*26 november 2021*

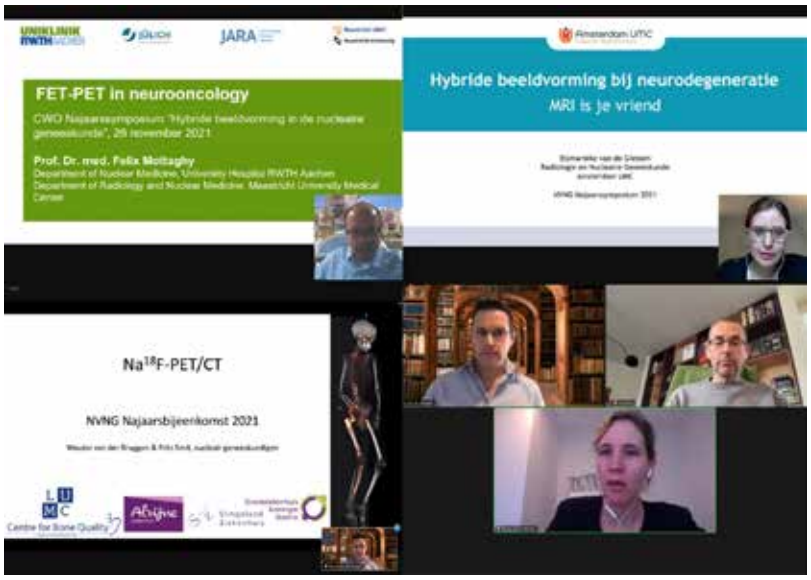
# **Online wetenschappelijke vergadering NVNG:** Recente ontwikkelingen binnen klinische nucleaire geneeskunde

### *Ochtendprogramma*

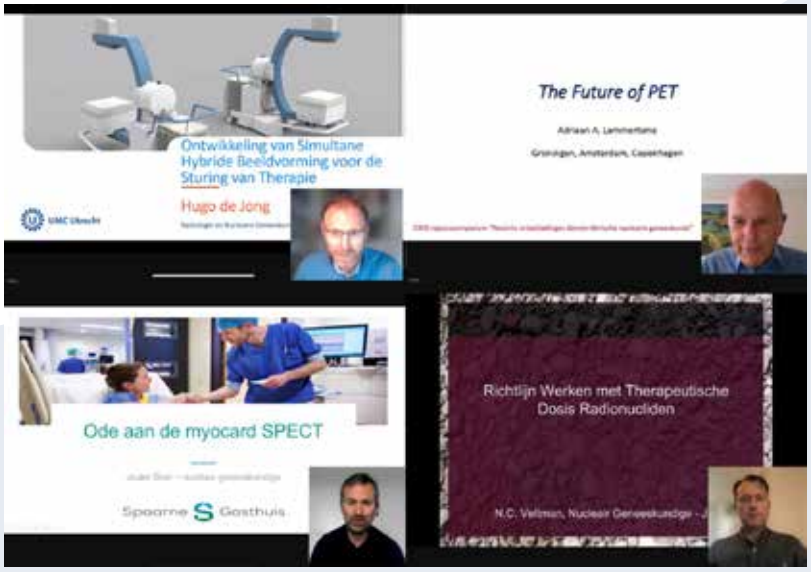
Net als de wetenschappelijke voorjaarsbijeenkomst werd op 26 november 2021 het najaarssymposium van de NVNG volledig virtueel gehouden met als thema "Recente ontwikkelingen binnen klinische nucleaire geneeskunde". Onder voorzitterschap van drs. Tineke van der Weijer startte het door de Commissie Wetenschappelijke Ontmoetingen (CWO) samengestelde programma met een presentatie van nucleair geneeskundige prof. dr. Felix Mottaghy (Maastricht UMC) over FET PET in neuro-oncologie. Vervolgens behandelde nucleair radioloog dr. Elsmarieke van de Giessen (Amsterdam UMC) diverse aspecten van hybride beeldvorming bij neurodegeneratie. De laatste presentatie van de eerste ochtendsessie was een duo-presentatie van drs. Wouter van der Bruggen en drs. Frits Smit (LUMC) met als onderwerp Na[$^{18}$F]F-PET/CT.

