Original article

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Correction of an image size difference between positron emission tomography (PET) and computed tomography (CT) improves image fusion of dedicated PET and CT

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Aim **Clinical work in software positron emission tomography/computed tomography (PET/CT) image fusion has raised suspicion that the image sizes of PET and CT differ slightly from each other, thus rendering the images suboptimal for image fusion. The aim of this study was to evaluate the extent of the relative image size difference between PET and CT and the impact of the correction of this difference on the accuracy of image fusion.**

Methods **The difference in real image size between PET and CT was evaluated using a phantom study. Subsequently, 13 patients with cancer in the head/neck area underwent both CT and [^{18}F]fluorodeoxyglucose PET in a custom-made mask for external beam radiotherapy, with multimodality markers for positional reference. The image size of PET relative to CT was determined by evaluating the distances between the markers in multiple directions in both scans. Rigid-body image fusion was performed using the markers as landmarks, with and without correction of the calculated image size difference.**

Results **Phantom studies confirmed a difference in real image size between PET and CT, caused by an absolute error in PET image size calibration. The clinical scans demonstrated an average relative difference in image size of 2.0% in the transverse plane and 0.8% along the longitudinal axis, the PET images being significantly smaller. Image fusion using original images demonstrated an average registration error of 2.7 mm. This error was decreased to 1.4 mm after size correction of the PET images, a significant improvement of 48% ($P < 0.001$).**

Conclusions **A significant deviation in PET image size may occur, either as a real image size deviation or as a relative difference from CT. Although possibly not clinically relevant in normal diagnostic procedures, correction of such a difference benefits image fusion accuracy. Therefore, it is advisable to calibrate the PET image size relative to CT before performing high-accuracy rigid-body image fusion.** *Nucl Med Commun* **27:515–519 © 2006 Lippincott Williams & Wilkins.**

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Introduction

Image fusion of positron emission tomography (PET) and computed tomography (CT) can improve the diagnostic value and diagnostic accuracy in oncological imaging of the head and neck area [1–3]. Image fusion may also be applied to incorporate functional information in external beam radiation treatment [4,5]. When performing image fusion, a high accuracy in anatomical registration of the images is required, because incorrect registration may induce diagnostic errors, such as erroneous localization or characterization of the lesions [6]. In particular, when using image fusion for the definition of target volumes in intensity-modulated radiation therapy (IMRT), the required accuracy is high as the error in dose delivery is in the range of only 2–3 mm [7]. Errors in image registration may influence the outcome of therapy and the level of complications of external beam radiation therapy.

For software image fusion of dedicated PET and CT, an accuracy of better than 2 mm has been demonstrated using phantoms [8]. The accuracy that can be achieved in patients will probably be lower as a result of complicating factors, such as small positioning errors, motion artefacts, the time interval between scans and limited comparability between scans due to visualization of different structures and processes on PET and CT. Furthermore, differences may exist in image size. In this article, real image size is defined as the discrepancy between the measured size of an object on an image and the true size of that object. Furthermore, relative differences in image size may occur between scanning modalities. The image

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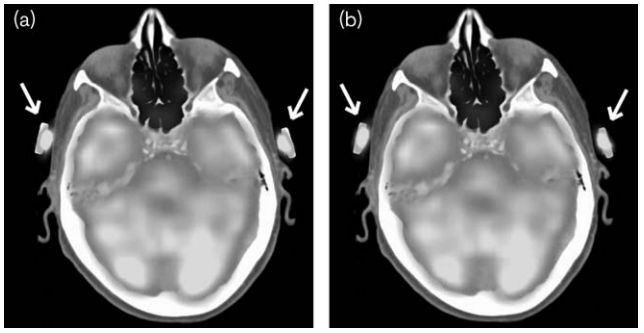
Fig. 1



Software image fusion of positron emission tomography (PET) and computed tomography (CT). A slice through the head is shown at the level of two multimodality fiducial markers positioned in front of the ears. (a) Original images: the markers on PET are closer to each other than on CT, and hence the PET image is somewhat smaller than the CT image. (b) After correction for image size differences: The markers are centred correctly.

size is often not considered in rigid-body image fusion as, in general, the scanner image sizes are fixed and validated for both PET and CT.

