Wetenschappelijke vergadering NVNG: Veiligheid voor alles

16 juni 2023

Ochtendprogramma

De wetenschappelijke voorjaarssbijeenkomst van de NVNG werd op 16 juni 2023 in Gelre ziekenhuizen, Apeldoorn gehouden met als thema "Veiligheid voor alles". Na een welkomstwoord van de voorzitter van de Commissie Wetenschappelijke Ontmoetingen (CWO) drs. Emilia Owers startte de eerste ochtendsessie van het door de CWO samengestelde programma onder voorzitterschap van drs. Emilia Owers en drs. Tineke van de Weijer met een presentatie van nucleair geneeskundige dr. Marcel Janssen (Radboud UMC, Nijmegen) betreffende "[^{117}Lu]Lu-PSMA I&T vs [^{117}Lu]Lu-PSMA-617". Vervolgens behandelde nucleair geneeskundige drs. Emilia Owers (NKI-AvL, Amsterdam) het onderwerp "[^{117}Lu]Lu-PSMA dosimetry". De laatste spreker van de eerste ochtendsessie was nucleair apotheker dr. Nanno Schreuder (GE HealthCare Radiofarmaca Apotheek Zwolle) met als presentatie "Bijwerkingen van diagnostische radiofarmaca, wat kunnen we leren van de patiënt?".

De tweede ochtendsessie, met dr. Marcel Janssen en dr. ir. Anke de Vries als voorzitters, startte met de presentatie "Inspectie ANVS op afdelingen nucleaire geneeskunde" door klinisch fysicus dr. ir. Bart Vermolen (Ziekenhuis Gelderse Vallei, Ede). Vervolgens werd het onderwerp "[^{117}Lu]Lu-PSMA - stralingsveiligheid" behandeld door klinisch fysicus dr. Pepijn Horssen (Meander Medisch Centrum, Amersfoort).

Sprekers van de eerste ochtendsessie: Marcel Janssen, Emilia Owers en Nanno Schreuder

Sprekers van de tweede ochtendsessie: Pepijn Horssen en Bart Vermolen

Aansluitend op het ochtendprogramma werd een algemene ledenvergadering van de NVNG gehouden.

Middagprogramma
In aansluiting op de presentatie "Huidige ontwikkelingen PALLAS en FIELD-LAB" door dr. Karlijn van der Schilden (NRG/PALLAS) volgden de vrije inzendingen.

Samenvattingen vrije inzendingen middagprogramma

First Experience with [^{195}mPt] Cisplatin Imaging in Lung Cancer Patients

D.S. Hoogenkamp[1]; E.A. Aalbersberg[1]; K. van der Schilden[2]; N.H. Hendrikse[3]; M.P.J. Mooijer[3]; U. Funke[3]; A.D. Windhorst[3]; B.J. de Wit-van der Veen[1]; W.V. Vogel[1]

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Aim/Introduction
Platinum-based chemotherapeutics are known to show heterogeneous responses and the development of nephrotoxicity is not uncommon. So, patient selection before therapy could aid in increasing effectiveness and decreasing toxicity. Radiolabeled [^{195m}Pt]Cisplatin is hypothesized to provide useful in vivo information on its distribution and aid in this process of patient selection. This imaging study evaluates the absorbed dose of [^{195m}Pt]Cisplatin SPECT/CT in lung cancer patients.

Materials and Methods
Five patients with non-small-cell lung cancer (NSCLC) who will receive 25 fractions radiotherapy with concurrent low-dose cisplatin were included. Patients received a single dose of 100 MBq [^{195m}Pt]Cisplatin in their second or third week of treatment. For the synthesis of [^{195m}Pt]Cisplatin a known procedure was modified (1). 195mPt was supplied by the Nuclear Research & Consultancy Group (Petten, Netherlands) and produced under GMP at the Amsterdam UMC (location Vumc, Netherlands) with a radiochemical purity of ≥95% at a radioactivity concentration of 11.1 ± 4.9 MBq/ml. Up to six SPECT/CTs (Intevo Bold Siemens, Germany) were acquired between 1 and 168 hours after injection. Time-activity curves were generated by mono-exponential fitting of organ specific activities acquired using automated full organ segmentations in 3DSlicer (TotalSegmentator). S-values for ^{195m}Pt were obtained from IDAC-Dose 2.1.

