-B to the reference.

The % differences between the AD calculated with Protocol-A/B and the reference are reported in Table-1.

	Protocol-A	Protocol-B
Cumulative-AD	5% [-16%,-0%,13%,25%]	1% [-15%,-4%,5%,14%]
AD-C2	15% [-47%,-5%,39%,102%]	2% [-27%,-7%,7%,16%]
AD-C3	0%	-1% [-17%,-5%,8%,26%]
AD-C4	2% [-54%,-10%,24%,69%]	4% [-26%,-5%,11%,29%]

Table-1: % differences between the AD calculated with Protocol-A and Protocol-B with respect to the reference. Data are reported as median [min,Q1,Q3,max], outliers excluded.

Conclusions The comparison between the AD calculated according to Protocol-A/B and the reference showed that the latter provides more accurate results. The introduction of this approach into the clinical routine would significantly reduce the number of required acquisitions.

OP-PHYS04

Radiation dose optimization of CT acquisitions in SPECT/CT examinations

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Aims: SPECT imaging for visualization of molecular processes is often combined with CT, which offers the possibility for anatomical localization of SPECT tracers. Additionally, the CT data is used for attenuation correction of the SPECT image, as such improving the quantitative value of the images. Besides the advantages of combined SPECT/CT, the main disadvantage of the CT is the additional radiation dose received by the patient. The objective of this study was to analyse the correlation between the recovery coefficient (RC) and the CTDI for several CT-settings in SPECT/CT acquisitions.

Methods: The NEMA PET body phantom with six spheres and a lung compartment was used and filled with a ^{99m}Tc activity concentration sphere-to-background ratio of 9,63. Images were acquired on two SPECT/CT cameras, Discovery NM/CT D670 (GE Healthcare) and BrightView XCT (Philips). For the D670, several kV values (80, 100 and 120) were used together with an mA range of 10 – 300 with tube current modulation. For each kV value several scans were performed with increasing noise index (NI). The obtained CTDI values were incrementally decreased from 12,98 mGy to 2,9 mGy. On the Brightview XCT, kV values and NI cannot be changed, so all acquisition were performed at 120 kV. The mA value was changed for each scan and ranged from 2 mA – 80 mA. The resulting CTDI values were incrementally decreased from 15 mGy to 0,65 mGy. Reconstruction with attenuation correction was performed using the software of the camera, while the measured activity in spheres, background and lung compartment was determined in PMOD.

Results: For both scanners, no clear correlation between RC and CTDI was found. Some fluctuations in RC were noticed for changing CTDI values, however this variation did not follow any clear trend. Additionally, the changes that can be noticed are so small that they likely will not have clinical relevance. The ratio between the activity in the lung compartment over the activity in the background was calculated as well. For all acquisitions on the D670, the difference between the highest and lowest value for this ratio was 0,007 and for the Brightview XCT this difference was 0,03.

Conclusions: From these results it seems that lower CT doses do not negatively impact the quantitative accuracy of the SPECT images.

OP-PHYS05

StarGuide Tc-99m imaging reconstruction parameters optimization

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Aims: StarGuide is a new GE Healthcare CZT-based SPECT/CT Camera, composed of 12 detectors mounted in a new ring architecture.

Following the installation of this SPECT/CT system in Jules Bordet Institute, this study aimed optimizing reconstruction parameters for both qualitative and quantitative ^{99m}Tc diagnostic imaging.

Methods: Two different phantom models were acquired with GE StarGuide SPECT/CT Camera. First, a homogeneous Jaszczak phantom was acquired with 5 different ^{99m}Tc activities (100-700 MBq) for calibration factor stability assessment. Second, a NEMA 2012/IEC 2008 phantom, was filled with different sphere to background ratios (cold background, 13:1, 4:1) for noise and Recovery Coefficient (RC) evaluation. Noise is the mean coefficient variation measured in four cylindrical volumes of interest in the background of the NEMA phantom. RC is defined by a curve describing the variation of the ratio (measured activity in sphere/theoretical activity in sphere,) in a function of the spheres' radius. To compare the RC of different reconstructions quantitatively, the integral of the RC curves was calculated.

