18F-FDG-PET and MRI in patients with malignancies of the liver and pancreas. Accuracy of retrospective multimodality image registration by using the CT-component of PET/CT

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Accuracy of retrospective multimodality image registration by using the CT-component of PET/CT

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Keywords
Magnetic resonance imaging, positron emission tomography, PET/MR; image fusion, multimodality imaging, PET/CT

Summary
Purpose: To evaluate the accuracy of retrospective rigid image registration and fusion between F-18 fluorodeoxyglucose positron emission tomography (FDG-PET) and magnetic resonance imaging (MRI) of the upper abdomen. Patients, material, methods: Image fusion of PET and MRI was performed in 30 patients with suspected malignancy of the liver or pancreas. Using a commercially available image fusion tool capable of rigid manual point-based registration, PET-Images were retrospectively registered and fused by matching eight homologous points in the 3D spoiled gradient echo (GRE) MRI sequences acquired in portal venous phase and in the CT-component of PET/CT. Two separate observers (R1, R2) assessed accuracy of image registration by determining the distances in the x-, y- and z-axis as well as the absolute distance between anatomical landmarks which differed from the landmarks chosen for registration. Quality of fusion was graded using a three point grading scale (1 poorly fused; 2 satisfactory fused; 3 correct fused) and compared to hybrid PET/CT fusion. Results: Mean time of registration per patient was less than 2 minutes. Objective registration assessment showed errors between 2.4–6.3 mm in x-axis: mean 3.6 mm (R1); 4.6 mm (R2), 2.3–9.3 mm in y-axis (mean 5.1 mm; 5.5 mm) and 3.3–12.0 mm in z-axis (mean 5.9 mm; 5.9 mm). The mean error in absolute distance between points was 6.0–16.8 mm (mean 9.9 mm; 10.6 mm). In visual assessment, most fusions were graded to be satisfactory or correctly fused: R1, R2: grade 3, 11/30 (36.7%); 22/30 (73.3%); grade 2, 13/30 (43.3%), 8/30 (26.7%); grade 1, 6/30 (20%), 0/30 (0%). Fusions were mostly comparable to hybrid PET/CT fusions. All of the fusions were defined as diagnostically relevant by both observers. Conclusion: Retrospective rigid image fusion of FDG-PET and MRI of the upper abdomen using the CT-component of PET/CT for registration is feasible without adaptation in image acquisition protocols and shows sub-centimeter registration errors in most cases.

Schlüsselwörter
Magnetresonanztomographie, Positronenemissionsuntomographie, PET/MR, Bildfusion, PET/CT

Zusammenfassung
Ziel: Evaluation der Genauigkeit der retrospektiven rigiden Bildregistrierung und -fusion von ¹⁸F-Fluordeoxyglukose Positronenemissions-

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Computed tomography (CT) and magnetic resonance imaging (MRI) are currently considered as the backbone for detection and characterization of malignancies of the liver and pancreas. Both imaging modalities provide accurate information with regard to anatomical location and size of the lesions and are helpful (1) in prediction of lesion malignancy, staging and restaging; assessment of therapeutic response and prediction of lesion malignancy, staging and restaging; assessment of therapeutic response and preoperative planning.

Over the last decade, positron emission tomography using 18F-fluorodeoxyglucose (FDG-PET) and in particular PET/CT have shown to be valuable in staging of primary and secondary tumours of the liver and pancreas, and especially in the assessment of distant metastases and tumour response (2–9). With the availability of PET/CT, fusion of detailed morphology obtained from CT with functional information from PET into a single image using an integrated device has shown to provide new possibilities for diagnosis and therapy. Furthermore, the fusion of PET and CT images into a single image has been shown to be more accurate in tumour staging than PET or CT alone and even more than PET and CT images viewed side by side (10–13).

