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High energy probe for detecting lymph node metastases with ^{18}F-FDG in patients with head and neck cancer

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Hochenergie-Sonde zur Detektion von Lymphknotenmetastasen mit ^{18}F-FDG bei Patienten mit Kopf-Hals-Tumoren

Keywords
High energy gamma probe, ^{18}F-FDG, PET, head and neck cancer

Summary
Aim of this study was to validate a newly developed high energy probe (positron emission probe, PEP) optimised for localising PET tracers in vivo. **Patients and methods:** Physical investigations included determination of full width at half maximum (FWHM) values at a distance of 1 cm and angular resolution using different point sources. Values obtained with the new probe were compared to those of a conventional gamma probe (CGP). Additionally, PET studies were performed in 36 patients (6 women, 30 men) with proven head and neck cancer and suspected lymph node metastases (Axis, Marconi/Philips) after administering 250–320 MBq ^{18}F-FDG. Subsequent to PET investigations ^{18}F-FDG uptake in cervical regions was measured using the PEP. PEP investigations were carried out bilaterally in 5 lymph node (LN) levels (Robbins' classification of the neck). Results of probe studies were correlated with visual and semiquantitative PET evaluations, US and histological findings. **Results:** FWHM of the new probe was 7 mm (CGP 22 mm) at 662 keV (^{137}Cs) and angular resolution resulted in 8° (CGP 60°). In 29 out of 36 patients LN metastases were suspected due to ultrasound investigations. After neck dissection, histology confirmed LN metastases in 21 patients. Sensitivity (sens.) of US amounted to 95% and specificity to 40%. In 18/21 patients LN metastases were detected by PET (sens. 86%). PET scans failed to diagnose the LN status correctly in 6/36 patients (accuracy 83%). Employing the PEP probe in 20/21 patients LN metastases were identified (sens. 95%), and LN status was determined accurately in 29/36 patients (accuracy 81%). Tumour/background ratios of PEP measurement and results of semiquantitative PET analyses were comparable. **Conclusions:** PEP measurement is a promising method for preoperative planning of the extent of neck dissection in patients with head and neck cancer and further for radioguided localising PET tracer accumulation during surgery.

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Schlüsselwörter
Hochenergiesonde, ^{18}F-FDG, PET, Kopf-Hals-Tumore

Zusammenfassung
Ziel dieser Arbeit war es, eine neu entwickelte Hochenergie-Sonde (Positronenemissionssonde, PES) die für die Lokalisation von PET-Tracern optimiert wurde, zu validieren. **Patienten und Methoden:** Die physikalischen Untersuchungen umfassten die Bestimmung der Ortsauflösung (FWHM) sowie der Winkelauflösung. Die ermittelten Werte wurde mit denen einer konventionellen Gammasonde (KGS) verglichen. Zusätzlich wurde bei 36 Patienten mit gesicherten Kopf-Hals-Tumoren und fraglicher Lymphknoten(LK)-Metastasierung eine PET-Untersuchung (Axis, Marconi/Philips) mit 250–350 MBq ^{18}F-FDG durchgeführt. Die Ermittlung des ^{18}F-FDG-Uptake in den zervikalen Regionen mit der PES erfolgte im Anschluss an die PET-Untersuchungen, bilateral in jeweils 5 LK-Level (Robbins' Klassifikation des Halses). Die Resultate der Sondenmessungen wurden mit den visuellen und semiquantitativen Auswertungen der PET-Untersuchungen sowie mit den Ergebnissen der Ultraschalluntersuchung (US) und der Histologie verglichen. **Ergebnisse:** Die FWHM der neuen Sonde betrug 7 mm (KGS 22 mm) für die 662 keV (^{137}Cs) Quelle, die Winkelauflösung betrug 8° (KGS 60°). Bei 29 der 36 Patienten wurden aufgrund der US LK-Metastasen vermutet. Nach der Neck-Dissektion wurde dies bei 21 Patienten bestätigt. Die Sensitivität (Sens.) der US betrug 95%, die Spezifität 40%. Die PET konnte bei 18/21 die LK-Metastasen nachweisen (Sens. 86%). Bei 6/36 Patienten wurde mittels PET der LK-Status nicht korrekt ermittelt (Richtigkeit 83%). Durch Einsatz der PES konnten bei 20/21 Patienten die LK-Metastasen detektiert werden (Sens. 95%), der LK-Status wurde bei 29/36 Patienten korrekt beurteilt (Richtigkeit 81%). Die Tumor/Background-Verhältnisse der PES-Messungen und der semiquantitativen PET-Auswertung waren vergleichbar. **Schlussfolgerungen:** Die PES-Messung ist eine vielversprechende Methode für die präoperativen Planung der Neck-Dissektion bei Patienten mit Kopf-Hals-Tumoren und zukünftig für die radioaktivitätsgeführte intraoperative Lokalisation von PET-Tracern.

