*11 juni 2021*

# Online wetenschappelijke vergadering NVNG: Radionuclide therapie

De wetenschappelijke voorjaarsbijeenkomst van de NVNG georganiseerd door de Commissie Wetenschappelijke Ontmoetingen (CWO) werd op 11 juni 2021 volledig virtueel gehouden met als thema "Radionuclide therapie". Het programma van de eerste ochtendsessie begon met een presentatie van radiochemicus dr. Robin de Kruijff (Reactor Instituut Technische Universiteit Delft) over radionuclide productie en radiochemie. Vervolgens behandelde nucleair geneeskundige dr. Tessa Brabander (Erasmus MC Rotterdam) diverse aspecten van peptide receptor radionuclide therapie (PRRT) bij neuroendocriene tumoren en de ervaringen met [$^{177}$Lu]Lu-DOTA-TATE. In de tweede ochtendsessie besprak nucleair geneeskundige/radiotherapeut dr. Wouter Vogel (Antoni van Leeuwenhoek Amsterdam) het gebruik van [$^{177}$Lu]Lu-PSMA. Vervolgens presenteerde prof. dr. Erik Verburg (Erasmus MC Rotterdam) de eerste ervaringen met [$^{225}$Ac]Ac-PSMA in relatie tot andere therapeutische mogelijkheden. De sessie werd afgesloten met een presentatie van ziekenhuisapotheker dr. Hendrikus Boersma (UMC Groningen) over implementatie van alfa en beta emitters in de ziekenhuissituatie.

Na een korte paneldiscussie vond een algemene ledenvergadering van de NVNG plaats. In de middag werden twee sessies gehouden met presentaties van een zestal vrije inzendingen zoals hieronder beschreven.

# Samenvattingen vrije inzendingen middagprogramma

## Denosumab reduces lesional fluoride uptake on [18F]NaF PET-CT in Fibrous Dysplasia

**W. van der Bruggen, MD[1,2], D. Vriens, MD, PhD[1], M.E. Meier, MD[3,4], F. Smit, MD[1,5], E.M. Winter, MD, PhD[3], L.F. de Geus-Oei, MD, PhD[1,6], N.M. Appelman-Dijkstra, MD, PhD[3]**

*[1]Section of Nuclear Medicine, dept. of Radiology, [3]Center for Bone Quality, dept. of Internal Medicine, division of Endocrinology, [4]Dept. of Orthopaedic surgery, Leiden University Medical Center (LUMC), Leiden, [2]Dept. of Nuclear Medicine, Slingeland Hospital, Doetinchem, [5]Dept. of Nuclear Medicine, Alrijne Hospital, Leiderdorp, [6]Biomedical Photonic Imaging Group, University of Twente, Enschede*

### Introduction

[99mTc]Tc-HDP uptake (bone scan) does not change after bisphosphonate-treated Fibrous Dysplasia (FD). We investigated whether [18F]NaF PET-CT can be used for treatment response measurement in FD.

### Methods

Fifteen consecutive patients with FD with baseline and follow-up [18F]NaF-PET-parameters of healthy bone and FD lesions, BTMs and pain scores at start of denosumab (n=8) and non-denosumab patients (n=7). The Volumetric measures of FD-burden (FTV) and 'Fraction affected skeleton' (FAS), represented the portion of the skeleton affected.

### Results

Individual healthy bone [18F]NaF PET-CT cut-offs remained unchanged in denosumab (p=0.237) and non-denosumab patients (p=0.575). Volumetric [18F]NaF PET-CT FD-burden decreased significantly after start of denosumab (median FTV 316cm$^3$ to 97cm3; p=0.018). FTV did not change significantly in non-denosumab patients (76 cm$^3$ to 54 cm$^3$; p=0.249). In the total 15 patients, serum P1NP and Alkaline Phosphatase (ALP) decreased significantly: 82ng/mL vs 55ng/mL, p=0.023 and 119 IU/L vs 84 IU/L, p=0.020, respectively. In denosumab-treated patients pain scores improved leading to pain medication reduction. This correlated with lesional FD-related uptake whilst healthy bone activity did not change. BTMs and FTV correlated positively, P1NP r=0.730; p<0.001 and ALP r=0.406; p=0.006, as did change in BTMs and FTV: P1NP (p=0.032) and ALP (p=0.024). FAS strongly correlated with treatment-induced decrease in ALP (p=0.027) and P1NP (p=0.009).