Different reconstruction parameters (number of updates (iterations*subsets), reconstruction algorithm (OSEM and Qclear), Gamma, Beta, Sens, Clarity, post reconstruction filter) were optimized to enhance resolution and decrease noise. Following the quantitative optimization, the nuclear medicine physicians have assessed qualitatively patients' images reconstructed.

Results: For quantification purposes, a specific protocol (^{99m}Tc Quantitation) has been used for all image reconstructions, presenting a stable CF = 1031 ± 10 cps/MBq, with activities (100-700 MBq), also for different updates (20-300). A low number of updates (20) has been chosen to avoid Gibbs-like artifact, which appeared at high number of updates (about 40 % of min/max intensity for the largest sphere with 10i10s (cold background)). With NEMA phantom acquisitions, the next reconstruction parameters have been proposed, which presented a good compromise between noise (10 %) and resolution (high RC integral): 4 iterations, 5 subsets, Qclear reconstruction algorithm, Relative Difference for Maximum regularization (RDP), Gamma of 10 and Beta of 2, Clarity (Power of 0.01).

According to physicians' visual analysis, the proposed parameters allowed better diagnosis than those used by default (OSEM, 2 iterations, 10 subsets, post reconstruction Gaussian filter of 3.69 mm.

Conclusions: By using ^{99m}Tc Quantitation reconstruction protocol, the stable CF calculated, will permit different quantitative patient diagnosis. In addition, despite that not all reconstruction parameters have been tested yet (FAME, Contrast Enhancement in Clarity); a good image quality is obtained permitting better diagnosis, than that based on the default reconstruction parameters.

TECHNOLOGIST TRACK**ORAL PRESENTATIONS****OP-TECH1****Logistical analysis of the individual “whole body” dosimetry of personnel professionally exposed to ionizing radiation in Belgium, over the last 10 years.**

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Aims: The organizations employing professionally exposed workers are responsible for monitoring the corresponding radiation doses. In order to ensure the correct observation of exposure doses, personnel are monitored using individual “whole body” dosimeters. Readings of individual dosimeters are not always possible however, due to the loss or damaging of the device. This generates unnecessary costs, and logistical problems. The management of individual dosimeter measurements has become an increasing challenge. The objective of this study is to analyse the logistical impact of lost dosimeters in Belgium over the last 10 years.

Methods: This is a retrospective quantitative study spanning the last 10 years, carried out with data collected at

Vinçotte Controlatom with a total sample size of 6 million data points. The number of distributed and lost dosimeters were analysed taking the following criteria into account: Belgian clients, for the period from 01/01/2011 to 30/04/2021, and including different parameters: dosimeter type (OSL), region, province, gender, activity sector and profession.

Results: Of the sample analysed, 2.152.079 dosimeters were distributed in Belgium, with an average of 215.208 (± 3.365,76 SEM) dosimeters per year. The amount of distributed dosimeters tended to increase yearly. From those, 39.770 dosimeters were considered lost or non-returned to the firm, and were billed to the client. This is equivalent to a loss of individual information related to 3.615 workers on average (± 424,97 SEM) per year. Further analysis showed that, 43% of the lost dosimeters were OSL4 type, 11% came from both educational sector and veterinary assistant, and 31% were related to industry. Moreover, 42% of the lost dosimeters are represented in Brussels-Capital but it's the province Brabant-Flamand who lost the most (13%) and it is men who account for a larger number of lost dosimeters.

Conclusions: The data analysis shows the importance of the additional logistics and loss of information generated by the loss of a dosimeter, having an impact on the individual protection and dose estimate of the worker, on the quality and reliability of the dose attribution. On top of that, the financial burden that is a direct consequence of the loss of dosimeters, should be considered as well in further studies. This work highlights the potential efficiency of education and training initiatives in the field of dosimetry that are still needed, as well as preventive measures or even work procedures so as to decrease (information and material) waste, by understanding the inherent causes.