Results
Tracer elimination depended on renal clearance and bladder voiding, with a half-life of 32 ± 18 hours. Blood clearance was relatively slow, with $T_{50\%}$ at 29,6 ± 15 hours. The liver received the highest [^{195m}Pt]Cisplatin amounts; 7.6% ± 1.1% of the total administered [^{195m}Pt]Cisplatin at T = 1.5 hours. Also, highest absorbed radiation dose was found in the liver (62.6 mGy ± 11.1 mGy), followed by bladder wall (48.5 mGy ±22.5) and kidneys (42.3mGy ± 9.6mGy). Patients received a mean effective dose of 15.6 ± 2.5 mSv per 100 MBq [195mPt]Cisplatin. Effective dose estimates were highly influenced by estimates of the bladder dose.

Conclusion
[^{195m}Pt]Cisplatin as a diagnostic tool is safe to use in patients with NSCLC, with a mean effective dose of 15.6±2.5 mSv (0.16±0.025 mSv/MBq). In following studies, tumour accumulation and imaging quality will be further assessed.

References
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Prognostic model based on ^{18}F-FDG PET radiomics features and correlation of radiomics parameters with the serum biomarker TARC in patients with relapsed or refractory classical Hodgkin lymphoma

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Part of this research in n=65 patients has been published: Driessen J, et al. *Leukemia*, 2022. doi: 10.1038/s41375-022-01717-8.

Introduction
Classical Hodgkin lymphoma (cHL) mainly affects young adults and generally has a favourable outcome.

However, patients who relapse or are primarily refractory (R/R) to chemo-radiation receive intensified salvage chemotherapy and autologous stem cell transplantation with cure rates of only 50-60%. Investigating prognostic factors for patients with R/R cHL is essential to optimize risk-adapted treatment strategies. We investigated the prognostic value of several quantitative PET features and assessed their correlation with the serum biomarker Thymus and Activation Regulated Chemokine (TARC), that is secreted by Hodgkin-Reed Sternberg (HRS)-cells.

Methods

We built a prognostic model on baseline quantitative ^{18}F-FDG PET radiomics features and clinical characteristics to predict freedom from progression (FFP) in R/R cHL patients. Metabolic tumour volume (MTV) and several novel radiomics dissemination features representing inter-lesion differences in distance, volume and standard uptake value (SUV) were extracted at patient level from the baseline PET. Logistic regression was applied to develop and train the model on a total of 111 patients from two clinical trials (NCT02280993 and NCT00255723) and validated on an independent external cohort of 68 patients (NCT01508312). In a subset of patients (n=56) we performed immunohistochemical (IHC) staining for TARC by HRS-cells on lymph node biopsies at baseline and we measured soluble (s)TARC in serum at several time points.

Results

The prognostic radiomics model consists of a selection of three PET features (MTV, Spread in distance and tumour-to-liver-ratio of SUVmean ($TLR_{SUVmean}$)) and two clinical features (R/R status and B symptoms) and yielded a high AUC of 0.822 and 0.758 in the training (cross-validated) and validation cohort, respectively.

We identified a subset of high-risk patients with inferior FFP outcomes who showed a 3-year FFP of 41.3% versus 88.4% for patients in the low-risk group in the training cohort ($p<0.0001$), and 33.3% versus 76.8% in the validation cohort ($p=0.003$), respectively. Baseline MTV and $TLR_{SUVpeak}$ showed significant correlations with baseline sTARC ($R=0.54$; $p<0.001$, and $R=0.40$; $p=0.002$, respectively). After one cycle of chemotherapy, patients with absolute sTARC levels <500pg/mL had a significantly lower risk of progression. Combining baseline $TLR_{SUVmean}$ and serum TARC after one chemotherapy cycle significantly increased the prognostic value of both independent parameters.