De tweede ochtendsessie, met dr. ir. Anke de Vries als voorzitter, startte met een presentatie van klinisch fysicus prof. dr. Hugo de Jong (UMC Utrecht) over ontwikkeling van simultane hybride beeldvorming voor sturing van therapie. Vervolgens werd de toekomst van PET door klinisch fysicus prof. dr. Adriaan Lammertsma (UMC Groningen) en myocard SPECT door nucleair geneeskundige drs. Jouke Boer (Spaarne Gasthuis) behandeld. De sessie werd afgesloten door nucleair geneeskundige drs. Niels Veltman (Jeroen Bosch Ziekenhuis) met een samenvatting van de nieuwe richtlijn "werken met therapeutische doses radionucliden".

In de middag werden twee sessies gehouden met de presentatie van een zestal vrije inzendingen zoals hieronder samengevat. Tussen beide middagssessies werd bekend gemaakt dat dr. Elly van der Veen de Woldring Prijs 2021 had gewonnen (zie bericht in kader).




*Presentaties van de eerste ochtendsessie van het najaarssymposium van de NVNG*




*Presentaties van de tweede ochtendsessie van het najaarssymposium van de NVNG*

Samenvattingen
vrije inzendingen
middagprogramma

# [18F]FDG-PET/CT to prevent futile surgery in indeterminate thyroid nodules:
## a blinded, randomised controlled multicentre trial

**E.J. de Koster, MD[1], Prof. L.F. de Geus-Oei, MD PhD[1,2,3], A.H. Brouwers, MD PhD[4], E.W.C.M. van Dam, MD PhD[5], L.T. Dijkhorst-Oei, MD PhD[6], A.C.H. van Engen-van Grunsven, MD PhD[7], W.B. van den Hout, PhD[8], T.K. Klooker, MD PhD[9], R.T. Netea-Maier, MD PhD[10], M. Snel, MD PhD[11], W.J.G. Oyen, MD PhD[1,12], D. Vriens, MD PhD[2*], for the *EfFECTS trial* study group.**

*[1]Radboud University Medical Centre, Department of Radiology and Nuclear Medicine, Nijmegen, [2]Leiden University Medical Centre, Department of Radiology, Section of Nuclear Medicine, Leiden, [3]University of Twente, Biomedical Photonic Imaging Group, Enschede, [4]University of Groningen, University Medical Centre Groningen, Department of Nuclear Medicine and Molecular Imaging Groningen, [5]Amsterdam University Medical Centres, location VU University Medical Centre, Department of Internal Medicine, Division of Endocrinology, Amsterdam, [6]Meander Medical Centre, Department of Internal Medicine, Amersfoort, [7]Radboud University Medical Centre, Department of Pathology, Nijmegen, [8]Leiden University Medical Centre, Department of Medical Decision Making, Leiden, [9]Amsterdam University Medical Centres, location Academic Medical Centre, Department of Endocrinology and Metabolism, Amsterdam Gastroenterology Endocrinology and Metabolism, Amsterdam; Flevo hospital, Department of Internal Medicine, Almere, [10]Radboud University Medical Centre, Department of Internal Medicine, Division of Endocrinology, Nijmegen, [11]Leiden University Medical Centre, Department of Medicine, Division of Endocrinology, Leiden, [12]Rijnstate Hospital, Department of Radiology and Nuclear Medicine, Arnhem; Humanitas University, Department of Biomedical Sciences and Humanitas Clinical and Research Centre, Department of Nuclear Medicine, Milan, Italy*

## Purpose
To assess the impact of an [18F]FDG-PET/CT-driven diagnostic workup to rule out malignancy, avoid futile diagnostic surgeries, and improve patient outcomes in thyroid nodules with indeterminate cytology.