OP-TECH2**Design of an integrated Radiopharmaceutical Supply Chain (SC) to enhance its overall Supply Chain Performance Methodology**

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Aims: From production, through transport to the patient ultimately benefiting from diagnosis or treatment, each entity is part of a Radiopharmaceutical supply chain (SC). Studies from academia and/or observations from the practitioners 'realm support the fact that a chain would perform better both on the individual level for each actor as for the whole chain, if considered and managed as a single entity. Encompassing disparate elements into a coherent, cohesive and dynamic system pertains to the concept of integration. This integration of actors as an inter-organizational process constitutes the essence of Supply Chain Management (SCM) which focuses on savvy operation and implementing the best strategies and to ensure the chain's successfulness. These focuses are even more crucial for radiopharmaceutical chains because of their complexity, various specificities, and the different paradigms imposed by the global market therefore, trade-offs become necessary. In Performance Management Science, the Supply Chain Performance Measurement System (SCPMS) framework orchestrates these trade-offs from a holistic perspective by evaluating SCM strategies. SCPMS comprises a set of measures quantifying the effectiveness and efficiency of SC processes and enable the organization of inter-organizational activities. This framework being absent in the radiopharmaceutical SC, this study ambitions to bridge the gap.

Methods: To implement this tool, the first step of this context-specific study consisted in interviews with direct and indirect actors, site visits and literature reviews which shed light on the dynamics of this chain, revealing its constraints and challenges. Second, strategies are defined, through a dual approach methodology: the bottom-up based on context analysis unveiled the relevant strategies and the top-down exposed the practitioners' vision and chosen strategies. Third, the metrics that mainly constitute the tool are designed. Fourth, scenarios are developed to express the strategies and are based on the best practices and inputs from stakeholders of the domain. Finally, the scenarios are measured then compared, with the optimal design being the one displaying the best overall performance and satisfaction for the end user/patients.

Results: Each step's methodology is outlined, and an integrated visual presentation of the radiopharmaceutical supply chain problems was developed based on the Molybdenum-99 SC constraints analysis. Strategies and metrics are proposed.

Conclusions: This study highlights the importance of the chain's actors' integration, proposing a new approach to the activity's management, firstly through performance measurement and moreover, through the holistic perspective. Although each radiopharmaceutical SC is unique, the tool proposed could be adapted on other radiopharmaceutical chains.

OP-TECH3

Can a third party software vendor (MIMVista) match the image quality of native software vendor?

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Aims:The DICOM image standard is a vendor neutral standard which allows viewing and processing in third party software. Brand specific reconstruction algorithms are only to be used on the vendor’s own processing software. The original vendors offer advanced resolution recovery as standard on native systems. Recently a new third party, MIMvista software, is available that claims to match image quality reconstruction of the original vendor.

Methods: Datasets obtained with three gammacamera’s, made by two prominent vendors (GE Healthcare, Siemens Healthineers). Reconstruction was performed using native vendor software settings and third party software (MIMvista). Reconstruction parameters were developed by MIMvista using an in-house database to obtain CT attenuation corrected images using resolution recovery. For this abstract, SPECT/CT images were used from bone scintigraphy studies with a variety of clinical indications and body regions. The reconstructions were blinded and compared by experienced nuclear medicine physicians.

Results: Visual analysis and comparison of the CT attenuation corrected images by 3 readers showed an equal image quality, when comparing MIMvista and the original vendor’s reconstruction.

Conclusions: MIMvista’s claim that the image quality can be matched, turns out to be valid. Further comparison with data from other types of examinations and camera’s is planned to evaluate full customer experience.

OP-TECH4

Implementing Lutetium-177 PSMA ligand therapy: practical aspects concerning radioprotection and dosimetry

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Aims: Since September 2021 Lutetium-177 (Lu177) prostate-specific-membrane-antigen (PSMA) ligand therapy is offered to our metastatic prostate cancer patients. We share our initial experience on the practical issues we encountered in the first 40 treatment sessions.

Methods: We describe the practical aspects of implementing Lu-177 PSMA I&T radionuclide therapy in a general hospital in Ghent. The radiopharmaceutical is provided by AZ Groeninge (Kortrijk) and prepared with carrier free Lu177. We designed our standard operating procedures to comply with the FANC requirements. Dose rates were measured at 1m in a standardized geometry post injection, at 4h and at 20h and confronted this with the Belgian guidelines to discharge the patient from the radionuclide therapy ward. In order to comply with the dosimetric requirements, we tested several post therapy imaging schemes and explored the MIMVISTA® software package.

