A Comparison of ^{18}F -FDG-PET/MRI and ^{18}F -FDG-PET/CT in the Cancer Staging of Locoregional Lymph Nodes

DAVID SLOUKA¹, JIRI KRCAL¹, TOMAS KOSTLIVY¹, PETR HRABACKA¹,
ALENA SKALOVA², HYNEK MIRKA³, ONDREJ TOPOLCAN⁴ and RADEK KUCERA⁴

¹Department of Otorhinolaryngology, University Hospital in Pilsen,
Faculty of Medicine in Pilsen, Charles University, Pilsen, Czech Republic;

²Department of Pathology, University Hospital in Pilsen,
Faculty of Medicine in Pilsen, Charles University, Pilsen, Czech Republic;

³Department of Medical Imaging, University Hospital in Pilsen,
Faculty of Medicine in Pilsen, Charles University, Pilsen, Czech Republic

⁴Department of Immunochemistry Diagnostics, University Hospital in Pilsen,
Faculty of Medicine in Pilsen, Charles University, Pilsen, Czech Republic

Abstract. *Aim: The aim of the study was to evaluate the yields of 2-deoxy-2-[^{18}F]-fluoro-D-glucose positron-emission tomography/magnetic resonance imaging (^{18}F -FDG-PET/MRI) and ^{18}F -FDG-PET/computed tomography (CT) for the detection of metastatic involvement of locoregional neck nodes in patients with head and neck malignancy. Patients and Methods: A total of 90 patients (66 men and 24 women) met the inclusion criteria. Preoperative staging was performed: 53 examinations using PET/CT and 37 using PET/MRI. Results: For PET/MRI, the study demonstrated a sensitivity of 89%, specificity of 64%, positive predictive value of 85%, and negative predictive value of 70%; PET/CT had a sensitivity of 95%, specificity 47%, positive predictive value of 82%, and negative predictive value of 78%. Conclusion: Both methods have a high yield in N-clinical staging with statistically insignificant differences. We assume PET/MRI to be the first-choice method in organ-targeted examinations, for pediatric patients and repeat examinations. In cases of MRI contraindication, PET/CT can be used with no impact on the quality of care.*

Head and neck tumours occur with an incidence of 4-5 cases per 100,000 population and affect twice as many males as females (1). Over 90% of these are tumours of epithelial origin, the rest made up of tumours of mesenchymal and neuroectodermal origin (2). The diagnostic-treatment protocol includes two basic modalities: Surgical resection, and radiotherapy, sometimes in combination with chemotherapy. Current oncology utilizes imaging techniques for staging and therapy planning, as well as for evaluating tumour response to therapy. The first hybrid versions of positron-emission tomography (PET)/computed tomography (CT) were developed in 1998 (3) and a hybrid version of PET/magnetic resonance imaging (MRI) has been available since 2000 (4). The hybrid versions of PET/CT and PET/MRI utilize a combination of a given imaging technique with a positron emitter. The most commonly used radiopharmaceutical is 2-deoxy-2-[^{18}F]-fluoro-D-glucose (^{18}F -FDG).

The aim of this study was to systematically evaluate ^{18}F -FDG-PET/CT imaging versus ^{18}F -FDG-PET/MRI for the detection of locoregional metastatic involvement of neck nodes in epithelial tumours in patients with head and neck malignancy, and make a comparison of clinical (cN) and pathological (pN) classification.

Patients and Methods

Groups of patients. Between 2017 and 2019, a retrospective, monocentric study was conducted at the Otorhinolaryngology Clinic to evaluate the performance of hybrid imaging methods when used to detect the involvement of locoregional metastatic neck lymph nodes in epithelial malignancies of the head and neck. The inclusion criteria were: Malignant epithelial tumour in the head and neck area, preoperative PET/CT or PET/MR staging followed by radical or selective neck dissection, histological examination of tissue

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Correspondence to: Radek Kucera, Ph.D., Associate Professor, Department of Immunochemistry, University Hospital Pilsen, Edvarda Benese 13, 305 99 Pilsen, Czech Republic. E-mail: kucerar@fnplzen.cz

Key Words: Head and neck tumours, hybrid imaging, PET/MRI, PET/CT, cancer staging, lymph node.

Table I. Characteristics of the patient groups.