Based on its inherent soft-tissue contrast, MRI provides several advantages over CT in evaluating malignancies of the liver as well as of the pancreas. In addition, MRI offers the possibility to use tissue-specific contrast agents which may be beneficial for detection and characterization of liver neoplasms. It has been shown that MRI in combination with standard gadolinium based extracellular contrast agents and/or with liver specific contrast agents is superior to contrast enhanced CT for imaging various primary liver neoplasms and metastases (14–17). Although MRI in combination with liver specific contrast agents provides some functional information, it may be desirable to combine MRI with functional PET data, especially regarding therapy response assessment. Whereas PET/CT hybrid systems for body applications are already commercially available, hybrid PET/MRI scanners are still under development and as yet not commercially available (18, 19).

Therefore, the only way to currently perform registration of FDG PET and MRI data is by software based image registration and fusion of the separately acquired data sets. Reports on PET/MRI image fusion in the upper abdomen are rare and to the best of our knowledge there are only two studies addressing feasibility of imaging fusion between PET and MRI in this body region (20, 21). Whereas Lemke et al. (20) reported on feasibility and impact of imaging fusion between FDG PET and MRI in various organ systems including the upper abdomen, Ruf et al. (21) reported on the impact of FDG-PET/MRI fusion in the detection of pancreatic cancer. However, neither study quantitatively investigated the accuracy of image registration between PET and MRI.

The purpose of this study was to evaluate the accuracy of interactive, retrospective, point-based, rigid image registration and fusion between standard clinical PET and MRI datasets in patients with suspected or confirmed malignancies of the liver or pancreas.

Patients, material, methods

This study was approved by the institutional ethical review board. Informed patient consent was waived for this retrospective evaluation.

Patients

Fulfilling the following inclusion criteria 30 patients were included:

- contrast enhanced MRI imaging of the upper abdomen within 30 days of the PET/CT scan,
- suspected or confirmed malignancy of liver or pancreas,
- no surgery, chemo- or radiotherapy between acquisition of PET/CT and MRI.

The study group consisted of 15 men and 15 women with an age range between 28 and 82 years (mean 61.2 ± 14). The mean time between MRI and PET/CT was 11.3 ± 9.2 days, ranging from 0 to 30 days. MRI and PET/CT scanning were ordered primarily for staging and preoperative planning purposes. The 30 patients included 4 patients with carcinoma of the pancreas, 9 with primary liver tumours (5 cholangiocellular carcinomas, 2 haemangioendothelioma, 2 focal nodular hyperplasia), 15 patients with liver metastasis (origin of metastases: 5 gastrointestinal carcinoma, 2 oropharyngeal carcinoma, 2 melanoma, 2 lung cancer, 1 neuroendocrine tumour of the pancreas, 1 cholangiocellular carcinoma, 1 hepatocellular carcinoma, 1 breast cancer). In two patients, liver metastases were clinically suspected but were ruled out by imaging follow-up.

**Fig. 1** The field of view (FOV) was chosen according to the patient’s individual body size (a). In axial direction (b), the FOV was chosen to include the area from the liver dome down to the lower poles of the kidneys.
Data acquisition

PET/CT- and MRI-images were acquired separately without taking special prerequisites with regard to the planned image fusion.

PET/CT

All data were acquired on either of two combined PET/CT in-line systems (Discovery ST or Discovery RX; GE Healthcare). These dedicated systems integrate a PET scanner with a multislice helical CT scanner (64 slice VCT / 16 slice Lightspeed 16; GE Healthcare) and permit the acquisition of coregistered CT and PET images in a single session.

The patients fasted for at least 4 h before scanning, which started approximately 60 min after the injection of 370–400 MBq of $^{18}$F-FDG and the glucose level (range, 80–120 mg/dl; 4.4–6.7 mmol/l) was measured. Patients with elevated glucose levels were rescheduled, prepared with insulin, and scanned when they had normal glucose levels. Patients were examined in the supine position. Initially, a low dose CT scan was acquired starting from the level of the head using the following parameters: 40 mAs, 140 kV, 0.5 s/tube rotation, a slice thickness of 4.25 mm, a scan length of 867 mm, and a data acquisition time of 22.5 s. The CT scan was acquired during breath holding in the normal expiratory position. The low dose CT data were used for attenuation correction, lesion localization and CT lesion characterization. The images were reconstructed using a standard iterative algorithm. Immediately after the CT acquisition, a PET emission scan was acquired with a time of 90 s to 3 min per cradle position with a 1-slice overlap in 2-D or full 3-D reconstruction mode (matrix 128 × 128). The 8–9 cradle positions starting from the head and continuing to the knees resulted in an acquisition time of approximately 12–27 min. PET/CT was performed according to the recently published procedure guideline for tumour imaging with $^{18}$F-FDG PET/CT (22).