Results: 2 syringe shields were tested: one specifically designed for the administration of Lu177, composed of an inner acrylic and an outer lead shielding compared to a standard PET lead shield. The latter was found to be the most convenient.

Patients with various types of urinary incontinence were present in this patient population. A shielded box was designed to safely store the urine in patients with a stoma or bladder catheter during their stay in the radionuclide ward. This box contains a 4 liter urinary reservoir and minimizes the exposure and handling of the radio-active urine by the personnel.

Dose rate was measured at 1 meter at various time points post injection and we found an excellent correlation with the whole body counts derived from whole body post therapy scintigraphies. The clearance of activity tends to be less pronounced in the first treatment session compared to the follow up sessions. Dose rates of all patients were below 20µSv/h at 1 m 20h post administration, in most cases even after a few hours. MIMVISTA® software is user friendly. However we doubt the clinical relevance of the obtained absorbed dose estimates in this patient population presenting with end stage disease. We were confronted with several patients who were not able to undergo the proposed post therapy scanning scheme because this turned out too demanding for these fragile patients.

Conclusions: We introduced Lu177 PSMA in our prostate clinic without encountering major safety issues. However it should be taken into account that implementing this treatment modality safely and in line with local legislation requirements was a time-consuming and costly process.

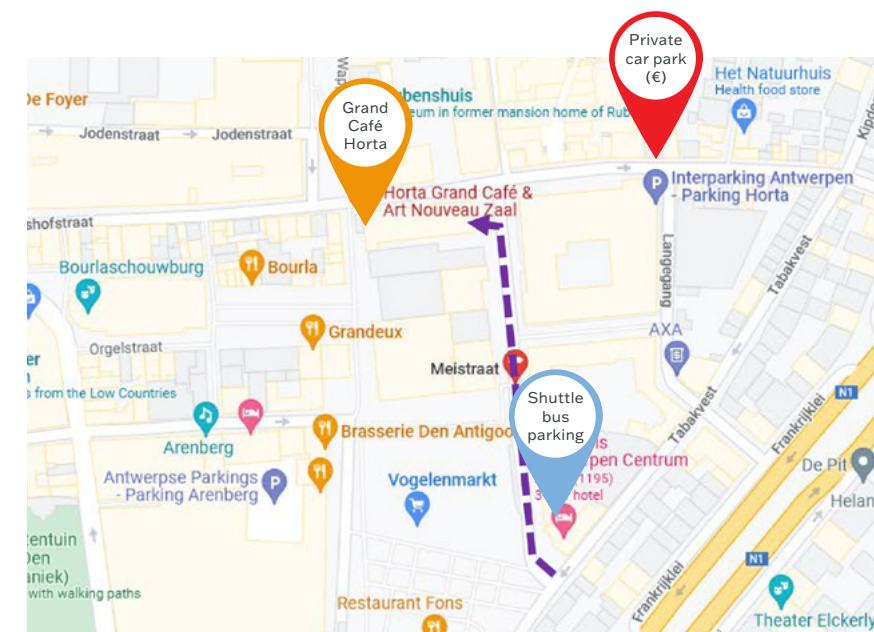
SATURDAY NIGHT MIXER

After the science, jump on the shuttle bus and join us on Saturday night (7/5/2022) to wind-down and socialize with your colleagues during the complimentary reception and walking dinner in the historic heart of Antwerp!

We welcome you from 19:15 in the Horta Art Nouveau hall (Hopland 2, 2000 Antwerp). Enjoy the food, a cultural intermezzo, and the late-night entertainment!

PROGRAM

19:15 – 19:55	Arrival and Welcome
19:55 – 20:00	Welcome by BELNUC President
20:00 – 21:30	Walking dinner
21:30 – 22:10	Live performance Soprano Julie Gebhart
22:10 – 22:45	Dessert
22:45 – 01:30	DJ & Party



SHUTTLE BUS

Chartered shuttle buses will depart from the Antwerp Expo bus parking at 19:00, located at the Vogelzang street (200m from the symposium entrance), and take you to the Meistraat (200m from the Horta Grand Café).

Return buses will leave from the Meistraat every 30 minutes from 22:00 and stop at the Crowne Plaza Hotel and the Antwerp Expo bus parking (Vogelzangstraat). The last bus leaves Horta at 02:00.

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