During software PET/CT image fusion with multimodality markers for IMRT planning of the head and neck area, we observed a small systematic scaling difference between CT and PET images. Patients were slightly smaller on PET images than on CT images. An example is shown in Fig. 1(a). It was suspected that the image size of the CT scanner and/or PET scanner was inaccurate. Attempts were made to correct these errors with patient-specific manual or automatic scaling procedures, but the results were variable and depended on other factors, such as small positioning differences and deformations. It was hypothesized that correction with an objectively determined systematic scaling factor would provide a better and more elegant solution.

The purposes of this study were to determine the extent of image size differences between PET and CT, to evaluate the impact of this problem on image fusion accuracy and, if needed, to determine a systematic scaling correction factor.

Materials and methods

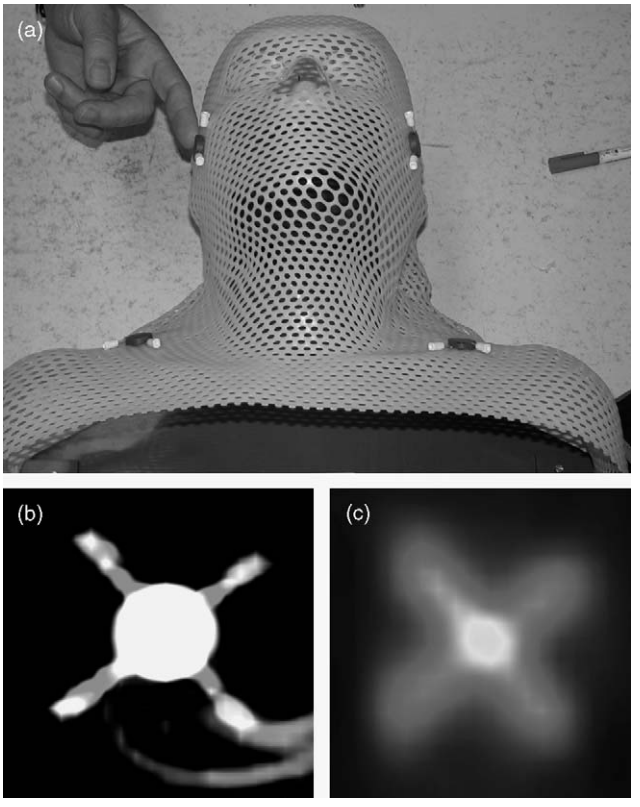
Phantom experiment

A linear phantom, 50 cm in length, with 11 multimodality markers positioned at 5 cm intervals, was used to estimate the real image sizes of PET and CT, and to detect the linearity of deviations. Each marker consisted of two glass capillaries positioned under a 90° angle, filled with either iodine-containing X-ray contrast solution or diluted [^{18}F]fluorodeoxyglucose ([^{18}F]FDG) solution. The visualization of a marker is demonstrated in Fig. 2. The phantom was scanned in three directions (i.e. x, y and z) in both PET and CT. The distances between the centres of all marker pairs were measured in three directions in both imaging modalities. Differences in the distances between corresponding marker pairs on PET and CT were evaluated throughout the field of view of the scanners to determine the linearity of deviations. The inter-operator variation of the manual localization of the centre of the markers was evaluated by the analysis of 12 markers in a separate session by two operators.