One of the most important nuclear medicine procedures in oncology is ^{18}F fluorodeoxyglucose positron emission tomography (^{18}F-FDG-PET) (17, 19, 21). Furthermore, radioguided surgery plays an important role combining diagnostic investigation and surgical intervention (2, 15, 24). In conventional gamma probes lead collimators discriminate target radioactivity from background. Lead collimators in a hand-held supply, however, can be primarily used only for low energy emitting isotopes. For high-energy emitters, such as PET tracers, a different technical principle is crucial since efficient shielding would be too heavy and bulky and thus could hardly be used during surgery. So far, physical properties of PET tracers hinder successful combination of PET and radioguided surgery. Similar to the development of gamma cameras to detect 511 keV quanta using PET collimators, first investigations using collimated conventional gamma probes to determine ^{18}F-FDG in vivo were reported (8, 9, 20). The usefulness of this approach has been demonstrated in first phantom studies and later in a few patients with colorectal cancer and melanoma. Other approaches are focussed on direct measurement of β^+ (3, 31).

The aim of our work was to develop and test a new gamma-sensitive probe with electronic collimation capable to detect 511 keV positron annihilation quanta. The first prototype was investigated using phantom studies. Additionally, the positron emission probe (PEP) was clinically validated by preoperative transcutane measurement of ^{18}F-FDG accumulation in lymph node metastases of patients with head and neck cancer. Results were compared to those of ultra-

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sound (US), PET, and – as gold standard – the histological findings.

Patients, material, methods

Physical data

We aimed at developing a new probe to detect high-energy gamma quanta and, as well, positron emission annihilation quanta (PEP). PEP works with electronic collimation using multiple CsI-crystals to measure tracer uptake and background activity and does not require lead or tungsten shielding (10). While target activity is preferably detected by the central crystal, background and scatter quanta are mainly detected by the concentric tapered detector ring (Fig. 2). Counts obtained from the central detectors and the crystals of the outer ring are compared to receive spatial information. Electronic collimation allocates target and background activity by special algorithms. Aperture angle for the central detector can be varied by algorithms. Therefore, electronic focusing can be individually optimised for different applications. For optimised results, detectors are calibrated daily using a point source located 1 cm from the central detector.

Physical characteristics of PEP were determined in comparison to a conventional gamma probe (Navigator (14 mm), USSC/Tyco). Measurements were carried out according to the methods described by Wengenmair et al. (27–29). Spatial resolution (lateral sensitivity distribution) was determined measuring different point sources at a distance of 1 cm orthogonally. Count rates were recorded in 1 mm steps along a line perpendicular to the central axis of the probe head. Full width at half maximum (FWHM) values represent a measure for the minimal distance at which two point sources can be detected separately, and, thus for spatial resolution. Therefore, FWHM values of both probes were analysed using point sources with different g-ray energies (^{57}Co (122 keV, 86%); ^{133}Ba (356 keV, 62%); ^{22}Na (511 keV, 64% +1275 keV, 36%) and ^{137}Cs (662 keV, 85%)) to cover the energy range of standard tracers, i.e. ^{99m}Tc, ^{131}I and PET isotopes. Additionally, full width at tenth maximum (FWTM) values of the PEP were determined. The angular resolution was evaluated at two defined distances to the central detector of 3 cm (nearfield) and of 30 cm, respectively, moving the probes in steps of 2°. Probe sensitivity was determined directly in front of the central detector using either $^{99m}TcO_4^-$ or ^{18}F-FDG. Lateral electronic "shielding" was determined by scanning the probe with ^{99m}Tc or ^{18}F hot spots.

Patient investigations

A total of 36 consecutive patients (6 women, 30 men), aged 34–84 years (m = 57) with biopsy-proven head and neck cancer and suspected lymph node metastases were scheduled for surgery including tumour ablation and lymph node dissection (localisations of the primary see Table 2). The indication for neck dissection was based on the dimension and localisations of the primary tumour and/or suspicious enlarged lymph nodes detected by ultrasound, CT or MRI. Depending on these criteria, neck dissection was carried out ipsilaterally in 20 and bilaterally in 16 cases.

Sonography

Ultrasound investigations (Siemens, 7.5 MHz linear transducer head) were carried out by an experienced investigator bilaterally in 5 lymph node levels according to the Robbins' classification of the neck (22).