		PET/CT	PET/MRI
Number of patients	Overall	53/100	37/100
	Men	41/77	25/68
	Women	12/23	12/32
Age, years*	Median (range)	61 (40-82)	62 (40-79)
Location of primary tumour	Diagnosis		
Oral cavity	Spinocellular carcinoma	2	2
Oropharynx	Spinocellular carcinoma	20	15
Hypopharynx	Spinocellular carcinoma	2	2
Larynx	Spinocellular carcinoma	19	5
Glandula parotis	Mucoepidermoid carcinoma	0	2
	Myoepithelial carcinoma	1	1
	Salivary ductal carcinoma	1	2
	Low differentiated large cell diffuse carcinoma	1	0
	Acinocellular carcinoma	0	2
	Biphasic adenocarcinoma	0	1
Glandula submandibularis	Epithelial-myoepithelial carcinoma	1	1
Skin	Spinocellular carcinoma	2	2
Thyroid gland	Papillary carcinoma	1	1
Primary tumour unknown	Spinocellular carcinoma	3	1
Total		53	37

*Test of equivalence ($p=0.0078$).

resection with findings of a sufficient number of lymph nodes to determine pN classification, according to the eighth edition of the TNM classification (5). The exclusion criteria were: Non-fulfilment of inclusion criteria and incomplete data in medical documentation. The inclusion criteria were met by 90 patients who were divided into two age-equivalent groups (test of equivalence $p=0.0078$) according to the type of examination performed. The results achieved in both groups were then compared with each other. Informed consent was obtained from all the participants. The study was approved by The Ethical Committee of University Hospital in Pilsen on August 12th 2014.

Methods used. PET/CTs were performed using hybrid scanner Biograph 128 mCT UltraHD (Siemens Healthineers, Erlangen/Knoxville, Germany/TN, USA). The CT data were acquired using a low-dose protocol during a venous phase after injection of 80-100 ml of iodine contrast agent dosed according to body weight (Ultravist 370, Bayer Pharma, Berlin, Germany). Data were reconstructed at an image width of 0.75 mm and 5 mm. PET data were acquired after injection of ^{18}F -FDG (fluorodeoxyglucose, UJV, Rez u Prahy, Czech Republic) at a dose of 2.5 MBq/kg in 5-7 bed positions with acquisition times of 1.5 min. per position. Total examination time was 13 min.

PET/MRI was performed using an integrated 3T MRI and PET system Biograph mMR, (Siemens Healthineers, Erlangen, Germany) using an 18 channel Total Image Matrix coil system. The dose of 7.5 ml of 1-molar contrast agent (Gadovist; Bayer Pharma) was injected for the purpose of MRI. The targeted examination of the head and neck was performed first including axial T2 short tau inversion recovery (STIR), coronal and sagittal T2 turbo spin echo, axial diffusion-weighted imaging with b-value of 50 and 800 s/mm^2 including ADC value calculation and postcontrast dynamic T1

Table II. Results of the clinical (cN) and pathological (pN) classification.

Imaging technique	Status	cN, n	pN, n	Conformity, %
PET/CT	N0	9	15	81.13
	N1	22	16	
	N2a	0	2	
	N2b	16	15	
	N2c	6	4	
	N3	0	1	
Total	N	53	53	81.07
PET/MRI	N0	10	11	
	N1	6	11	
	N2a	0	0	
	N2b	13	9	
	N2c	6	2	
	N3	2	4	
Total	N	37	37	

PET: Positron-emission tomography; CT: computed tomography; MRI: magnetic resonance imaging.

volumetric interpolated breath-hold examination (VIBE) sequences. This was followed by a complete examination of the body (from head to thigh) using coronal T1 VIBE Dixon two-point and axial turbo inversion recovery magnitude T2 STIR sequences. PET data were acquired after injection of ^{18}F -FDG (UJV) at a dose of 2.5 MBq/kg in 5-7 bed positions with acquisition times of 4 min per position. Total examination time was 53 min. Lymph nodes with a maximum standardized uptake value of 3.0 or more were considered as positive.

Table III. Comparison of positron-emission tomography/computed tomography (PET/CT) with PET/magnetic resonance imaging (MRI).

Imaging technique	n	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Odds ratio	p-Value*
PET/CT	53	94.74	46.67	81.82	77.78	15.75	>0.99
PET/MRI	37	88.46	63.64	85.19	70.00	13.42	

*Fisher's test.

Statistical methods. Statistical analysis was performed using S.A.S. software (Statistical Analysis Software release 9.2; SAS Institute Inc., Cary, NC, USA). The following statistical parameters are presented: sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and odds ratio. The TOST test was used to demonstrate age equivalence between patient groups. Fisher's exact test was used to compare the difference in frequency of successful determination of node positivity/negativity. A *p*-value of less than 0.05 indicated statistical significance.