Clinical experiment

Thirteen patients with newly diagnosed malignancy in the head and neck area were included. All patients had squamous cell carcinoma of the oral cavity or larynx, and were candidates for external beam therapy. None of the patients had a history of diabetes mellitus, and fasting glucose levels were within the normal range. In addition to standard planning CT, an [^{18}F]FDG PET scan was performed to provide biological parameters for optimized target volume definition. Both CT and [^{18}F]FDG PET were acquired in a

Fig. 2



Example of the multimodality markers used for landmark registration and image fusion accuracy evaluation. (a) Markers as placed on the mask. (b) Markers as seen on computed tomography (CT) filled with iodine contrast. (c) Markers as seen on positron emission tomography (PET) filled with [^{18}F]fluorodeoxyglucose solution. The centre of the markers could be determined with an inter-operator variability well below 1 mm on both CT and PET images.

custom-moulded mask to provide identical positioning. Four multimodality markers were attached to each mask at corner positions outside the target field (Fig. 2).

Image acquisition

CT scans were acquired using a multislice spiral CT scanner (Marconi AcQsim, Marconi Corporation, Cleveland, Ohio, USA). The scanning parameters comprised a scan range from the skull base to the lung top, intravenous contrast in the arterial phase, 100 mA, 130 kV. The pixel size of the images was 0.938 mm^2 in the transaxial plane. The voxel size in the axial direction was defined by a slice thickness of 3 mm.

PET scans were acquired using a full-ring dedicated PET scanner (Siemens ECAT Exact 47, Siemens/CTI, Knoxville, Tennessee, USA). An activity of 250 MBq of [^{18}F]FDG was injected intravenously. The scans were acquired 1 h post-injection, using three-dimensional emission for 6 min per bed position, and employing attenuation correction based on two-dimensional germanium-68 transmission images for 2 min per bed position. All PET scans were reconstructed using an iterative two-dimensional ordered subset expectation maximization (OSEM) algorithm [9] using four iterations, 16 subsets and a three-dimensional Gaussian filter of 5 mm. A zoom factor of 1.5 was applied to generate voxels with a size of 3.432 mm in all directions.

Evaluation of image size difference

The difference in real image size between PET and CT was evaluated by measuring the distances between the centres of multiple markers in the transverse and axial planes for both imaging modalities. For each patient, four markers were placed in a rectangular configuration, providing 26 marker pairs in the transverse plane and 26 pairs in the axial direction. Three markers in three separate patients were excluded from evaluation because of poor visibility. Thus, 24 evaluable marker pairs in the transverse plane and 23 pairs in the axial direction were used for the analysis. The relative difference in pixel size between PET and CT was calculated using the formula: $(\text{Distance}_{PET} - \text{Distance}_{CT})/\text{Distance}_{CT} \times 100\%$.

Impact on image fusion

Image fusion was performed twice, with the original PET images and with PET images that had been corrected for the image size difference relative to CT by adaptation of the pixel size in the DICOM header of the source files.

Rigid-body landmark-based registration of PET images to CT images was performed with in-house-developed software, based on the visualization toolkit VTK [10]. First, the centre of all markers was identified manually. Subsequently, rigid-body registration, that is based on three translation and three rotation parameters, of PET to CT images was performed automatically by minimizing the sum of the square distances between corresponding marker centres [11]. Scaling of the images in the image registration software was not necessary, because image size corrections had already been performed in the DICOM source files.

The accuracy of the image registration procedure was evaluated mathematically by determining the remaining positional difference between corresponding markers on PET and CT after image registration. Statistical analysis of the difference in image registration accuracy between the two image sets was performed using a two-sided paired *t*-test. The level of significance was set at 0.05.

Results

The inter-operator variability in the determination of the centre of the markers was well below 1 mm in both types of scans. For CT images, the average difference between the two operators was 0.54 mm [standard deviation (SD), 0.28 mm]. For PET images, the average difference was 0.42 mm (SD, 0.19 mm).

Image size difference

In the phantom experiment, in the horizontal direction (*x*-axis), the measured distance between the outermost markers on PET was 490.4 mm. On CT images, the measured distance was 499.2 mm, a relative difference from PET of 1.8%. In the vertical direction (*y*-axis), the respective distances were 499.0 and 490.1 mm, a relative difference of 1.8%. In the longitudinal direction, the distances were 500.5 and 497.2 mm, a relative difference of 0.7%. For both PET and CT, the markers were distributed evenly along the phantom in all directions. The difference in distance between marker pairs on PET and CT was detected throughout the field of view, indicating a linear image size difference.