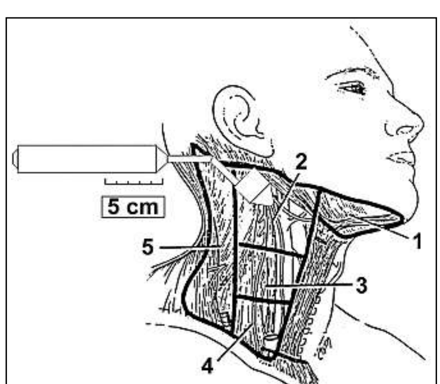

Fig. 1 PEP measurement in five anatomically defined levels (1–5) of the neck according to Robbins' classification (22)

Criteria for malignant lymph node involvement were size, shape, status of echogenic hilus, echogenicity, micronodular appearance and intranodal necrosis.

PET

Within a 2-week period prior to surgery each patient underwent ^{18}F-FDG-PET. Whole body PET scans were performed under routine conditions after application of 250–350 MBq ^{18}F-FDG. Acquisition was started 1 h p. i. using a dual head coincidence gamma camera (Philips AXIS) in 2-D mode (128^2 matrix, 180° rotation, 6° steps, 70 s/step). Emission data were rebinned and reconstructed using an iterative algorithm (OSEM) with implemented attenuation correction. Target/background ratios were calculated from count rates obtained by generating ROIs over the tumour and contralateral regions.

Probe investigations

PEP measurements in patients were performed bilaterally in 5 lymph node levels (Robbins' classification, 22) 2–3 h p. i. in most patients subsequent to the PET scan (Fig. 1). Lymph node levels were slowly scanned using the PEP, and maximum count rate was documented after integration over 15 s, irrespective of the results of PET or US. Investigation time was 10–15 min for each patient. A cut-off criterion for lymph node involvement was derived from maximum background count rates in lymph node levels without pathological findings. ^{18}F-FDG uptake in the primary tumour was measured (if accessible without administering sedatives) and compared to count rates over shoulder and brain.

Data analysis

Since PET scans could not be evaluated level-dependent, suspect findings in the concordant regions were rated as true positive. Sonography and PEP measurements of each level were directly compared with histology. Non-dissected neck sides were used to define the criteria of lymph node involvement for PEP measurements. Sensitivity, specificity, positive and negative predictive values as well as accuracy were calculated from these data.

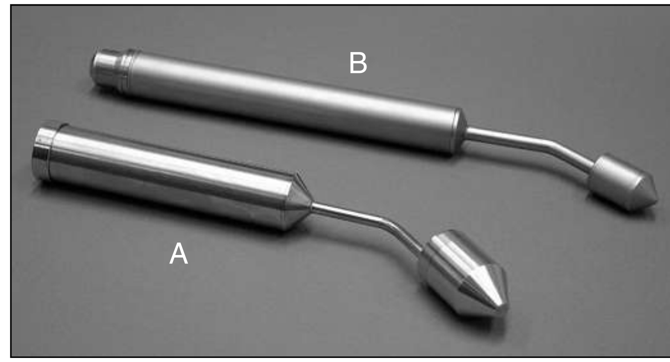

Fig. 2
Picture of the first prototype positron emission probe (A) used in this paper and the actual version (B). Weight of investigated probe was 350 g.

Results

Physical data

Before measurements on patients were carried out, basic physical properties such as spatial and angular resolution of the new preliminary prototype were determined and compared to those of a conventional gamma probe (CGP). In contrast to the CGP, the spatial resolution of the PEP was almost independent of the source energy as shown in Table 1. Thus, two ^{137}Cs point sources positioned at a distance of 1 cm could be distinguished with the PEP. FWTM values of PEP were lower than the FWHM values of CGP. FWHM values of CGP increased from 18 mm (^{57}Co) up to 27 mm (^{22}Na). Depending on energy, angular resolution of the PEP was 6°-8° (GP 60°-75°). Probe sensitivity increased with source energy from 5 cps/kBq for ^{99m}Tc to 18 cps/kBq for ^{18}F. Due to the special construction without collimators, leak sensitivity of PEP was time-dependent. It reached a maximum of 9 cps/MBq 1 s after exposure with a ^{18}F hot spot, decreasing to >1 cps/MBq after 3 s at the surface of detector's cylinder, 1.5 cm from its tip.

Patient investigation

Table 2 shows a summary of the results. Histology revealed lymph node metastases in 21/36 patients. In 12 patients only one affected level could be found. In 9 patients extensive metastatic spread to more than one level (in 6 patients ipsilateral, in 3 patients bilateral) was confirmed by histology. In 15/36 patients histology showed no lymphatic metastatic spread.

