Wetenschappelijke vergadering NVNG: "Nuclear Medicine: from bench to bedside"

7 oktober 2022

Ochtendprogramma

De wetenschappelijke najaarsbijeenkomst van de NVNG werd op 7 oktober 2022 in het Meander MC te Amersfoort gehouden met als thema "Nuclear Medicine: from Bench to bedside". Na de welkomstwoorden 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 dr. Hendrikus Boersma met een presentatie van onderzoeker dr. Frank Nijssen (associate professor at Radboudumc) over "Holmium therapy for liver metastases; from bench to bed side". Vervolgens behandelde Kristell Chatalic (Head of Development at Radboud Translational Medicine) het onderwerp "The production process of [^{18}F]PSMA". De laatste spreker van de eerste ochtendsessie was klinisch fysicus Anne Meijerink (St. Antonius Ziekenhuis Nieuwegein) met als presentatie "Implementatie van nieuwe richtlijn radionuclidentherapie met betrekking tot [^{131}I]NaI".

De tweede ochtendsessie, met drs. Tineke van den Weijer en dr. ir. Anke de Vries als voorzitters, startte met de presentatie "Inrichten van een afdeling nucleaire geneeskunde" door klinisch fysicus dr. ir. Roel Wierts (MUMC+). Vervolgens werd het onderwerp "Beheersbaarheid van afvalstromen van radionuclide therapieën" behandeld door Mattijs Maris (ZerEau). De sessie werd afgesloten door arts onderzoeker medische oncologie Jasper van Geel (UMCG) met de presentatie "Current advances in the application of [^{18}F]FES-PET in breast cancer".

Sprekers van de eerste ochtendsessie: Frank Nijssen, Kristell Chatalic en Anne Meijerink.

Presentaties van de tweede ochtendsessie: Roel Wierts (virtuele presentatie), Mattijs Maris (rechts) en Jasper van Geel (links onder).

In aansluiting op de uitreiking en presentatie van de winnaar van de Woldring Prijs (zie rubriek Woldring Prijs In de Kijker verder in deze editie) werden in de middag twee sessies gehouden met de presentatie van een viertal vrije inzendingen zoals hieronder samengevat.

Samenvattingen vrije inzendingen middagprogramma

Impact of [18F]FDG-PET/CT and laparoscopy in staging of locally advanced gastric cancer – a cost analysis in the prospective multicenter PLASTIC-study

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Background

In advanced gastric cancer patients scheduled for D2-gastrectomy with curative intent, [18F]FDG-PET/CT and staging laparoscopy (SL) may reduce futile gastrectomies by detecting non-curable (distant metastases and/or irresectable) disease. However, the cost impact of these modalities is unclear. Therefore, this study determined the cost impact of [18F]FDG-PET/CT and SL in staging advanced gastric cancer by reducing futile gastrectomies after detecting non-curable disease.

Methodology

In this cost analysis, four staging strategies were modeled in a decision tree: 1) [18F]FDG-PET/CT first, then SL, 2) SL only, 3) [18F]FDG-PET/CT only and 4) neither SL nor [18F]FDG-PET/CT. Costs were assessed using data from the prospective multicenter PLASTIC-study, which evaluated adding 18F]FDG-PET/CT and SL to staging with CT for advanced gastric cancer (cT3–4 and/or cN+) in eighteen Dutch hospitals. The Dutch Healthcare Authority provided unit costs of [18F]FDG-PET/CT and biopsy/cytology. SL unit costs were calculated bottom-up. Gastrectomy-associated costs were collected with hospital claim data until 30 days postoperatively, and until 90 days as additional scenario analysis with longer follow-up. A probabilistic sensitivity analysis with 1000 iterations was performed to assess uncertainty.

Results

[18F]FDG-PET/CT including biopsy/cytology cost €1104 per patient. Bottom-up calculations totaled €1531 per SL, and €1703 including biopsy/cytology during SL. Preventing a single D2-gastrectomy reduced costs by €21,437. Total costs if all patients would undergo gastrectomy were €18,584 per patient (strategy 4; without [18F]FDG-PET/CT and SL). Total costs per patient were €17,725 for strategy 1, €16,668 for strategy 2 and €19,305 for strategy 3 (table 1). Compared to strategy 4 (without [18F]FDG-PET/CT and SL), performing 'SL only' resulted in net cost savings of €1916 per patient. Adding [18F]FDG-PET/CT to SL (strategy 1) increased costs by €1057 per patient, but still resulted in net cost savings of €859 per patient due to good diagnostic performance by SL. The probabilistic sensitivity analysis (figure 1) resulted in net cost savings when comparing strategy 2 (SL only) versus strategy 1 ([18F]FDG-PET/CT first, then SL) in all 1000 iterations (100%); at minimum–maximum €201–€2108 per patient. In contrast, strategy 3 ([18F]FDG-PET/CT only) showed a net cost increase of €721 per patient. Results from the 90-day scenario analysis yielded equivalent conclusions with even greater cost differences.