Conclusion

We developed a prognostic model combing radiomics and clinical features that calculates a risk profile for individual patients which can be applied to develop risk-stratified treatment strategies in R/R cHL. In addition, we established the prognostic value of sTARC and its correlation with quantitative PET parameters.

Cardiac one-stop-shop: Performance of a Rapid Diagnostic Outpatient Clinic using Rubidium-82 PET-CT Imaging

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Introduction

Atherosclerotic vascular disease is a major cause of death worldwide, and in the Netherlands, coronary heart disease affects a large number of people. To speed up the diagnosis of myocardial ischemia due to severe atherosclerotic narrowing of coronary arteries, a rapid diagnostic outpatient clinic was introduced that utilizes myocardial perfusion PET-CT imaging (^{82}Rb PET-CT). The aim of this clinic is to analyse patients within a week and all appointments on the department

Sprekers eerste middagsessie: (vlnr) Julia Driessen, Denise Hoogenkamp en Karlijn van der Schilden.

of cardiology and nuclear medicine take place on the same day. The study aims to determine whether the use of the rapid diagnostic outpatient clinic results in shorter throughput times, thus decreasing the risk for patients with severe coronary artery disease without compromising efficiency and healthcare costs.

Methods

The study was conducted by retrospectively comparing the throughput times between the rapid diagnostic outpatient clinic and the traditional outpatient clinic. The date of referral and the date of the follow-up appointment after the examination for all patients referred for examination at the rapid diagnostic outpatient clinic were recorded, as well as the number of patients who actually underwent an examination. The Duke score was calculated, and a pre-test likelihood of >15% indicated the need for additional testing according to the guideline of the European Society of Cardiology (ESC). The study's main outcome was the potential reduction in days of the diagnostic process through the use of the rapid diagnostic outpatient clinic compared to the control group.

Results

In total, 152 patients were analysed, and the results showed that the throughput times in the rapid diagnostic outpatient clinic were on average 9 days compared to 68 days in the control group. Ischemia was found in 25% of patients in the rapid diagnostic outpatient clinic and 10% of controls. Six percent of patients dropped out of the rapid diagnostic outpatient clinic because the indication was rejected by the cardiologist, and 8% of patients in the rapid diagnostic outpatient clinic had a pre-test likelihood of below 15%. Examinations with a Duke score below 15% or with non-specific symptoms were considered not useful and deemed as over diagnosis.

Conclusion

The study concludes that the implementation of a rapid diagnostic outpatient clinic utilizing ^{82}Rb PET-CT imaging has the potential to dramatically expedite the diagnosis of myocardial ischemia in patients with suspected coronary artery disease with an average reduction of 59 days. The rapid diagnostic outpatient clinic was more effective in selecting patients with ischemia, where 25% of patients had ischemia compared to 10% in the control group. Dropout rates and overdiagnosis occurred in 14% of cases. These findings suggest that the rapid diagnostic outpatient clinic is an effective and efficient way to diagnose myocardial ischemia due to severe atherosclerotic narrowing of coronary arteries.

The Effect of Folate on [^{68}Ga]Ga-PSMA-11 Organ and Tumor Uptake: Predictions Using Physiologically Based Pharmacokinetic Modelling

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Introduction

It is hypothesized that folate intake might reduce accumulation of PSMA-directed peptides due to competitive binding to the PSMA-receptor and, thus, folates could affect diagnostic imaging and radioligand therapy in prostate cancer. However, the exact relationship between folates and PSMA-ligands is not well established. Therefore, we aimed to develop a physiologically based pharmacokinetic (PBPK) model to predict the effect of folate intake on [^{68}Ga]Ga-PSMA-11 uptake in salivary glands, kidney and tumours.