## Methods
In the Efficacy of [18F]FDG-PET in Evaluation of Cytological indeterminate Thyroid nodules prior to Surgery (EfFECTS) trial, 132 adult euthyroid patients with scheduled diagnostic surgery for a Bethesda III or IV thyroid nodule underwent [18F]FDG-PET/CT and were randomised to an [18F]FDG-PET/CT-driven or diagnostic surgery group. In the [18F]FDG-PET/CT-driven group, management was based on the [18F]FDG-PET/CT result: when the index nodule was visually [18F]FDG-positive, diagnostic surgery was advised; when [18F]FDG-negative, active surveillance was recommended. The nodule was presumed benign when it remained unchanged on ultrasound surveillance. In the diagnostic surgery group, all patients were advised to proceed to the scheduled surgery, according to current guidelines. The primary outcome was the fraction of unbeneficial patient management in one year, i.e., diagnostic surgery for benign nodules and active surveillance for malignant/borderline nodules. Intention-to-treat analysis was performed. Subgroup analyses were performed for non-Hürthle cell and Hürthle cell nodules.

## Results
Patient management was unbeneficial in 42% (38/91 [95% confidence interval [CI], 32%-53%]) of patients in the [18F]FDG-PET/CT-driven group, as compared to 83% (34/41 [95% CI, 68%-93%]) in the diagnostic surgery group (p<0.001). [18F]FDG-PET/CT-driven management avoided 40% (25/63 [95% CI, 28%-53%]) diagnostic surgeries for benign nodules: 48% (23/48 [95% CI, 33%-63%]) in non-Hürthle cell and 13% (2/15 [95% CI, 2%-40%]) in Hürthle cell nodules (p=0.02). No malignant or borderline tumours were observed in patients under surveillance. Sensitivity, specificity, negative and positive predictive value, and benign call rate (95% CI) of [18F]FDG-PET/CT were 94.1% (80.3%-99.3%), 39.8% (30.0%-50.2%), 95.1% (83.5%-99.4%), 35.2% (25.4%-45.9%) and 31.1% (23.3%-39.7%), respectively.

## Conclusion
An [18F]FDG-PET/CT-driven diagnostic workup of indeterminate thyroid nodules leads to practice changing management, accurately and oncologically safely reducing futile surgeries by 40%. For optimal therapeutic yield, application should be limited to non-Hürthle cell nodules.

*lisanne.dekoster@radboudumc.nl* ♦

## [$^{18}$F]FDG PET radiomics for the prediction of genetic clusters in pheochromocytomas and paragangliomas

**W.A. Noortman[1,2], D. Vriens[1], E.H. Aarntzen[3], A. van Berkel[4], H. J. L. M. Timmers[4], L.F. de Geus-Oei[1,2], F.H.P. van Velden[1]**

*[1]Department of Radiology, section of Nuclear Medicine, Leiden University Medical Centre, Leiden, [2]Biomedical Photonic Imaging Group, University of Twente, Enschede, [3]Department of Radiology and Nuclear Medicine, Radboud University Medical Centre, Nijmegen, [4]Department of Internal Medicine, Division of Endocrinology, Radboud University Medical Centre, Nijmegen*

### Introduction

Pheochromocytomas and paragangliomas (PPGLs) are rare neuroendocrine tumours. Up to 40% harbour an underlying germline mutation. Furthermore, somatic mutations are found in at least one-third of sporadic PPGLs. Hereditary PPGLs can be segregated into 2 clusters based on their transcription profiles: cluster 1 (SDH, VHL) is enriched for genes that are associated with the hypoxic response, and cluster 2 (RET, NF1) implicates gene mutations that activate kinase signaling. Cluster 1 PPGLs are associated with increased [$^{18}$F]FDG accumulation (i.e. $SUV_{max}$). This study compared the use of radiomics, $SUV_{max}$ and biochemical profile for the prediction of the genetic clusters of PPGLs.