MRI

All MR imaging was performed on a 1.5 T MR scanner (Signa EchoSpeed EXCITE® HD or HDx, GE Healthcare, Waukesha, Wisconsin, USA) using an 8-channel anteroposterior phased-array surface coil which was placed around the individual and covered the entire liver. The field of view (FOV) was chosen according to the patient’s individual body size. In transverse direction, the FOV was chosen to include the area from the liver dome down to the lower poles of the kidneys (Fig. 1). Imaging protocol included an unenhanced two-dimensional T2-weighted breathhold single shot fast spin echo sequence (SSFSE)
in coronal plane, a transverse T2-weighted fat suppressed respiratory-triggered fast spin echo sequence (FSE) and a transverse T1-weighted breathhold fast spoiled gradient-recalled echo sequence (FSPGR) in-phase and out-of-phase. In patients with suspected cholangiocarcinoma or patients with visible bile duct dilation in the other unenhanced sequences MR cholangiography (MRC) using a three-dimensional 3D fast spin recovery fast spin echo sequence (FRFSE) was performed.

Following acquisition of the unenhanced sequences contrast-enhanced dynamic MR imaging was performed following intravenous administration of a standard dose (0.1 mmol/kg bodyweight) of either gadobutrol (Gadovist, Bayer-Schering AG) or gadolinium-EOB DTPA (Primovist, Bayer-Schering AG). For dynamic contrast enhanced imaging, a parallel three-dimensional (3D) spoiled gradient echo (GRE) sequence (LAVA (Liver Acquisition with Volume Acceleration), version 12.0M4; GE Healthcare) was performed during a breath hold in transverse plane with a nominal measured voxel dimension of 1.5 × 1.5 × 4.0 mm³ in acquisition along the frequency-encoding times phase-encoding times section-encoding direction, and an interpolated reconstructed voxel dimension of 0.75 × 0.75 × 2.0 mm³. Dynamic contrast-enhanced parallel GRE imaging was performed in the arterial (20 s after injection), portal venous (60–80 s after injection) and hepatic phase (240 s after injection). Comparable to previous studies (20,21), the portal venous phase was chosen for image registration with the CT-component of PET/CT because this sequence best demonstrates anatomical detail.

**Image registration**

MRI and PET/CT data were transferred in DICOM format to a workstation running

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**Table 1** Overview of PET / MRI registration errors separated by observer and anatomical landmark