### Conclusions

[18F]NaF PET-CT captured treatment-induced lesional changes which correlated with BTMs and pain reduction, whilst no changes were seen in healthy bone NaF-metabolism during antiresorptive treatment. Therefore [18F]NaF PET-CT can be used as an objective local parameter of response to denosumab treatment in FD.

*vanderbruggen@gmail.com*

## The added value of digital [18F]FDG PET/CT in disease staging and restaging in patients with resectable pancreatic cancer: an interim analysis

**T.L. de Jong[1], D. Koopman[1], C.A.J. van der Worp[2], H. Stevens[1], F.A. Vuijk[3], A.L. Vahrmeijer[3], J.S.D. Mieog[3], J.W.B. de Groot[4], M.A.C. Meijssen[5], L.F. de Geus-Oei[6], P.L. Jager, MD, PhD[1], G.A. Patijn[7]**

*[1]Department of Nuclear Medicine, [2]Department of Radiology, [4]Department of Internal Medicine, [5]Department of Gastroenterology and Hepatology and [7]Department of Surgery Isala Hospital, Zwolle, [3]Department of Surgery and [6]Department of Radiology, Leiden University Medical Center, Leiden*

### Introduction

Disease staging and restaging in patients with resectable pancreatic cancer is routinely done with contrast enhanced computed tomography (ceCT), and is challenging. We studied the added value of digital [18F]FDG PET/CT in staging and restaging, in comparison to ceCT and Ca19-9 serum levels, in patients with resectable pancreatic cancer receiving neo-adjuvant therapy.

### Methods

We prospectively included 24 patients. Digital [18F]FDG PET/CT scans and ceCT scans were acquired before (T1) and after neo-adjuvant therapy, but before surgery (T2). Ca19-9 serum levels were also measured. A team of nuclear medicine specialists, a radiologist, and a pancreatic surgeon examined all scans. We monitored new findings on [18F]FDG PET/CT as compared to ceCT at T1 and T2 for each patient. Treatment response was evaluated by measuring tumor diameter change on ceCT, by CA19-9 change in plasma, and by changes in [18F]FDG PET/CT uptake.

### Results

Four of the 24 patients did not undergo resection, because the surgeon found liver metastases during surgical exploration. All of these four patients had suspected liver metastasis on PET, whereas only one was suspected of liver metastasis on ceCT. From T1 to T2, the medians for all treatment response parameters decreased: tumor diameter on ceCT (32 mm [25-37] to 26 mm [19-32]), Ca19-9 serum levels (298 U/mL [70-526] to 42 U/mL [27-134]), and [18F]

FDG PET/CT uptake (SUL 4.5 [3.8-5.5] to 1.9 [1.7-3.1]).

## Conclusion

Digital [$^{18}$F]FDG PET/CT was able to assess undetected small liver metastasis at the baseline. Based on these preliminary findings, we expect that the addition of digital [$^{18}$F]FDG PET/CT to the staging and restaging of pancreatic cancer may be of added value.

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*dejongtonke@gmail.com*

# The value of [$^{18}$F] fluorodeoxyglucose Positron Emission Tomography / Computed Tomography for the diagnosis of device related infections in patients with a Left Ventricular Assist Device: A dual centre study

**D. Ten Hove[1,2], A. Wahadat[3,4,5], R.H.J.A. Slart[1,6], M. Wouthuyzen-Bakker[2], G. Mecozzi[7], P.P. Van Geel[8], K. Caliskan[4], O. Manintveld[4], B. Sinha[2], R.P.J. Budde[3]*, A.W.J.M. Glaudemans[1]* (*shared authorship)**

*[1]Department of Nuclear Medicine and Molecular Imaging, [2]Department of Microbiology and Infection Prevention, [7]Department of Cardiothoracic Surgery, [8]Department of Cardiology, University of Groningen, University Medical Centre Groningen, Groningen, [3]Department of Radiology and Nuclear Medicine, [4]Department of Cardiology, Erasmus University Medical Centre, Rotterdam, [5]Department of Cardiology, HagaZiekenhuis, The Hague, [6]Department of Biomedical Photonic Imaging, Faculty of Science and Technology, University of Twente, Enschede*