### Methods

Forty patients underwent a [$^{18}$F]FDG-PET/CT scan prior to surgery. Forty-two lesions (13 cluster 1, 19 cluster 2, 10 sporadic) were delineated using an adaptive threshold of 41% SUVpeak, wherefrom 105 radiomic features were extracted. Stratified 5-fold cross-validation for the prediction of the genetic cluster was performed using multinomial logistic regression. Dimensionality reduction using redundancy filtering of the Spearman correlation matrix and factor analysis was incorporated in the folds; 1 factor was obtained for every 10 patients in the training set. Predictive performances were presented as mean multiclass areas under the receiver operating characteristic curves (AUC) over the five folds for the test sets. Results were validated using a sham experiment, in which the outcome labels were shuffled in 100 iterations. AUCs of the biochemical profile (noradrenergic, adrenergic and dopaminergic), $SUV_{max}$ and the radiomics model were compared to sham data.

### Results

A multivariate model with biochemistry alone could predict the genetic cluster with a mean AUC for the test set of 0.57. $SUV_{max}$ resulted in a mean test AUC of 0.86 (0.83 combined with biochemistry, in brackets for all AUCs). The three radiomic factors reached an AUC of 0.85 (0.80). Cluster 1 and 2 could be distinguished with AUCs of 1.00 (0.96) and 0.98 (0.93) for the $SUV_{max}$ and radiomic factors, respectively. AUCs for $SUV_{max}$ and radiomic factors were 0.91 (0.91) and 0.83 (0.81) for characterization of cluster 1 and sporadic PPGLs and 0.68 (0.62) and 0.74 (0.66) for cluster 2 and sporadic PPGLs. All sham AUCs were around 0.50.

### Conclusion

Identification of cluster 2 PPGLs and sporadic PPGLs might be better achieved by radiomics when compared to biochemistry, $SUV_{max}$ or sham data. $SUV_{max}$ could already predict cluster 1 PPGLs with high certainty, therefore radiomics could not enhance the classification performance for this cluster.

*w.a.noortman@lumc.nl* ♦

## External validation of PET-based radiomic models to identify patients with residual esophageal cancer after neoadjuvant chemoradiotherapy

**M.J. Valkema[1], R.J. Beukinga[2], A. Chatterjee[3], H.C. Woodruff[3], P. Lambin[3], R.J. Bennink[4], W. Schreurs[5], M. Roef[6], R. Valkema[1], S.M. Lagarde[1], B.P.L. Wijnhoven[1], J.T.M. Plukker[2], J.J.B. van Lanschot[1]**

*[1]Erasmus MC Cancer Institute, University Medical Centre Rotterdam, [2]University Medical Centre Groningen/ Medical Imaging Centre, Groningen, [3]Department of Precision Medicine, GROW - School for Oncology and Developmental Biology, Maastricht University, Maastricht, [4]Amsterdam University Medical Centre, Amsterdam, [5]Zuyderland Medical Centre, Heerlen, [6]Catharina Hospital Eindhoven, Eindhoven*

### Background

High-throughput quantitative imaging ("radiomics") has been proposed to predict tumor response in various types of cancer. Internally validated radiomic models based on post-treatment [$^{18}$F]FDG-PET features plus CT-stage have been developed (Beukinga et al. 2018) to detect residual tumor after neoadjuvant chemoradiotherapy for esophageal cancer. The aim of the present study was to externally validate the published models.

### Methods

The external validation cohort comprised esophageal cancer patients who underwent chemoradiotherapy according to the CROSS regimen followed by immediate resection in four Dutch institutes between 2013-2019. Outcome was tumor regression grade (TRG) 1 (0% residual vital tumor) versus TRG-2-3-4 (≥ 1% tumor). Preoperative [$^{18}$F]FDG-PET/

CT was performed 6-12 weeks after nCRT. Gross tumor volumes on CT were transposed to post-treatment PET scans and were manually adapted in consensus by two investigators. Radiomic features were extracted using the software of the published models, in which the same settings for feature calculation were applied. Discrimination and calibration were assessed for the 6 internally validated models with optimism-corrected AUCs>0.77.