<table>
<thead>
<tr>
<th>anatomical landmark</th>
<th>measurement direction</th>
<th>F1/F2 observer 1</th>
<th>F1/F2 observer 2</th>
</tr>
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<tr>
<td></td>
<td>mean / min / max</td>
<td>mean / min / max SD</td>
<td>max / SD</td>
</tr>
<tr>
<td>AL</td>
<td>x-axis</td>
<td>4.65 / 2.49 / 12.00</td>
<td>3.84 / 2.47 / 17.93</td>
</tr>
<tr>
<td></td>
<td>y-axis</td>
<td>8.27 / 6.81 / 28.80</td>
<td>6.25 / 6.24 / 7.44</td>
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<tr>
<td></td>
<td>z-axis</td>
<td>6.60 / 6.63 / 20.00</td>
<td>5.35 / 5.74 / 4.68</td>
</tr>
<tr>
<td></td>
<td>dist</td>
<td>13.13 / 11.19 / 31.08</td>
<td>9.16 / 16.53 / 21.3 / 3.95</td>
</tr>
<tr>
<td>LL</td>
<td>x-axis</td>
<td>4.39 / 3.96 / 10.80</td>
<td>2.88 / 3.08 / 4.03</td>
</tr>
<tr>
<td></td>
<td>y-axis</td>
<td>7.53 / 7.21 / 17.70</td>
<td>4.77 / 2.30 / 3.75</td>
</tr>
<tr>
<td></td>
<td>z-axis</td>
<td>5.74 / 7.77 / 20.05</td>
<td>5.11 / 6.27 / 4.01</td>
</tr>
<tr>
<td></td>
<td>dist</td>
<td>10.07 / 8.34 / 23.84</td>
<td>5.62 / 6.35 / 7.90</td>
</tr>
<tr>
<td>TC</td>
<td>x-axis</td>
<td>4.05 / 2.32 / 8.20</td>
<td>2.36 / 2.03 / 4.10</td>
</tr>
<tr>
<td></td>
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<td>7.46 / 6.72 / 25.30</td>
<td>5.80 / 5.92 / 9.27</td>
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<tr>
<td></td>
<td>z-axis</td>
<td>5.65 / 12.02 / 20.00</td>
<td>5.35 / 8.98 / 11.51</td>
</tr>
<tr>
<td></td>
<td>dist</td>
<td>12.04 / 14.89 / 32.90</td>
<td>6.09 / 9.55 / 16.76</td>
</tr>
<tr>
<td>PV</td>
<td>x-axis</td>
<td>3.37 / 2.58 / 15.20</td>
<td>3.38 / 2.32 / 3.18</td>
</tr>
<tr>
<td></td>
<td>y-axis</td>
<td>5.00 / 4.19 / 13.00</td>
<td>3.95 / 3.18 / 3.89</td>
</tr>
<tr>
<td></td>
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<td>5.52 / 6.11 / 16.00</td>
<td>3.77 / 6.05 / 3.69</td>
</tr>
<tr>
<td></td>
<td>dist</td>
<td>9.42 / 8.89 / 19.98</td>
<td>7.26 / 8.75 / 7.26</td>
</tr>
<tr>
<td>RA</td>
<td>x-axis</td>
<td>3.63 / 2.36 / 13.90</td>
<td>2.82 / 2.76 / 3.41</td>
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<tr>
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<td>2.65 / 2.40 / 3.60</td>
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<td>3.73 / 5.11 / 12.05</td>
<td>3.11 / 3.45 / 4.05</td>
</tr>
<tr>
<td></td>
<td>dist</td>
<td>7.94 / 7.23 / 16.03</td>
<td>3.18 / 3.55 / 7.28</td>
</tr>
<tr>
<td>LE</td>
<td>x-axis</td>
<td>6.31 / 3.43 / 12.60</td>
<td>3.90 / 2.46 / 5.86</td>
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<td>2.67 / 2.29 / 3.96</td>
</tr>
<tr>
<td></td>
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<td>6.14 / 3.25 / 20.00</td>
<td>6.78 / 2.62 / 4.84</td>
</tr>
<tr>
<td></td>
<td>dist</td>
<td>11.25 / 5.97 / 26.14</td>
<td>6.10 / 3.09 / 9.65</td>
</tr>
</tbody>
</table>

all measurements in mm; AL: anterior liver border; LL: lateral liver border; TC: celiac trunk; PV: left portal vein; RA: right adrenal gland; LE: liver lesion; dist: Euclidean distance; F1: registration performed by physician 1; F2: registration performed by physician 2
Mac OS X 10.5 (Apple Computer, Inc., Cupertino, CA, USA). For the registration of MRI and PET images we used OsiriX (OsiriX Medical Image software, version 3.3, OsiriX Foundation, Geneva, Switzerland), available under a free software license. OsiriX implements manual landmark-based rigid registration of two image data sets, computing the best transform (three translational and three rotational degrees of freedom) to fit corresponding, user-selected anatomical landmarks in a least squares sense. Registration between the transaxial PET images and the portal venous phase of the 3D GRE sequence was performed by two physicians resulting in two separate fused datasets (F1 and F2). Eight anatomical landmarks (the most cranial and most caudal located points of the liver, spleen and both kidneys) were marked in the portal venous phase of contrast enhanced MRI and in the low dose, non-contrast enhanced CT-component of PET/CT (Fig. 2). These landmarks were then copied from the CT-component to the PET-component of PET/CT which was already registered with the CT-component by hardware registration in the hybrid PET/CT-system. Due to the fact, that the PET- and the CT-component were already anatomically registered by the hybrid PET/CT-System, the landmarks could be copied one-to-one from the CT-component to the PET-component. Finally, the PET data set was registered to the MRI data set by using the landmark-based algorithm, resampled onto a common grid and fused with the MRI data set.