## Background

Left ventricular assist devices (LVADs) are increasingly used for the treatment of end-stage heart failure. LVADs improve quality of life and long-term survival, but device specific infections remain cumbersome. These infections can lead to life threatening complications and are difficult to diagnose with conventional radiological imaging. In this study, [$^{18}$F]FDG PET/CT accuracy for the diagnosis of LVAD specific infections was evaluated with specific focus on potential confounders and the additive value of semi-quantitative analysis.

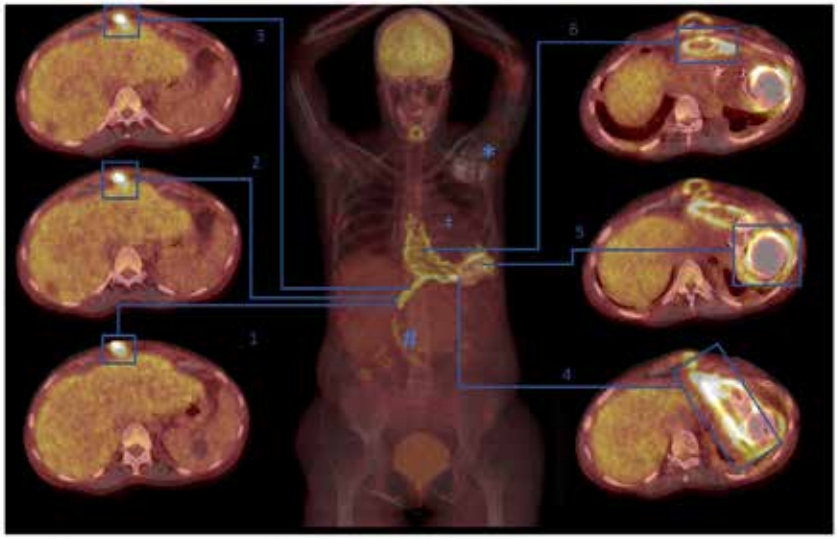
## Materials/methods

All LVAD recipients who underwent [$^{18}$F]FDG PET/CT between September 2013 and August 2020 in two LVAD centres in the Netherlands: University Medical Centre Groningen (UMCG) and Erasmus Medical Centre (EMC), with a suspicion of driveline and/or central device infection were included. [$^{18}$F]FDG PET/CT was performed according to European Association of Nuclear Medicine (EANM) guidelines. Potential confounders were documented and assessors were blinded to the clinical context of included patients. Assessment of [$^{18}$F]FDG PET/CT was performed visually and semi-quantitatively with six regions of interest alongside the driveline and central device components. The final clinical diagnosis of either driveline infection or central device infection, based on findings during surgical intervention or multidisciplinary consensus, was used as the reference for diagnosis.

## Results

In total 38 patients (average age 55 years, 84% males) were evaluated for a total of 55 episodes of suspected device-specific infection. Clinical evaluation established driveline infection in 28 cases, central device infection in 7 and combined infection in 4. Visual analysis obtained a sensitivity and specificity of 0.83 and 0.75 respectively, in differentiation between infected and non-infected drivelines. Visual analysis of [$^{18}$F]FDG PET/CT of central device components showed excellent sensitivity: 1.0,

Figure 1. Areas of interest alongside LVAD driveline and at central device components (both infected)



Legend: 1: Driveline exit site, 2: Suprafascial driveline, 3: Subfascial driveline, 4: Intrathoracic part driveline 5: Pump housing, 6 : Outflow tract. NB: Note also the ICD (*), an MVP without signs of infection (†) and the residual FDG uptake below the insertion of the driveline after surgical debridement and shortening of the driveline 2 months before (#).

but suffered from poor specificity: 0.23. Semi-quantitative analysis using a $SUV_{max}$ was comparable to visual analysis for establishing driveline infections, with a sensitivity and specificity of 0.80 and 0.84 respectively, while for central device infections, semi-quantitative analysis using a SUVratio outperformed visual analysis, with a sensitivity and specificity reaching 0.88 and 0.90 respectively.