## Results

Some 189 patients were included in the external validation cohort. Baseline characteristics and outcome (TRG-1: 40/189 patients (21%); TRG2-3-4: 149/189 patients (79%)) were comparable to the derivation sample. The model including cT-stage and the feature "median absolute deviation" had highest AUC of 0.65 (95% CI 0.56-0.73), and a calibration slope and intercept of 0.15 and -1.49 respectively. At a probability threshold of 0.8 (using Youden's index), sensitivity was 81%, specificity 31% and accuracy 69%.

## Conclusion

The predictive performance of the previously developed radiomic models could not be replicated in the present multicentre external validation cohort. The decreased overall performance indicates overfitting of the models to the derivation sample. Possible causes are unintentional dependency of radiomic features on scanner types, scanning protocols, tumor delineation methods and timing of post-treatment [18F]FDG-PET/CT. We aim at improving the generalizability of the models, to enable future application in clinical decision-making for individual patients.

*m.valkema@erasmusmc.nl* ♦


*Presentaties en sprekers van de eerste middagsessie van het najaarssymposium van de NVNG.*

# [18F]FET PET/MRI: a novel and improved technique for detection of pituitary microadenoma

**I. Pruis, MSc[1], S. Neggers, MD, PhD[2], F. Verburg, MD, PhD[1], S. Veldhuijzen van Zanten, MD, PhD[1]**

*[1]Department of Radiology and Nuclear Medicine, [2]Department of Internal Medicine, Erasmus MC, Rotterdam*

## Introduction

Pituitary adenoma can cause severely disabling symptoms resulting from hormonal dysregulation. In 40% of patients, diagnostic MRI is inconclusive as microadenoma by definition are <10mm and not always sufficiently contrasting. We here introduce a novel method for detection of microadenoma by O-(2-[18F]-fluoroethyl)-L-tyrosine ([18F]FET) PET/MRI.

## Methods

Patients with suspected microadenoma underwent PET/MR-imaging at 20 minutes post-injection of 200 (median, range 50-207) MBq [18F]FET. A positive scan was defined as focal uptake exceeding local background (i.e., normal pituitary tissue). Outcomes were compared with results of selective inferior petrosus sinus sampling (IPSS), post-operative pathology reports, and clinical follow-up.

## Results

Nineteen patients, 73.7% female, median age 56 (11-68), with Cushing's disease (n=12; 63.2%) or acromegaly (36.8%) but with a negative/inconclusive MRI were included. Fifteen patients (78.9%; 10 Cushing, 5 acromegaly) showed positive focal [18F]FET PET/MRI uptake. Four patients underwent surgery upon which pathology confirmed presence of an adenoma. Nine out of eleven Cushing patients also had positive IPSS, however, in five IPSS could not differentiate between left/right, and in two the designated side by IPSS did not correlate with imaging. In the

patients with a negative [18F]FET PET/MRI, one proved true-negative after surgery, one was diagnosed with a Rathke's cleft/non-metabolic cystic adenoma instead, one appeared to have minimal symptoms that not required therapy, and one had a later confirmed microadenoma that was possibly not detected by [18F]FET PET/MRI because of ACTH normalizing medication at the time of the scan.

## Conclusion

[18F]FET PET/MR-imaging shows high accuracy for localizing microadenoma in patients with hormonal dysregulation. The diagnostic yield of this hybrid imaging technique showed to exceed that of MRI alone and IPSS. This novel approach herewith provides an important addition for planning of selective transsphenoidal adenomectomy.