Ultrasonography

In 20/21 patients affected lymph nodes were detected by ultrasound. However, 9/15 patients without lymphatic metastatic spread exhibited suspect findings in at least one cervical level. In this subgroup, false positive cases due to inflammatory processes had to be considered. The resulting ultrasound sensitivity was 95%, while specificity amounted only to 40%. Accuracy was 72%.

PET

In 5/36 patients primary tumours had already been removed. In 30 of the remaining 31 patients, increased glucose metabolism in primary tumours was visualized by PET. In one patient suffering from adenoid cystic carcinoma of the tongue the primary could not be detected. As to lymphatic metastatic spread, PET resulted true positive in 18/21 patients amounting to a sensitivity of 86%. Semiquantitative analyses resulted in target/background ratios of 1.3 : 1 to 6.2 : 1. Findings were true negative in 12/15 patients (specificity 80%). False negative results were obtained in 3 patients. Micro-anatomy of lymph nodes revealed large cystoid and necrotic areas in one of those patients. The other two patients presented a total of 3 predominantly small metastases with a max. diameter of 0.7, 0.8, and 1.7 cm, respectively. False positive findings were caused by unspecific lymphadenitis (2 patients) and sarcoidosis (1 patient). No differences in visual or semiquantitative estimation of data were found. In 3 patients distant metastases or secondary carcinomas were suspected. In those, histology confirmed one distant metastasis in the lung (Fig. 3) and metastatic breast cancer in another patient (Fig. 4). The third patient suffered from sarcoidosis (false positive finding).

Probe measurement

Count rates varied individually (range: 100–350 cps over sholder, 270–1400 cps at cervical region and 700–1650 cps over brain). Cut-off criterion for lymph node involvement was a count rate exceeding 15% of the respective rate in contralateral and/or adjacent levels. Based on this criterion, PEP investigation resulted true positive in 20/21 individuals, and a sensitivity of 95%, respectively. Tumour/background ratios of PEP measurements and results of semiquantitative PET analyses were comparable. Analyses resulted in target/background ratios of 1.2 : 1 to 4.8 : 1. In 9/15 patients probe measurement demonstrated no evi-

Tab. 1 Head-to-head comparison of spatial resolution
(FWHM: full width at half maximum values; FWTM: full width at tenth maximum)

point source		^{57}Co	^{133}Ba	^{22}Na	^{137}Cs
gamma-ray energy intensity		122 keV, 86%	356 keV, 62%	511 keV, 64%, 1275 keV, 36%	662 keV, 85%
positron emission probe	FWHM	7 mm	9 mm	9 mm	7 mm
	FWTM	12 mm	12 mm	20 mm	12 mm
convential gamma probe (FWHM)		18 mm	19 mm	27 mm	22 mm

dence of cervical lymph node involvement (specificity 60 %). In analogy to PET, false positive results were caused by unspecific lymphadenitis (n = 2) and sarcoidosis (n = 1). In 3 patients extensive ^{18}F-FDG uptake in the primary tumour superimposed the signal in the adjacent cervical level. In 4 cases with false negative PET results (3 patients with lymph node metastases and one patient with adenoid cystic carcinoma of the tongue) PEP was able to detect the foci. Histology revealed cystic degeneration of metastases in 2 of these cases and two-dimensional growth of metastasis in one patient.

Tab. 2 Clinical data and lymph node involvement due to histology and diagnostics prior to neck dissection (f: female; m: male; ipsi: ipsilateral; bilat: bilateral; l: left; r: right; L: level; –: no suspect findings; +: lymph node involvement suspected; met: distant metastasis or secondary carcinoma)