Data analysis and validation

Two observers independently determined the x-, y- and z-coordinates of a second set of corresponding anatomical landmarks on the registered CT component of PET/CT as well as on the 3D GRE sequence of MRI in each patient. The following landmarks were used: the most anteriorly (ventrally) located point of the liver surface (called anterior liver border, AL); the point on the surface of the liver which was located most laterally at the level of the left portal vein (PV); the location of the celiac trunk at the level of the aortic origin (TC); the location of the right adrenal (RA); and if present, the center of the smallest clearly detectable liver lesion (LE). At the level of the right adrenal gland, the intersection of the lateral and medial limb was chosen as the reference point. If a liver lesion was present, the center of the smallest lesion detectable on both studies was chosen as reference point. All anatomical landmarks used for data validation are shown in Figure 3.

Coordinates of all these points were noted and the absolute distance between corresponding points in X-, Y- and Z-axis were determined separately. Additionally,
the Euclidean distance (D) between those chosen points in the two data sets was calculated using the following equation, where p and q represent the coordinates of points P and Q:

\[ D_{pq} = \sqrt{(p_x - q_x)^2 + (p_y - q_y)^2 + (p_z - q_z)^2} \]

In addition, each observer separately assessed the quality of image fusion on a 3-point scale (1 poorly fused; 2 satisfactory fused; 3 correctly fused). Finally, each PET/MR fusion was compared to integrated PET/CT fusion on a 3-point scale for image quality with regard to diagnostic purposes (1 worse than PET/CT and not diagnostic; 2 worse than PET/CT but diagnostic; 3 equal to PET/CT). Observers were asked to concentrate on the accuracy of the alignment in the region of the liver, of the kidneys and where available in the region of liver lesions.

Bland-Altman analysis for inter-observer agreement was used to assess differences in measurements with the mean of observations (23, 24). The differences in measurements were plotted against their means. The mean of the differences between values provided a measure of the bias or systematic error between measurements of both observers. The SD of the differences represented the variability between the techniques, with bias of plus or minus 1.96 (SD) denoting the limits of agreement. Inter-observer agreement was assessed for each of the fused datasets (F1 and F2) separately.

### Results

Mean time of image registration and fusion was less than 2 minutes (mean, 2.0 ± 0.4 minutes; range, 1.4–2.9 minutes for F1, and 1.4 ± 0.3 minutes; range, 0.9–2.2 minutes for F2) including identifying the landmarks.

The anterior liver border was not accessible for measurement in 7/60 (11.7%), the lateral liver border in 4/60 (6.7%), the celiac trunk in 14/60 (23.3%) and the right adrenal gland in 2/60 (3.3%) of patients. The origin of the left portal vein was visualized and accessible for measurement in all cases.

When averaging the distances as measured by R1 and R2, the percentage of lesions misregistered by less than 10 mm were 95.1% and 91.0% in the x-axis, 86.7% and 86.1% in y-axis, 85.7% and 86.1% in z-axis and 60.8% and 60.3% in absolute distance. For R1 and R2, 83.2% and 82.9% of errors in absolute distance, respectively were smaller than 15 mm.

Objective registration assessment showed mean errors of all registered anatomical points of 2.4–6.3 mm in x-axis (mean R1 3.6 mm; R2 4.6 mm), 2.3–9.3 mm in y-axis (mean 5.1 mm; 5.5 mm) and 3.3–12.0 mm in z-axis (mean 5.9 mm; 5.9 mm). The mean error in 3-dimensional distances between points was 6.0–16.8 mm (mean 9.9 mm; 10.6 mm) (Table 1).