Materials and Methods

A PBPK model was developed for [^{68}Ga]Ga-PSMA-11 and folate (folic acid and its metabolite 5-MTHF), with compartments added that represent salivary glands and tumour. Model evaluation for [^{68}Ga]Ga-PSMA-11 was performed with patient data from two different studies (1,2), while for folate data from literature were used (3,4). Using the final model, the effect of varying folate doses on relative differences in [^{68}Ga]Ga-PSMA-11 accumulation in salivary glands, kidney and tumour compartments was predicted. Folate doses were selected to represent intake by means of folate-containing food (150 µg), vitamin supplements (400 µg) and folate tablets (5 and 10 mg). In addition, predictions were made for patients with different tumour volumes (10-1000 mL).

Results

PBPK model predictions adequately described data for both [^{68}Ga]Ga-PSMA-11 and folates. Predictions of folate doses of 150 and 400 µg showed no clinically relevant effect (<23.5% relative difference) on salivary gland and kidney uptake. However, for 5 and 10 mg, a relevant decrease in salivary glands (34 and 36%, respectively) and kidney uptake (32 and 34%, respectively) was predicted. None of the included folate doses showed a relevant effect on tumour accumulation. Lastly, different tumour volumes did not influence the effects of folate intake on [^{68}Ga]Ga-PSMA-11 distribution.

Conclusion

High folate doses (5 and 10 mg) were predicted to decrease [^{68}Ga]Ga-PSMA-11 salivary gland and kidney

uptake, while intake by means of folate-containing food or vitamin supplements was predicted to show no relevant effects. [^{68}Ga]Ga-PSMA-11 tumour uptake was not affected by folate intake in the dose range studied and tumour volume differences were not expected to impact folate effects. These predictions could guide trial design aimed at using folates to reduce toxicity during PSMA-based radioligand therapy.

References

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Characterization and correction of dead-time effects for I-131 intra-therapeutic dosimetry in differentiated thyroid cancer

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Introduction

Several studies are exploring re-differentiation therapies that might re-enable radioactive iodine (RAI) therapy in RAI-refractory differentiated thyroid cancer (DTC) patients. Intra-therapeutic I-131 dosimetry is essential to assess dose-effect relationships for tumours and organs-at-risk in this new therapy strategy. However, quantitative imaging of high I-131 activities in vivo includes several challenges such as dead-time-induced count losses, attenuation, scatter and limited spatial resolution. In this preliminary work, dead-time effects were investigated.

Methods

I-131 capsules with varying activities up to 7,400 MBq were scanned in a neck scatter phantom on a gamma camera (Discovery NM/CT 670 Pro SPECT/CT; GE Healthcare). The two detectors were positioned anterior and posterior of the phantom at 180 degrees. Spot-view (256x256 matrix and 2.2 mm pixel size) count rates were measured using a photopeak window of 364 keV ±10% and High Energy General Purpose (HEGP) collimators. A total of 21 measurements were performed with I-131 activities ranging from 85 to 7,338 MBq. For both detectors a curve was fitted to the measurements using Sorenson's paralyzable model. In addition, six measurements were performed with varying capsule-detector distances (10-35 cm with increments of 5 cm) using a capsule of 3,242 MBq. For one DTC patient receiving I-131 therapy (5,710 MBq), a total body scan was performed 1.5 hours post-administration without micturition using five non-overlapping spot-views. The activity in each spot-view was assessed using the fitted curves and its sum was compared to the administered activity.

Results

Dead-time effects were observed for activities above 710 and 801 MBq for the anterior and posterior detector, respectively. Measured count rate peaks and Sorenson's dead-time constants were 27.2 kcps (at 1,104 MBq) and 0.91 µs for the anterior detector and 23.0 kcps (at 3,367 MBq) and 0.30 µs for the posterior detector. At capsule-detector distance 15 cm, count rates increased 1.9 and 0.2 kcps every 5 cm and a total increase of 75.6 and 3.1% at 35 cm was observed for the anterior and posterior detectors, respectively. In the DTC patient, the activity was 6,903 MBq (i.e. 122% of the real activity) using this initial naive approach.