patient-no.	age (years) / sex	location of primary	neck dissection	histology	sonography	PET	PEP measurement
1	47/m	tonsil	ipsi (r)	+ / L2r	-	+	+
2	53/m	larynx	bilat	+/L2,3l	+	+	+
3	67/m	tongue	ipsi (l)	-	-	-	-
4	61/w	hypopharynx	ipsi (l)	+/L2l	+	+/met	+
5	65/w	tonsil	ipsi (l)	-	-	-	-
6	59/m	tonsil	ipsi (l)	+/L2l	+	+	+
7	56/m	larynx	ipsi (r)	+ L2/4r	+	+	+
8	58/m	tongue	bilat	+L2l/L1r	+	+	+
9	55/m	larynx	bilat	-	+	+	-
10	51/m	larynx	bilat	+L2/r	+	-	+
11	69/m	tonsil	ipsi (r)	+L2/r	+	+	+
12	84/m	lip	bilat	-	-	+/met	+
13	44/m	tonsil	ipsi (l)	+L2/l	+	-	+
14	47/m	uvula	bilat	+L2/l	+	+	+
15	49/m	oropharynx	ipsi (r)	-	-	-	-
16	44/w	hypopharynx	ipsi (r)	-	+	-	+
17	62/m	larynx	bilat	+/L1–3r	+	+	+
18	48/m	tonsil	ipsi (l)	-	+	+	+
19	53/m	larynx	ipsi (l)	+/L2l	+	+	+
20	62/m	tonsil	ipsi (l)	+/L2l	+	+	+
21	48/m	larynx	bilat	+/L2,3l	+	+	+
22	70/m	larynx	bilat	-	-	-	+
23	34/w	tongue	bilat	-	+	-	-
24	59/w	oropharynx	ipsi (l)	-	+	-/met	-
25	57/w	tongue	bilat	+L1–4r,2–3l	+	+	+
26	59/m	larynx	bilat	-	+	-	-
27	65/m	larynx	ipsi (r)	-	+	-	+
28	53/m	larynx	bilat	+/L2,3l	+	+	+
29	57/m	uvula	ipsi (l)	-	-	-	-
30	56/m	larynx	bilat	+/L3l	+	+	+
31	60/m	tonsil	ipsi (r)	+/L3,5l	+	-	-
32	64/m	parotis	ipsi (r)	+/L2r	+	+	+
33	48/m	oropharynx	bilat	-	+	-	-
34	54/m	tonsil	ipsi (l)	-	+	-	+
35	47/m	tonsil	ipsi (r)	+/L1r	+	+	+
36	66/m	larynx	bilat	+/L3–4r, L4l	+	+	+

Comparison of methods

Sonography and PEP investigation were both found to exhibit a high sensitivity of 95% in detecting cervical lymph node involvement. PET investigations had the highest specificity (80%) of the investigated methods (PEP 60%, US 40%). Using different cut off criteria for PEP measurements, specificity could be further increased but sensitivity would be inversely reduced. As shown in Table 3, accuracies of PET and PEP measurement were nearly identical (83, 81%) and thus nearly 10 % higher than accuracy of ultrasonography (72%).

Discussion

In nuclear medicine and especially in PET techniques, the development of new methods for clinical applications was at most preceded by a wide diversification of technical solutions. In the field of PET, beside the use of scanners multiple variants like gamma cameras with collimators (4, 26), coincidence gamma cameras (33), different detector types and detector materials have been investigated.

While radioguided surgery became more important during the last years, the development of new probes including imaging probes is still in progress (14, 20). Conventional gamma probes have been optimised for the application of low-energy isotopes using various probe types and collimators (27–29). Lead collimators have also been proposed to detect positron annihilation quanta (8, 9, 32). However, due to their large size and high weight they can hardly be used intra-operatively under routine conditions. Thus, the in vivo detection of positron annihilation quanta was an unsolved problem up to now.

As a consequence, different other solutions are under investigation. Axially orientated dual detector systems using either phoswich detectors composed of a plastic scintillator and a BGO crystal or an aligned photo diode and a CsI crystal are able to distinguish between β^+ decays and gamma quanta from scatter or annihilation (3, 31). The additional use of a collimator was described to obtain spatial information at primary intraoperative orientation (3). Hickernell et al. described another dual detector probe to detect low energy gamma quanta. This probe contained two concentric collimated detectors (13, 30). In analogy to electronic collimation in gamma cameras and PET-scanners, an approach for electronic collimation for hand-held devices based on single photon measurement was developed in our project (patent pending, 10). The electronic background reduction by a concentric tapered ring of crystals is definitely effective, not only in the high energy range. Head-to-head comparison of CGP and PEP resulted in significantly higher spatial resolution of PEP (PEP 7 mm, CGP 20 mm) in the high energy range as was primarily expected, since CGP was not optimised for measurements in the high energy range. Additionally, spatial resolution of PEP was superior in the low energy range (PEP 7 mm, CGP 14 mm). Data obtained with the CGP were in the range as previously reported (28, 29). However, spatial resolution of the used CGP was rather low compared to other devices as reported in that overview. Even in the high energy range FWHM values of our preliminary prototype were superior to those of the conventional gamma probe in the low energy range. Additionally, angular resolution was found to be improved. These results indicated the usability of the new principle for investigations in vivo, too. Since the probe described is a preliminary prototype restricted to one default mode, this article is not focused on the complete physical characterisation of this device. Up to now, the third version of PEP is under approval as a medical device. In this new probe lager crystals are implemented to achieve a higher sensitivity and shorter integration times. Supplementary data will be presented at maturity phase of the PEP project.