Results

A total of 90 patients (66 men and 24 women) met the inclusion criteria. Preoperative staging was performed: 53 examinations using PET/CT and 37 using PET/MRI. We have demonstrated a high efficacy of both hybrid methods in identification of positive lymph nodes, a base condition for subsequent N-clinical staging. The conformity of cN and pN classification was almost the same for both imaging techniques. The conformity of cN and pN was 81.13% for PET/CT and 81.08% for PET/MRI. PET/CT achieved better sensitivity than PET/MRI (94.74% vs. 88.46%), but worse specificity (46.67% vs. 63.64%). In both methods, the NPV, PPV and odds ratios of positivity were comparable. Namely, PET/CT achieved PPV of 81.82%, NPV of 77.78%, and odds ratio of 15.75, and PET/MRI achieved: PPV of 85.19%, NPV of 70.00%, and odds ratio of 13.42. Statistically, the performance of both methods was equal (*p*>0.99). The results are shown in Tables II and III.

Discussion

Determining the extent of the primary tumour as well as the locoregional metastatic process in the head and neck area is challenging, especially for the boundary between the tumour and the surrounding soft tissue. Differences between CT imaging yield and MRI are already known (6). The use of MRI reduces the dose of radiation to the patient compared to CT (7). A combination of CT or MRI with PET-derived metabolic parameters improves imaging accuracy and thus makes a more accurate determination of target tumour tissue volume for radiotherapy planning (8, 9). The differences between the benefits of PET/CT and PET/MR methods are currently being evaluated by comparison with the results of histological examinations. Kubiessa *et al.* (10), in a study involving 22

patients with head and neck cancer undergoing both hybrid modalities, reported results with statistically insignificant differences between PET/MRI and PET/CT in accordance with Beyer *et al.* (11), Antoch *et al.* (12), and Castelijns *et al.* (13). Kubiessa *et al.* emphasised the importance of correlating findings with anamnestic data. The absence of anamnestic data may be one of the factors reducing the specificity of hybrid methods; for example, when a PET examination precedes surgery, including mini-invasive surgery or radiochemotherapy. Results presented by Kubiessa *et al.* (10) are inconsistent with the conclusions of the study by Huang *et al.* (14) with a set of 17 patients in which a higher yield with PET/MRI *versus* PET/CT was demonstrated in patients with oropharyngeal carcinomas. By contrast, the work of Kubiessa *et al.* is in accordance with a study by Partovi *et al.* (15), whereby the authors confirmed comparable results of both methods for the detection of locoregional and distant metastases of head and neck tumours in a group of 14 patients. This reflected another study by Varoquaux *et al.* of 32 patients. Varoquaux *et al.* demonstrated the comparable capability of both methods regarding image quality and fusion, and the imaging number, size and anatomical localization of malignant lesions (16). Szyszko *et al.* (17) and Grosse *et al.* (18) reported the main benefits of PET/MRI as being the reduction of the radiation dose and improvement in the anatomical details in the soft-tissue area due to MRI properties. Samolyk *et al.* assessed the utility of PET/MRI in preoperative staging in a group of 21 patients with head and neck tumours, reporting sensitivity at 55%, specificity of 98%, PPV of 71%, and NPV of 97% in the detection of metastatic neck lymph nodes (19). In accordance with a number of authors, our study confirmed the comparable results of PET/CT and PET/MRI for locoregional neck lymph node detection. In concordance with Szyszko *et al.* (17) and Grosse *et al.* (18), we see the great advantage of PET/MRI in its superior display of anatomical details in the soft-tissue area. In paediatric patients and patients requiring repeated imaging, PET/MRI offers the major benefit of lower radiation exposure. On the other hand, PET/CT is less time consuming, which may be an essential factor in examining patients with other health restrictions that do not allow them to remain in the supine position for an extended period of time.

In conclusion, we have demonstrated a high efficacy for both hybrid imaging techniques in N-clinical staging, with

statistically insignificant differences between PET/MRI and PET/CT. In accordance with the above-mentioned findings of recent studies, we assume PET/MRI to be the method of choice for organ-targeted examinations of the brain, head and neck, pelvic organs and liver as well as in examinations of paediatric patients and patients requiring repeated examinations using the hybrid imaging techniques where it is especially desirable to reduce the radiation burden of the patient. In cases of MRI contraindication, PET/CT can be used without any impact on the quality of care. A larger study incorporating a larger number of participants is required to evaluate the exact differences between PET/CT and PET/MRI imaging techniques.

Conflicts of Interest

All Authors declare no conflicts of interest.

Authors' Contributions

Conceptualization: D.S. and J.K.; methodology: D.S., A.S. and H.M.; investigation: T.K., P.H., and J.K.; writing – original draft preparation: D.S. and R.K.; writing – review and editing: R.K., O.T.

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