Conclusions

For advanced gastric cancer, performing SL resulted in substantial cost savings by reducing futile gastrectomies. In contrast, routine use of [18F]FDG-PET/CT did not substantially reduce futile gastrectomies due to limited diagnostic performance and increased costs considerably, and is therefore not recommended.

Table 1. Decision tree to assess the cost impact of staging laparoscopy (SL) and [^{18}F]FDG-PET/CT by modelling four staging strategies: 1) [^{18}F]FDG-PET/CT first, then SL, 2) SL only, 3) [^{18}F]FDG-PET/CT only and 4) Neither SL nor [^{18}F]FDG-PET/CT.

Staging strategies		PROBABILITY	COSTS					30 days	90 days
			PET	Biopsy after PET	SL	Biopsy and/or cytology after SL	Gastrectomy*	Total costs	Total costs scenario analyses*
1 PET → Positive →	No gastrectomy	0,03	€ 1.040	€ 643	€ 0	€ 0	€ 0	€ 1.683	€ 1.683
1 PET → Negative → SL → Positive →	No gastrectomy	0,17	€ 1.040	€ 45	€ 1.537	€ 302	€ 0	€ 2.925	€ 2.925
1 PET → Negative → SL → Negative →	Gastrectomy	0,80	€ 1.040	€ 45	€ 1.537	€ 151	€ 18.791	€ 21.564	€ 25.182
	TOTAL PER PATIENT	1	**€ 1.040**	**€ 64**	**€ 1.489**	**€ 172**	**€ 14.961**	**€ 17.725**	**€ 20.605**
2 SL → Positive →	No gastrectomy	0,20	€ 0	€ 0	€ 1.537	€ 302	€ 0	€ 1.839	€ 1.839
2 SL → Negative →	Gastrectomy	0,80	€ 0	€ 0	€ 1.537	€ 151	€ 18.791	€ 20.479	€ 24.096
	TOTAL PER PATIENT	1	**€ 0**	**€ 0**	**€ 1.537**	**€ 182**	**€ 14.949**	**€ 16.668**	**€ 19.545**
3 PET → Positive →	No gastrectomy	0,03	€ 1.040	€ 643	€ 0	€ 0	€ 0	€ 1.683	€ 1.683
3 PET → Negative →	Gastrectomy	0,97	€ 1.040	€ 45	€ 0	€ 0	€ 18.791	€ 19.877	€ 23.494
	TOTAL PER PATIENT	1	**€ 1.040**	**€ 64**	**€ 0**	**€ 0**	**€ 18.201**	**€ 19.305**	**€ 22.809**
4 No PET and no SL →	ALL GASTRECTOMY	1	**€ 0**	**€ 0**	**€ 0**	**€ 0**	**€ 18.584**	**€ 18.584**	**€ 22.201**

SL = staging laparoscopy. PET = [^{18}F]FDG-PET/CT; ^{18}F-Flurodeoxyglucose positron emission tomography/computed tomography. The probability is based on the observed frequencies in the PLASTIC-cohort. For instance, the top row shows a probability of 0.03 because distant metastases were detected in 3% of the patients undergoing [^{18}F]FDG-PET/CT. In addition, as not all patients underwent for example biopsy/cytology, the costs for this procedure were averaged per patient.
Results are shown including 30 postoperative days of follow-up and also 90 postoperative days as scenario analysis.
Marked green indicates the staging strategy reduces costs relative to staging strategy 4 (in blue), whereas red indicates the strategy leads to higher costs.

All 1000 runs lie below €0, indicating that staging strategy 2 (staging laparoscopy only) is cost saving in total costs per patient compared to strategy 1 (first [^{18}F]FDG-PET/CT, then staging laparoscopy) in all iterations (100%), underlining the robustness of our conclusions. The cost benefit was at minimum €201 and at maximum €2108.