In visual assessment, most fusions were graded to be satisfactory or correctly fused: R1, R2: grade 3, 11/30 (36.7%), 22/30 (73.3%); grade 2, 13/30 (43.3%), 8/30 (26.7%); grade 1, 6/30 (20%), 0/30 (0%). Fusions were mostly comparable to hybrid PET/CT fusions (Fig. 4). Fusions, which were rated to be poorly fused also showed a higher degree of registration error (Fig. 5). All of the registrations were defined as “diagnostic” by both observers (Table 2).

Even if an image fusion showed an objectively larger misregistration, observers were able to mentally assign the focus of FDG-uptake to the corresponding liver lesion on CT and therefore judging the study as diagnostic.

Bland-Altman analysis revealed small limits of agreement for measurement of registration errors for F1 (i.e. AL 1.2±7.0 mm; LL 0.7 mm).

### Tab. 2 Results of visual assessment

<table>
<thead>
<tr>
<th>fusion quality</th>
<th>observer 1</th>
<th>observer 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
<td>SD</td>
</tr>
<tr>
<td>in general*</td>
<td>2.17</td>
<td>0.75</td>
</tr>
<tr>
<td>compared to hybrid PET/CT**</td>
<td>2.40</td>
<td>0.50</td>
</tr>
</tbody>
</table>

*1: poor; 2: satisfactory; 3: correct; **1: worse, not diagnostic; 2: worse, diagnostic; 3: equal to hybrid PET/CT; SD: standard deviation

### Fig. 6

Patient (age: 62 years) with liver metastasis of colon carcinoma: ceMRI (a) and PET (b) after registration. PET/MR-fusion (c) with misregistration of SUV-uptake (arrowhead) and morphologic correlate of liver metastasis (arrow). Fusion is worse than hybrid PET/CT-fusion (d) but still diagnostic (grade 2). In addition benign liver cysts are noted in liver segments II and IVa.
2.1±5.1 mm; PV 2.2±3.2 mm; TC –2.9±6.7 mm; RA 0.6±3.6 mm; LE 0.3±3.6 mm) as well as for F2 (i.e. AL –5.3±7.5 mm; LL –2.6±6.7 mm; PV –0.6±3.6 mm; TC –1.4±8.9 mm; RA –2.1±4.5 mm; LE –2.2±3.9 mm). Also, mean differences between the measurements of both observers were minimal (i.e. AL –2.5±7.9 mm; LL –0.4±6.4 mm; PV 0.9±3.6 mm; TC –2.2±7.6 mm; RA –0.4±4.1 mm; LE –0.8±3.9 mm) (Fig. 7).

Discussion

This study demonstrates the feasibility to obtain reasonably accurate anatomical fusion images of PET and MRI of the upper abdomen by using the low dose CT-component of hybrid PET/CT and ceMRI even without the use of prerequisites such as immobilization in a vacuum mattress (25) or the application of external markers (26).

Whereas accurate hardware-based registration of FDG-PET and CT data is currently standard of care for all anatomical body regions, there is less experience with registration of FDG-PET and MRI data sets in body imaging. While the accuracy and clinical value of PET/MRI-registration in the brain has been extensively validated (27–34), reports on the image fusion of FDG-PET and MRI data in the abdomen are rare. With regard to malignancies of the liver and pancreas, functional information derived from PET may provide useful information about the presence and suspected malignancy of a lesion as well as assessment of therapy. Presence or absence of FDG-activity may improve the level of confidence in determining the malignancy of a liver lesion of unclear origin and thereby help for staging and restaging of the tumour.

The validation of PET/MRI registration techniques for clinical applications remains particularly challenging, because each image type and organ requires separate evaluation of achievable accuracy (7). Whereas the brain is encased by a rigid shell which does not change shape or size between different imaging studies, the organs in the upper abdominal region are subject to breathing-dependent movement and deformation (35).