*s.veldhuijzenvanzanten@erasmusmc.nl* ♦

# [18F]MFBG PET/CT as promising new neuroblastoma specific imaging – a prospective feasibility study compared to [123I]MIBG SPECT/CT

**A. Samim[1,2], T. Blom[1], A.J. Poot[1,2], N. Tolboom[1,2], A.J.A.T. Braat[1,2], M.M. van Noesel[1,2], M.G.E.H. Lam[1,2], A.D. Windhorst[3], M. Fiocco[1,4], G.A.M. Tytgat[1,2*], B. de Keizer[1,2*]**
*** G.A.M. Tytgat and B. de Keizer share senior co-authorship**
*[1]Princess Máxima Centre for Paediatric Oncology, Utrecht, [2]Division Imaging & Oncology, UMC Utrecht, [3]Department of Radiology & Nuclear Medicine, Cancer Centre Amsterdam, Amsterdam UMC, [4]Mathematical Institute, Leiden University*

## Background and Aims

Meta-[18F]fluorobenzylguanidine ([18F]MFBG), the fluorine-18 labeled analogue of [123I]MIBG, is a new tracer for imaging of neuroblastoma. It allows for fast, high-resolution PET imaging in a single day protocol without requiring thyroid blocking medication. The aim of this study was to investigate the feasibility and diagnostic performance of [18F]MFBG PET/CT compared to [123I]MIBG scanning in patients with neuroblastoma.

## Methods

From July 2020 to June 2021, we performed 20 paired total body [18F]MFBG PET/CT and [123I]MIBG scans (total body scintigraphy and SPECT/CT) in 14 patients (13/14 INRG stage M, median age 4.3 years, range 0.17–16 years). Two independent readers and a third consensus reader assessed skeletal lesions (using the SIOPEN skeletal segments and score) and soft tissue lesions.

## Results

Compared to [123I]MIBG scanning, [18F]MFBG PET/CT detected more lesions (both skeletal and soft tissue lesions) in 75% (15/20), equal in 20% (4/20) and less in 5% (1/20) of the scans. [18F]MFBG PET/CT detected more skeletal lesions in 55% (11/20), equal in 30% (6/20), and less in 15% (3/20) of the scans. [18F]MFBG PET/CT detected skeletal lesions in 40 segments that were negative on [123I]MIBG scanning (in 11/20 paired scans). There were only 4 [123I]MIBG positive/[18F]MFBG negative segments. The median effective dose of [18F]MFBG was significantly lower than [123I]MIBG (0.9 vs. 3.3 mSv, respectively, P<0.001). The majority (8/10) of patients who required sedation for [123I]MIBG scanning, were able to undergo [18F]MFBG PET/CT without sedation. We observed no adverse events related to [18F]MFBG injection.

## Conclusions

The results of this pilot study indicate that [18F]MFBG PET/CT is safe and feasible in pediatric patients with neuroblastoma and has superior tumor detection capability compared to [123I]MIBG scanning. [18F]MFBG PET/CT shows promise to become future standard of care.

*a.samim-4@prinsesmaximacentrum.nl* ♦

# [18F]FDG-PET/MR for the determination of antibiotic treatment response in necrotizing external otitis

**W.L. van der Meer[1,5], C, Mitea[1], J.J. Waterval[2,5], H.P.M. Kunst[2,3,4,5], A.A. Postma[1,4,5]**
*[1]Department of Radiology & Nuclear Medicine, Maastricht University Medical Centre, [2]Department of Otorhinolaryngology and Head and Neck Surgery, Maastricht University Medical Centre, [3]Department of Otorhinolaryngology and Head and Neck Surgery, Radboud Institute for Health Sciences, Radboud University Medical Centre, Nijmegen, [4]School for Mental Health & Neuroscience, Maastricht University, Maastricht, [5]Dutch Academic Alliance Skull Base Pathology, Maastricht University Medical Centre, Radboud University Medical Centre, Maastricht/Nijmegen*

## Purpose or learning objective

Necrotizing external otitis (NEO) is a rare and serious complication of external otitis. The determination of treatment response is difficult to establish clinically. This study demonstrates the role of standardized uptake values (SUV) on [18F]FDG-PET/MR for the determination of antibiotic treatment response.