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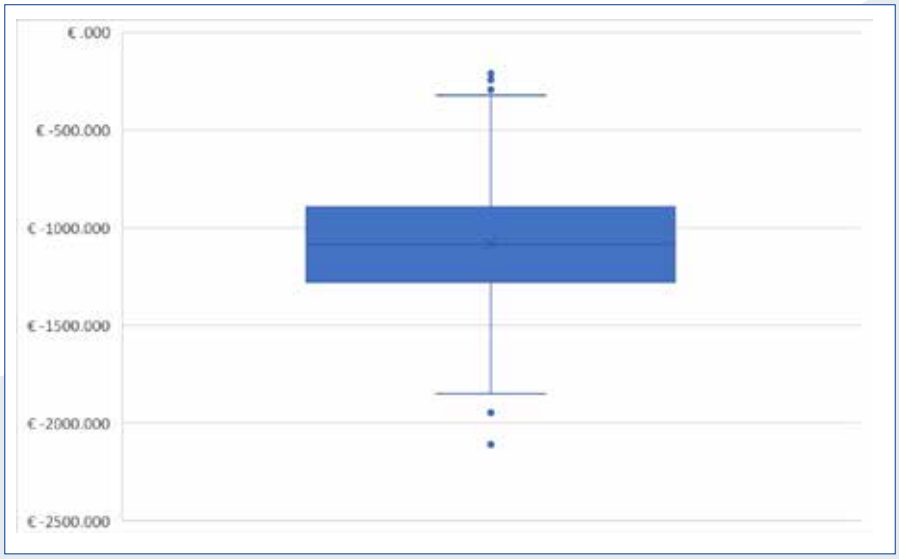

Figure 1. Boxplot displaying the probabilistic sensitivity analysis that compared the net cost savings of staging strategy 2 (staging laparoscopy only) versus strategy 1 (first [^{18}F]FDG-PET/CT, then staging laparoscopy) in 1000 iterations.

The Siemens Biograph Quadra PET/CT: performance characteristics and first clinical experiences

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Introduction

The new long axial field of view (LAFOV) Siemens Biograph Vision Quadra PET/CT system (Siemens Healthineers, Knoxville, USA) was installed at the University Medical Center Groningen, the Netherlands in August 2021. Objectives of this study are (1) to test the performance of the new Biograph Vision Quadra according to the NEMA NU 2-2018 standard with additional tests to assess the performance of the system throughout the LAFOV, and to test compliance to the European Association of Nuclear Medicine (EANM) Research Ltd (EARL) harmonization criteria, (2) to explore and demonstrate improvements in clinical image quality compared with state of the art systems.

Methods

Performance characteristics were assessed according to the NEMA NU 2-2018 standard with additional tests to assess the performance of the system throughout the LAFOV. Furthermore, EARL performance measurements were conducted to evaluate its ability to meet EARL standards. In addition, patients referred for an oncological PET scan were enrolled to undergo a dual imaging protocol (Biograph Vision and Biograph Vision Quadra) for a comparison in image quality. Patients received a single [^{18}F]FDG injected dose of 3 MBq/kg body weight and images were acquired at 60 and 90 min post injection in a balanced order of system use. Images were blindly reviewed by four nuclear medicine physicians and scored 1-5 on lesion demarcation, overall image quality, and image noise.

Results

The Biograph Vision Quadra PET/CT essentially consists of four interconnected Biograph Vision PET/CT systems resulting in an axial field of view (FOV) of 106 cm. The huge increase in sensitivity due to the longer axial FOV is the most prominent improvement in performance with respect to the Biograph Vision PET/CT. In addition, the system was able to comply with EARL SUV recovery criteria. Furthermore, 20 oncological patients were enrolled. Images acquired on the Biograph Vision Quadra were scored significantly higher on lesion demarcation according to Kendal's W test statistic ($Z = -2.69$; $P = 0.015$). Overall image quality and image noise were superior for the Quadra system using overall equal whole body scan times on both systems and were comparable between systems, when scan time on the Quadra system was already reduced by a factor ~7.

Conclusions

With regard to system performance, the Biograph Vision Quadra has an increased sensitivity resulting in improved image quality. Furthermore, the system is able to meet European harmonizing performance standards consistently throughout the LAFOV.

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Sprekers van de middagsessie: Cas de Jongh, Joyce van Sluis, Wyanne Noortman en Tineke van de Weijer

Development and external validation of a PET radiomic model for prognostication of head and neck cancer

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Introduction

External validation of radiomic studies is limited, although of utmost importance for the clinical implementation of radiomic models. The purpose is to build and externally validate a [^{18}F]FDG PET radiomic model to predict overall survival in patients with head and neck squamous cell carcinoma (HNSCC).