## Conclusions

[$^{18}$F]FDG PET/CT is a valuable tool for the assessment of device-specific infections in LVAD recipients. Semi-quantitative analysis can significantly increase diagnostic accuracy of [$^{18}$F] FDG PET/CT for the analysis of the central device components and should be considered in cases where the diagnosis cannot be rejected based on visual analysis.

*d.ten.hove@umcg.nl*

# Dose-response and dose-toxicity relationships for yttrium-90 glass radioembolization in patients with colorectal cancer liver metastases

**A.A. Alsultan, C. van Roekel, M.W. Barentsz, M.L.J. Smits, B. Kunnen, M. Koopman, R.C.G. Bruijnen, B. de Keizer and M.G.E.H. Lam**

*Department of Radiology and Nuclear Medicine, UMC Utrecht*

## Introduction

Radioembolization based on personalised treatment planning requires established dose-response and dose-toxicity relationships. The aim of this study was to investigate dose-response and dose-toxicity relationships in patients with colorectal liver metastases (CRLM) treated with glass Yttrium-90 ($^{90}$Y)-microspheres.

## Methods

All CRLM patients treated with glass [$^{90}$Y]Y-microspheres in our institution were retrospectively analysed. The tumour-absorbed dose was calculated for each measurable metastasis (i.e., [$^{18}$F]FDG-positive and >5 ml tumour volume) on post-treatment $^{90}$Y-PET. Metabolic tumour response was determined on [$^{18}$F]FDG PET/CT by measuring the total lesion glycolysis at baseline and at three months post-treatment. Response was categorized according to the PERCIST criteria. The relationship between tumour-absorbed dose and metabolic response was determined on a per lesion and per patient basis using a linear mixed-effects regression model. Clinical and laboratory toxicity were correlated with healthy liver-absorbed dose.

## Results

Thirty-one patients were included. The median tumour-absorbed dose of 85 measurable metastases was 133 Gy (range 20-1001 Gy). Per response category this was 196 Gy for complete response (CR), 177 Gy for partial response (PR), 72 Gy for stable disease, and 95 Gy for progressive disease (PD). A significant dose-response relationship was found on a tumour level with a significantly higher tumour-absorbed dose in metastases with CR (+94%) and PR (+74%) compared to metastases with PD, $p<0.001$. A similar relationship was found on a patient level, with PR having a higher tumour-absorbed dose compared to PD (+58%, $p=0.044$). A tumour-absorbed dose of >139 Gy predicted three-month metabolic response with the greatest accuracy (89% specificity, 77% sensitivity), while a tumour-absorbed dose of >189 Gy predicted response with 97% specificity and 45% sensitivity. The median healthy liver-absorbed dose was 63 Gy (range: 24-113 Gy). Toxicity was mostly limited to grade 1-2. There was one case of radioembolization-induced liver disease, this patient received the highest healthy liver-absorbed dose. A positive trend was seen for most laboratory parameters in our dose-toxicity analysis.

## Conclusion

A significant relation was observed between dose and response in CRLM patients treated with glass $^{90}$Y-radioembolization.

*a.a.n.alsultan@umcutrecht.nl*

# Safety and efficacy of holmium-166 radioembolization in hepatocellular carcinoma - the HEPAR Primary study

**M.T.M. Reinders[1], K.J. van Erpecum[2], M.L.J. Smits[1], A.J.A.T. Braat[1], J. de Bruijne[2], R.C.G. Bruijnen[1], D. Sprengers[3], R.A. de Man[3], E. Vegt[4], J.N.M. IJzermans[5], A. Moelker[4], M.G.E.H. Lam[1]**

*[1]Department of Radiology & Nuclear Medicine, [2]Department of Gastroenterology & Hepatology Utrecht University - University Medical Centre Utrecht, [3]Department of Gastroenterology & Hepatology, [4]Department of Radiology & Nuclear Medicine and [5]Department of Surgery Erasmus MC-University Medical Centre, Rotterdam*

## Introduction

In contrast to Yttrium-90, Holmium-166 ($^{166}$Ho) is a combined beta and gamma emitter, allowing quantitative nuclear imaging with perspective of individualized treatment planning. The aim of this prospective clinical phase I/II study was to establish the toxicity profile of $^{166}$Ho-radioembolisation in patients with intermediate to advanced stage hepatocellular carcinoma (HCC).