## Methods or background

Patients with NEO that underwent a diagnostic and follow-up [18F]FDG-PET-MR between 2016-2019

were included. [$^{18}$F]FDG-PET/MR scans acquired within 14 days of CT diagnosis were regarded as diagnostic, and after 14 days as follow-up. The SUV max of the affected and the unaffected ear were measured by a nuclear medicine specialist. The imaging findings were correlated with clinical response outcomes.

## Results or findings

In total 22 PET/MR scans from 11 patients were included. The average time between scans was 149 days. Diagnostic and follow-up [$^{18}$F]FDG-PET/MR scans showed a higher SUV max of the ear affected with NEO in comparison to the unaffected ear. Overall, $SUV_{max}$ (7.6 ± 2.1) of the affected ear is the highest within the first 14 days after NEO diagnosis in comparison to the healthy ear (2.1 ± 0.7). The SUV difference of the affected ear (2.8 ± 0.8) in comparison to the healthy ear (2.0 ± 0.9) persists, although no longer statically significant after successful antibiotic treatment.

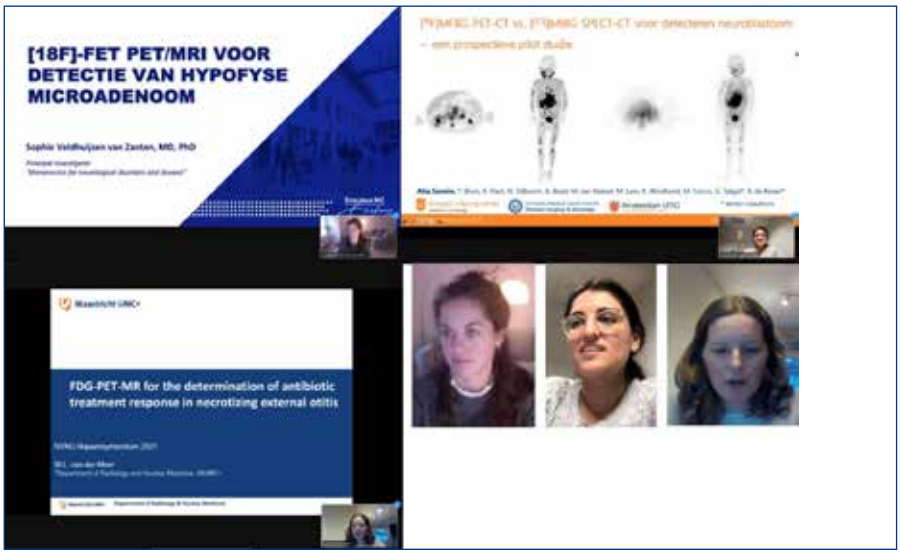
## Conclusion

SUV measurements on [$^{18}$F]FDG-PET/MR are correlated with clinical response outcomes after antibiotic treatment for necrotizing external otitis. Close collaboration with treating clinical physicians is advised, as the interpretation of SUV values is dependent upon knowledge of time of diagnosis, clinical patient status, and start and cessation of successful antibiotic treatment.

## Limitations

A small number of patients affected with NEO was included, as not every known patient received both a diagnostic and a follow-up [$^{18}$F]FDG-PET-MR.