Using data from 30 patients, we studied the anatomical accuracy of rigid PET/MRI registration provided by an open-source software tool. For this purpose, we measured the absolute distances of well-defined and reproducible anatomical landmarks in MRI and the CT component of hybrid PET/CT.

Recently, Lemke et al. published data of 59 patients in which software-based image fusion of PET and unenhanced T1- and T2 weighted and contrast media enhanced MRI (20) was performed in various anatomical regions including the abdomen. As in our study, mainly contrast enhanced T1-weighted sequences were used for image fusion. The authors concluded that
retrospective PET/MRI fusion is feasible although evaluation did not include a quantitative validation of registration error. Ruf et al. (21) evaluated the impact of FDG-PET and MRI image fusion on the detection of pancreatic cancer. The authors concluded that PET/MRI fusion improved the anatomical assignment and interpretation of FDG foci. Also in this study, contrast enhanced 3D GRE images obtained in the portal venous phase were used for PET/MR image fusion. In accordance to these two studies, our study demonstrated that registration of FDG PET and MRI data sets is feasible without special adaptations in data acquisitions. As an adjunct to these aforementioned studies, our study assessed quantitatively the accuracy of image fusion in the upper abdomen using an open-source software tool. The results of our study are comparable to the results obtained for retrospective image registration of FDG-PET and CT data sets (36). Inagaki et al. (37) reported on the accuracy of retrospective PET/CT registration of the upper abdomen without external markers in seven patients. In the study of Inagaki et al. (37), the mean error was 3.4 mm in X-, 4.7 mm in Y- and 9.2 mm in Z-axis. Similar results were also reported by Nakamoto et al. and Rizzo et al. (38, 39).

**Limitations**

Our study has several limitations. First, by using the CT-component of hybrid PET/CT and therefore using an indirect registration technique, we propagate a potential misregistration emerging from the hybrid PET/CT registration into the retrospective registration process. However, misregistration errors of hybrid PET/CT are generally small (40) and it has been shown that indirect PET/MR registration through the CT-part of hybrid PET/CT is subjectively more accurate than direct retrospective PET/MR registration (26). In the mentioned study, automatic voxel similarity based coregistration and external fiducial markers were used. A second limitation is that the mean time interval between PET/CT and ceMRI was 11.3 days which may have influenced the misregistration error. On the other hand, the fact that retrospective fusion using the described method shows accurate registration even though registration of PET and MR was not planned at the time of data acquisition and therefore no special prerequisites in image acquisition protocols had been made can also be looked at as a strength of the described fusion method.

A third limitation of our study is a possible imprecision with regard to the manual localization of the anatomical landmarks chosen. Accuracy of image registration may be improved by using non-rigid registration but is more computationally expensive and questionably adds clinical value (41).

Finally, we only used the portal venous phase for image registration with the CT-component of PET/CT as has been shown in other comparable studies (20, 21). However, the anatomical landmarks used for image registration (e.g. the upper and lower poles of the liver, kidneys and spleen) can also easily and accurately be detected in unenhanced MRI sequences.

While integrated PET/MRI is currently being developed and first results have been published for head-only imaging systems (19), it has yet to be proven that there is substantial clinical value until first hybrid PET/MRI scanners are introduced into clinical routine. Meanwhile, in selected clinical cases, retrospective image fusion of PET- and MRI data can be done with satisfying accuracy using routine protocols without taking special measures to prospectively standardize imaging protocols. Since we performed image registration between PET and MRI in a limited anatomical volume (the upper abdomen), no statement concerning the accuracy of whole body image fusion which is one of the advantages of hybrid PET/CT can be made. Finally, we did not investigate the diagnostic usefulness of PET/MRI in patients with malignancies of the upper abdomen.

**Conclusion**

Retrospective rigid image fusion of PET and MRI of the upper abdomen using an open-source freeware software is feasible without adaptation in image acquisition protocols and shows sub-centimeter registration errors in most cases.

**Conflict of interest**

This study was partially supported by Bayer AG (Schweiz), Bayer Schering Pharma.

**References**