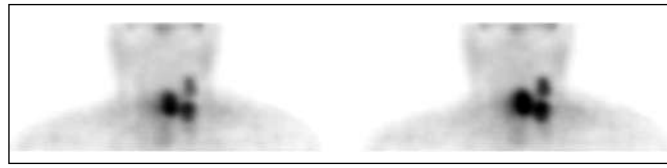

Fig. 3
Coronal slices of ^{18}F-FDG-PET of a 48 year-old man (patient no. 21, Tab. 2) with larynx carcinoma and lymph node metastases

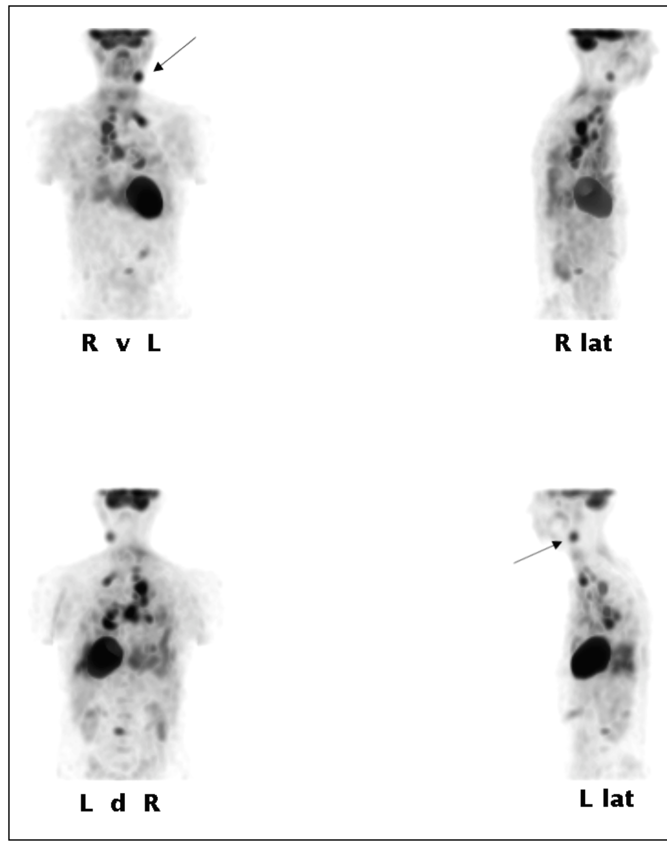

Fig. 4
^{18}F-FDG-PET images (3D, maximum pixel raytrace) of a 61 year-old woman (patient no. 4, Tab. 2) with lymph node metastasis of recurrent hypopharynx carcinoma (arrow), distant metastases and metastases of breast cancer.

As physical data are only one important criterion, we evaluated the potential of the new principle under clinical conditions. The biodistribution of ^{18}F-FDG was a powerful counterpart in this respect.

Tab. 3 Comparison of diagnostic modalities for detection of lymph node involvement; patient-based results (n = 36)

%	US	PET	PEP
true positive	95	86	95
true negative	40	80	60
positive predictive value	69	85	77
negative predictive value	86	80	90
accuracy	72	83	81

Patient investigations

Patient investigations were performed in individuals with head and neck cancer (HNC), because ^{18}F-FDG uptake is significantly enhanced in most entities of these tumours and their metastases (7, 23). In addition, the absence of cervical lymph node metastases at the time of diagnosis is one crucial determinant of survival (6). Thus, FDG-based diagnostic allows correct staging as a basis for optimal patient management. However, as already demonstrated in a patient with recurrence of thyroid carcinoma (18) the new probe might be helpful during surgery, especially in cases of scar tissue in the operative field.