Methods

Two multicentre datasets of patients with operable HNSCC treated with neoadjuvant afatinib who underwent a baseline [^{18}F]FDG PET/CT scan were included (EORTC 90111 trial: n=23, Unicancer Predictor trial: n=20). Tumours were delineated using an adaptive threshold of 50% SUV_{peak}, wherefrom 48 radiomic features were extracted. Each cohort was used once as training and once as an external validation set for the prediction of overall survival. Features were scaled (centred around 0, standard deviation of 1) and redundancy filtering was performed (r=0.95). Supervised feature selection was performed using variable hunting with variable importance, which was repeated 1,000 times, selecting the top 2 features (i.e. 1 feature per 10 subjects) ranked in terms of occurrence. A Cox proportional hazards regression model using selected radiomic features and clinical characteristics (age and HPV status) was fitted on the training dataset and validated in the external validation set. Model performances are expressed by the concordance-index (C-index).

Results

Based on the EORTC dataset, a radiomic signature with the features sphericity (shape) and interquartile range (first order) was constructed and returned a C-index of 0.69. External validation in the Unicancer

Table 1. C-indices, features selected using variable hunting with variable importance.

C-indices ± SE	Training (EORTC)	Validation (Unicancer)	Selected features	Training (Unicancer)	Validation (EORTC)	Selected features
HPV + Age	0.53 ± 0.13	0.32 ± 0.10		0.66 ± 0.09	0.47 ± 0.14	
2 radiomic features	0.69 ± 0.12	0.70 ± 0.11	Sphericity (shape) + Interquartile range (first order)	0.73 ± 0.11	0.60 ± 0.14	Cluster prominence (grey level cooccurrence matrix) + Grey level non-uniformity normalized (grey level run length matrix)
2 radiomics features + HPV + age	0.70 ± 0.12	0.64 ± 0.11	Sphericity (shape) + Interquartile range (first order)	0.77 ± 0.09	0.57 ± 0.11	Cluster prominence (grey level cooccurrence matrix) + Grey level non-uniformity normalized (grey level run length matrix)

dataset resulted in a C-index of 0.70. Vice versa, the Unicancer radiomic signature using the features cluster prominence (grey level cooccurrence matrix) and grey level non-uniformity normalised (grey level run length matrix) resulted in a C-index of 0.73. External validation in the EORTC dataset resulted in a C-index of 0.60. Clinical characteristics alone were unable to predict overall survival with C-indexes for the EORTC and Unicancer models of 0.53 (Unicancer validation: 0.32) and 0.66 (EORTC validation: 0.47), respectively. The combination of radiomic features and clinical characteristics resulted in overfitted models with C-indexes for the EORTC and Unicancer model of 0.70 (Unicancer validation: 0.64) and 0.77 (EORTC validation: 0.57), respectively.

Conclusion

Although assessed in two small, but independent, cohorts, a [^{18}F]FDG-PET radiomic signature seems promising for the prediction of overall survival in HNSSC treated with neoadjuvant afatinib. The robustness and clinical applicability of this radiomic signature will be further investigated by increasing the Unicancer cohort by 20 patients.

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Limited value of a CT Thorax in staging with PET/MRI

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Introduction

PET is recommended for the staging of many types of cancer. Hybrid PET/MRI systems are being used more frequently. One of the pitfalls of PET/MRI imaging is the inferiority to detect lung nodules, when compared to CT, and therefore is often combined with a CT thorax. However, this leads to concomitant detection of additional non-specific lung nodules. The clinical relevance remains an issue of discussion. Therefore, the aim of this study was to assess the sensitivity of detection of malignant versus benign nodules with PET/MRI.

Methods

The study retrospectively assessed all oncological PET/MRI whole body scans combined with CT performed at our center between May 2014 and December 2020. In total 328 patients were included. The presence of any lung nodules, their size, and presence or absence of any identifiable tracer uptake was registered, and compared with histological biopsy or follow-up over 2 years. Nodule-by-nodule comparison was performed for both modalities.

Results

Only 6% of the patients presented with lung metastases. The sensitivity and specificity of PET/MRI for lung metastases was 85% and 100% respectively. The average size of the detected lung metastases was 11.8±9.3 mm and of the non-detected lung metastases 6.3 ±0.6 mm ($p>0.05$). The incidence of non-specific lung nodules was 30%. Here the sensitivity of PET/MRI was poor (23.0%). The average size of the lung nodules detected on PET/MRI was 7.0±4.1 mm and the missed nodules 3.6±1.1 mm ($p< 0.001$).

Conclusion

The detection of lung metastases is fairly good with PET/MRI, whereas the sensitivity of the PET/MRI for the detection of non-metastatic lung nodules was size dependent with a poor sensitivity. This may be an advantage, limiting unnecessary follow-up of these lung-nodules, with adequate detection of metastases. Hence, one might consider not to perform these CTs in parallel to the PET/MRI in future clinical practice.

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