*lieke.vander.meer@mumc.nl* ♦




*Presentaties en sprekers van de tweede middagsessie van het najaarssymposium van de NVNG.*

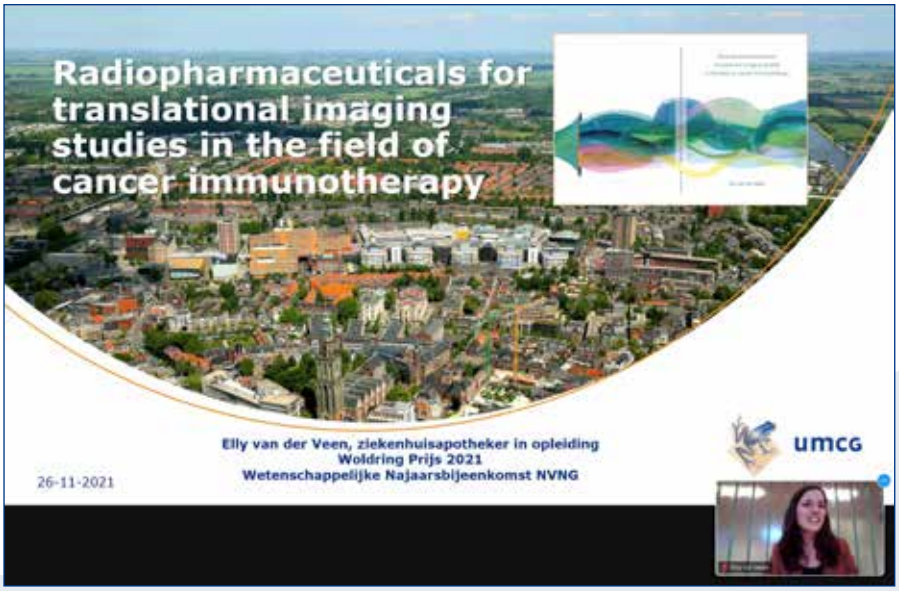
Terugkijken van de webinar met de presentaties van de vrije inzendingen van de wetenschappelijke NVNG-najaarsbijeenkomst van 26 november 2021 is mogelijk via de volgende link: *https://www.nvng.nl/nascholing/wetenschappelijke-ontmoetingen*

## ELLY VAN DER VEEN WINT WOLDRING PRIJS 2021

Tijdens de online gehouden wetenschappelijke najaarsvergadering van de NVNG op 26 november jl. maakte de voorzitter van de jury, dr. Vivian Bongers, bekend dat de Woldring Prijs 2021 naar dr. Elly van der Veen ging. Haar proefschrift getiteld "Radiopharmaceuticals for translational imaging studies in the field of cancer immunotherapy" werd uitverkozen uit zeven inzendingen. Elly van der Veen verdedigde haar proefschrift op 8 juli 2020 aan de Rijksuniversiteit Groningen en had als promotors prof. dr. E.G.E. de Vries en prof. dr. M.N. Lub-de Hooge. Hoewel de Woldring Prijs 2021 via teleconferentie werd aangekondigd vond de uitreiking fysiek plaats. Zoals te zien op onderstaande foto ontving Elly van der Veen de prijs uit handen van de voorzitter van de sessie, dr. Hendrikus Boersma. De samenvatting van het proefschrift van Elly van der Veen werd gepubliceerd in de editie van september 2020 van het TvNG *(https://www.tijdschriftvoornucleairegeneeskunde.nl/september-2020-volledige-uitgave-18-artikelen)*. Meer over de geschiedenis van de Woldring Prijs is te vinden op *https://www.tijdschriftvoornucleairegeneeskunde.nl/de-woldring-prijs-toen-en-nu.*

Voor informatie over het reglement van de Woldring Prijs zie: *www.nvng.nl/commissies/woldring-prijs.*


*Elly van der Veen ontvangt de Woldring Prijs 2021 uit handen van de voorzitter van de sessie dr. Hendrikus Boersma tijdens het najaarssymposium van de NVNG.*




*Online presentatie Elly van der Veen n.a.v. Woldring Prijs 2021.*

### Aankondiging

Het CWO-voorjaarssymposium van de NVNG zal worden gehouden op 10-6-2022 met als thema "Theranostics". Beoogde locatie: Gelre Ziekenhuis te Apeldoorn met ook de mogelijkheid om het symposium digitaal bij te wonen. Verdere details volgen op de internetsites van de NVNG en TvNG.