All diagnostic approaches in HNC patients, as investigated in the present study, should be aimed at the highest achievable sensitivity to avoid insufficient treatment of cases diagnosed as false negative. This is also accepted for ultrasound (11). Despite of this, sensitivity of ultrasound to localise lymph node involvement was reported to reach only 70% (1, 12, 25). Higher sensitivities between 70 and 89% are associated with a rather low specificity in the range of 70%. Limited specificity is generally tolerated to avoid false negative results which could reduce patients' life expectancy. Ultrasound evaluations in our study were carried out with an even higher sensitivity (95%), accepting a further decreased specificity (40%) in this clinical setting. Use of the PEP resulted in a comparably high sensitivity in diagnosing lymph node involvement (20 out of 21 cases, sensitivity 95%). Only in one patient with histologically proven metastases of a tonsil carcinoma with diameters of 8 mm and 17 mm, respectively, results obtained with PEP turned out to be false negative. Considering the rather large sizes of the metastases (5), this may be explained by an only slightly increased glucose metabolism, since PET was false negative, too. Interestingly, PEP was able to detect ^{18}F-FDG-uptake in 3 patients with lymph node metastases, which were PET negative. One reason for the superiority of PEP in this application might be that the method does not require complex 3-D reconstruction algorithms. The method is simply based on planar measurement at a close distance. In addition, the good physical properties of the probe which could be documented promote the superiority in the in vivo applications. Direct measurement of glucose metabolism via PEP turned out to be superior to PET even in cases with cystic degeneration of metastases (2 cases) or primary (1 case). When weighing these results, a small bias caused by the larger delay from tracer application to measurement has to be taken into account.

In summary, PEP measurements had a higher sensitivity in accessible regions than PET. However, one limitation of PEP is that it can be applied to superficial localisations, only. Preoperative PEP measurements can therefore only be supplementary to PET investigation, especially when considering the need to detect distant metastases or when additional primary tumours are suspected to be present. Specificity of PEP was found to be considerably higher (60%) than ultrasound (40%) at a comparable level of sensitivity, but it was lower than in PET (80%). However, due to the immanent fact that not only malignant but also inflammatory processes in adjacent structures cause increased glucose uptake (16), a high specificity (e. g. in the range of 90%) would be unrealistic.

Conclusions

In this study, a newly developed high energy probe, being capable to detect positron annihilation quanta, too, was introduced. We were able to demonstrate preliminary physical properties, a first view at clinical usefulness and to estimate the future potential of the device. The investigated first prototype matched the capability of established routine methods in detecting cervical lymph node metastases, and resulted superior in some respects. This prototype was intended to prove the principle of electronic collimation, and does not provide the complete functionality of standard probes. Therefore, an improved probe e.g. with shorter and variable integration time is being developed. Additional features like a threshold function are planned to optimise localisation of radiopharmaceuticals like ^{18}F-FDG with widespread accumulation in the patients' body. In our view, PEP has the potential to become a further valuable option to anchor nuclear medicine procedures in interventional patient care.

References

1. Adams S, Baum RP, Stuckensen T et al. Prospective comparison of ^{18}F-FDG PET with conventional imaging modalities (CT, MRI, US) in lymph node staging of head and neck cancer. Eur J Nucl Med 1998; 25: 1255–60.
2. Alex JC, Sasaki CT, Krag DN et al. Sentinel lymph node radiolocalization in head and neck squamous cell carcinoma. Laryngoscope 2000; 110: 198–203.
3. Bärwolff H, Göbel T, Hug O et al. Vorrichtung und Verfahren zur Bestimmung der Position eines Positronenemitters in einem Material. Patent no. DE 10112297 A1.
4. Botsch H, Beringer K, Petersen J et al. Single-photon emission tomography studies of rubidium-81 in the detection of ischaemic heart disease, using a stress-reinjection protocol. Eur J Nucl Med 1994; 21: 407–14.
5. Brink I, Klenzner T, Krause T et al. Lymph node staging in extracranial head and neck cancer with FDG PET--appropriate uptake period and size-dependence of the results. Nuklearmedizin 2002; 41: 108–13.
6. Brown AE, Langdon JD. Management of oral cancer. Ann R Coll Surg Engl 1995; 77: 404–8.
7. Buell U, Wieres FJ, Schneider W et al. ^{18}FDG-PET in 733 consecutive patients with or without side-by-side CT evaluation: analysis of 921 lesions. Nuklearmedizin 2004; 43: 210–6.
8. Essner R, Daghighian F, Giuliano AE. Advances in FDG PET probes in surgical oncology. Cancer J 2002; 8: 100–8.
9. Essner R, Hsueh EC, Haigh PI et al. Application of an ^{18}F fluorodeoxyglucose-sensitive probe for the intraoperative detection of malignancy. J Surg Res 2001; 96: 120–6.
10. Gerl J, Kojouharov I, Ameil F et al. High energy gamma probe with position sensing capability. Patent no. EP 04011020.7.
11. Goerres GW, Haenggeli CA, Allaoua M et al. Direct comparison of ^{18}F-FDG PET and ultrasound in the follow-up of patients with squamous cell cancer of the head and neck. Nuklearmedizin 2000; 39: 246–50.
12. Gritzmann N, Czembirek H, Hajek P et al. Sonography in cervical lymph node metastases. Radiologe 1987; 27: 118–22.
13. Hickernell TS, Barber HB, Barrett HH et al. Dual-detector probe for surgical tumor staging. J Nucl Med 1988; 29: 1101–6.
14. Hoffman E-J, Tornai M-P, Janecek M et al. Intraoperative probes and imaging probes. Eur J Nucl Med 1999; 26: 913–35.
15. Hyde NC, Prvulovich E, Newman L et al. New approach to pretreatment assessment of the N0 neck in oral squamous cell carcinoma: the role of sentinel node biopsy and positron emission tomography. Oral Oncol 2003; 39: 350–60.
16. Kubota R, Yamada S, Kubota K et al. Intratumoral distribution of fluorine-18-fluorodeoxyglucose in vivo: high accumulation in macrophages and granulation tissues studied by microautoradiography. J Nucl Med 1992; 33: 1972–80.
17. Landoni C, Gianolli L, Lucignani G et al. Comparison of dual-head coincidence PET versus ring PET in tumor patients. J Nucl Med 1999; 40: 1617–22.
18. Meller B, Sahlmann C, Horstmann O et al. Conventional gamma probe and high energy probe for radioguided dissection of metastases in a patient with recurrent thyroid carcinoma with ^{99m}Tc-MIBI and ^{18}F-FDG. Nuklearmedizin 2005; 44: N23–5.
19. Minn H, Lapela M, Klemi PJ et al. Prediction of survival with fluorine-18-fluoro-deoxyglucose and PET in head and neck cancer. J Nucl Med 1997; 38: 1907–11.
20. Pitre S, Menard L, Ricard M et al. A hand-held im-