## Methods

Inclusion criteria: HCC without curative options, Child-Pugh (CP) ≤B7 and good performance state. Patients were treated with $^{166}$Ho scout and therapeutic radioembolisation, aiming for an average absorbed dose of 60 Gy in the target volume. The primary endpoint was the rate of unacceptable toxicity (i.e. total bilirubin increase grade ≥3 with ascites and low albumin) or any serious adverse event (SAE) that was related to study treatment.

## Results

Thirty-one HCC patients were included, of whom 87% had multifocal disease. Twenty patients had liver cirrhosis on imaging, resulting in 45% BCLC stage B and 20% BCLC C. Median diameter of the largest tumour was 56 mm (range 15-195 mm). Unacceptable treatment-related toxicity occurred in three patients with 4 SAEs (two spontaneous bacterial peritonitis and one cholecystitis with subsequent bile duct stenosis and biliary fistula). Other side effects included fatigue (71%), back pain (55%), ascites (32%), dyspnoea (23%), nausea (23%) and abdominal pain (23%). At three and six months follow-up respectively, 54% and 84% of the target liver lesions showed complete or partial response.

## Conclusion

$^{166}$Ho-radioembolisation toxicity in this study for a selected group of patients with HCC was within the pre-defined limits. Response data support further evaluation.

*m.t.m.reinders@umcutrecht.nl*

# Value of regional myocardial flow reserve measurements using Rubidium-82 PET

**S.S. Koenders[4]; J.A. van Dalen[2]; P.L. Jager[1]; M. Mouden[3]; C.H. Slump[4]; J.D. van Dijk[1]**

*Department of [1]Nuclear Medicine, [2]Medical Physics, [3]Cardiology, Isala Hospital, Zwolle, [4]Technical Medical Centre, University of Twente, Enschede*

## Introduction

Visual assessment of Rubidium-82 ($^{82}$Rb) PET images is usually combined with global myocardial flow reserve (MFR) measurements. However, small regional flow deficits may go unnoticed when only looking at global flow values. Our aim was to compare the diagnostic value of regional and global MFR using $^{82}$Rb PET in the detection of obstructive coronary artery disease (CAD).

## Methods

We retrospectively included 1519 patients referred for rest and regadenoson-induced stress $^{82}$Rb PET/CT without prior history of CAD. Regional MFR was calculated per vessel and per segment. Vessel MFR was defined as the lowest MFR of LAD, LCX or RCA and segmental MFR as the lowest MFR of the 17-segments. Patients were classified to have obstructive CAD if follow-up from medical records included a positive invasive coronary angiography, percutaneous coronary intervention or coronary artery bypass grafting.

## Results

The total population consisted of 1519 patients with no prior history of CAD. The 154 patients classified as having CAD had a lower global MFR (median 1.9 vs. 2.4), vessel MFR (1.6 vs. 2.2) and segmental MFR (1.3 vs. 1.8) in comparison to the non-CAD patients ($p<0.001$). Receiver-operating characteristic analysis showed that the area under the curve for segmental MFR (0.80) was significantly larger ($p\leq0.006$) than that of global MFR (0.73) and vessel MFR (0.77).

## Conclusion

The use of regional MFR measurements improved the diagnostic performance of quantitative $^{82}$Rb PET in the detection of CAD as compared to global MFR measurements. We therefore recommend to use segmental MFR in combination with visual assessment of $^{82}$Rb PET scans.

*s.s.koenders@isala.nl*

Terugkijken van de webinar van de wetenschappelijke NVNG-voorjaarsbijeenkomst van 11 juni 2021 is mogelijk via de volgende link: *https://www.nvng.nl/nvng-nascholing/terugkijken-wetenschappelijke-voorjaarsbijeenkomst-11-juni-2021*

Het CWO-najaarssymposium van de NVNG zal worden gehouden op 26 november 2021 met als thema “Hybride beeldvorming”. Beoogd locatie: Meander MC, Amersfoort met waarschijnlijk ook mogelijkheid om het symposium digitaal bij te wonen. Verdere details volgen ♦