Conclusion

Dead-time effects are observed for I-131 activities >710 MBq and can adequately be described using Sorenson's paralyzable model. However, the current model overestimates the whole body activity before any excretion of therapeutic I-131. For the anterior detector, an increase up to 75.6% is observed with increasing capsule-detector distance. Effects of activity outside the field-of-view on measured count rates and incorporation of attenuation correction within the model are currently under investigation.

Guideline on radiation exposure after radionuclide therapies: implementation in clinical practice in three different hospitals in The Netherlands. Aiming for more uniformity

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Sprekers tweede middagsessie: (vlnr) Hinke Siebinga, Larissa van Golen, Jouke Boer en Friso Schoffelen

Introduction

National guidelines on radionuclide therapies have long been based on a 2005 report (*Aanbevelingen 'Het werken met therapeutische doses radionucliden'*), mainly based on iodine-131 ([^{131}I]NaI) therapies. With the introduction of new therapies, particularly ^{177}Lu based therapies which have less environmental radiation burden, and with the implementation of the 2013 basic safety standards directive in European legislation, an update was necessary. Until an update was available dose rate levels for discharge after [^{177}Lu]Lu were used in the way they were used for [^{131}I]NaI (20 µSv/h at 1m). The national guidelines were revised and implemented by the FMS in 2021, in hope of achieving more uniformity between hospitals. We investigated this pursued uniformity and have provided insights into its implementation.

Methods

Three different hospitals participated: an academic centre (UMC Utrecht), a peripheral centre (St Antonius Nieuwegein) and a cancer centre (AVL Amsterdam). These centres provided their institutional guidelines for comparison. An online meeting was held to seek more information on differences and similarities and to discuss the rationales behind the institutional considerations made. Data collection was focused on the two most used radionuclide therapies: [^{177}Lu]Lu-PSMA and ^{131}I-NaI.

Results

Some general practical uniformities could easily be adjusted (e.g. the general measure to flush the toilet twice was unanimously considered not useful, and the restrictions on dish washing and intimacy after [^{131}I]NaI therapy could be adapted). A radiation alert pop-up or symbol in the patient file was considered very practical as were travel information letters. For [^{177}Lu]Lu-PSMA, all centres discharged patients after 6 hours without measuring dose rate levels and requested that patients adhere to instructions and restrictions for three days. Most differences were encountered for [^{131}I]NaI therapies, especially dose rate level at discharge (20 µSv/h versus 40 µSv/h at 1m versus no measurement at all), and the duration of admission, restrictions after discharge and durations of those restrictions.

Conclusion

The implementation of the FMS guideline in each hospital has been different, based on different assumptions and considerations. For [^{177}Lu]Lu-PSMA the implementation was more uniform than for [^{131}I]NaI. Radionuclide therapies are increasing and becoming more patient tailored.

A more uniform approach could be helpful to patients as this prevents confusion between patient information leaflets from different institutions and discourages 'healthcare shopping' between hospitals. We intend to initiate further discussion and pursue uniformity on a national level in the future. ♦

Vlak vóór de presentatie van de vrije inzendingen van de tweede middagsessie werd door prof. Jan Pruim de "Fellowschip in de spotlight" gebracht met het uitreiken van diploma's aan (vlnr) Suzanne van den Berg (laudatio door Emilia Owers, AVL, niet op foto), Michael Ananta (laudatio door Roelf Valkema, Erasmus MC) en Eidrees Ghariq (laudatio Richard Raghoo, LUMC)

Tijdens de algemene ledenvergadering werd het nieuwe logo van de NVNG gepresenteerd door nucleair geneeskundige Peter Kaldeway. Op de achtergrond zichtbaar vlnr bestuursleden Ruth Keijsers, Andor Glaudemans, Christian Guillaume en Lenka Pereira Arias - Bouda