aging probe for radio-guided surgery: physical performance and preliminary clinical experience. Eur J Nucl Med Mol Imaging 2003 ;30: 339–43.
21. Reske SN, Bares R, Büll U et al. Clinical value of positron emission tomography (PET) in oncologic questions: results of an interdisciplinary consensus conference. Nuklearmedizin 1996; 35: 42–52.
22. Robbins KT. Classification of neck dissection: current concepts and future considerations. Otolaryngol Clin North Am 1998; 31: 639–55.
23. Schmidt M, Schmalenbach M, Jungehulsing M et al. ^{18}F-FDG PET for detecting recurrent head and neck cancer, local lymph node involvement and distant metastases. Comparison of qualitative visual and semiquantitative analysis. Nuklearmedizin 2004; 43: 91–101.
24. Shoaib T, Soutar DS, MacDonald DG et al. The accuracy of head and neck carcinoma sentinel lymph node biopsy in the clinically N0 neck. Cancer 2001; 91: 2077–83.
25. van den Brekel MW, Stel HV et al. Cervical lymph node metastasis: assessment of radiologic criteria. Radiology 1990; 177: 379–84.
26. Van Lingen A, Huijgens PC, Visser FC et al. Performance characteristics of a 511-keV collimator for imaging positron emitters with a standard gamma-camera. Eur J Nucl Med 1992; 19: 315–21.
27. Wengenmair H, Kopp J, Sciuk J. Quality criteria of gamma probes: requirements and future developments. In: Schauer A, Becker W, Reiser MF et al. (eds). The Sentinel Lymph Node Concept. Berlin, Heidelberg: Springer 2004: 113–25.
28. Wengenmair H, Kopp J, Vogt H et al. Qualitätskriterien für Meßsonden zur intraoperativen Lokalisation ^{99m}Tc-markierter Lymphknoten. Z Med Phys 1999; 9: 122–8.
29. Wengenmair H, Kopp J, Vogt H et al. Qualitätskriterien und Vergleich von Gammasonden zur Sentinel-Lymphonodektomie. Der Nuklearmediziner 1999; 4: 271–80.
30. Woolfenden JM, Barber HB. Radiation detector probes for tumor localization using tumor-seeking radioactive tracers. AJR Am J Roentgenol 1989; 153: 35–9.
31. Yamamoto S, Matsumoto K, Sakamoto S et al. An intra-operative positron probe with background rejection capability for FDG-guided surgery. Ann Nucl Med 2005; 19: 23–8.
32. Zervos EE, Desai DC, De Palatis LR et al. ^{18}F-labeled fluorodeoxyglucose positron emission tomography-guided surgery for recurrent colorectal cancer: a feasibility study. J Surg Res 2001; 97: 9–13.
33. Zimny M, Wildberger JE, Cremerius U et al. Combined image interpretation of computed tomography and hybrid PET in head and neck cancer. Nuklearmedizin 2002; 41: 14–21.

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