In the series of clinical scans, in the transverse plane, a significant average relative difference in distance between markers on PET and CT of 2.0% was observed (range, 0.2–3.7%; SD, 0.76%), the patient being smaller on the [^{18}F]FDG PET images than on the CT images in all cases. In the axial direction, an average difference of 0.8% (range, −0.6 to 2.5%; SD, 0.65%) was found, the patient being smaller on the [^{18}F]FDG PET images than on the CT images in the majority of cases.

To compensate for the detected differences in the clinical series, the pixel size of the PET images was increased by 2.0% to 3.501 mm in the transverse plane, and increased by 0.8% to 3.459 mm along the longitudinal axis, by adaptation of pixel size values in the DICOM file header. Repeated evaluation using the corrected PET images showed an image size difference of 0.2% (range, −1.4 to 1.8%; SD, 0.69%) in the transverse plane, and a

difference of 0.0% (range, −1.5 to 1.7%; SD, 0.68%) in the axial direction. Thus, a significant relative difference in image size between PET and CT could no longer be demonstrated.

Accuracy of image fusion

Image fusion using the original uncorrected [^{18}F]FDG PET images demonstrated an average mathematical registration error of 2.7 mm (range, 0.8–5.5 mm) at the position of the markers. When image fusion was performed using PET images corrected for relative image size differences, the error was 1.4 mm (range, 0.3–3.8 mm). This represented a significant decrease in the error in image fusion at the location of the markers of 48% ($P < 0.001$). Figure 1(b) shows a fused image after pixel size correction.

Discussion

The suspected relative difference in real image size between PET and CT was confirmed using both phantom studies and clinical scans. In the clinical scans, a series of separate measurements over multiple patients demonstrated the deviation with statistical significance. The manual identification of the centre of the markers was excluded as a possible source of error in the analysis procedure, because the inter-operator variability was negligible.

The results of the phantom measurements and the clinical scans were concordant (the size differences in the phantom measurements were well within the standard deviations of the clinical series). The deviation was shown to be linear, and thus the results from the phantom study and the clinical data were theoretically exchangeable. The image size difference derived from the clinical series was considered to be the most accurate, because statistical analysis of a series of measurements is less prone to bias in the manual evaluation of markers than a single measurement in the phantom experiment. Therefore, the image size difference derived from the clinical series was applied as the correction factor. This approach was validated by repeated measurements after correction, which no longer demonstrated significant image size differences.

The observed difference in image size between PET and CT was larger in the transverse plane than in the axial direction (2.0% versus 0.8%). The exact cause of this discrepancy remains unclear. There is no apparent reason why image size calibration of PET images would be more difficult in one direction than in another.

The relative difference in real image size between PET and CT was caused by an absolute error in calibration of the PET image size. With a pixel size and effective resolution (full-width at half-maximum) in the range of 5 mm in PET imaging, accurate image size calibration may be difficult. For example, to detect a deviation of 1%, the difference to be found in a marker distance over a length of 20 cm is only 2 mm, which is well below the resolution. Therefore, the procedure to determine the image size of a PET scanner will always be less accurate relative to a CT scanner. Furthermore, in IMRT planning, CT must be the gold standard by default because planning of the radiation fields depends on the electron density information derived from CT. For these reasons, we have adapted the PET images to match CT, regardless of the possibility of a hypothetical small remaining error in CT real image size.

Correction of the image size differences alone will not result in perfect image fusion. Other causes of inaccuracies remain, such as slight deformation of the mask between scans (as a result of small patient positioning differences) and patient motion during scanning (for example, swallowing). These factors, in combination with the sampling errors of the marker locations, contribute to the detected remaining error in rigid-body landmark-based image registration.

It can be argued that image size correction should be applied to all PET scanning, but the relevance of an error of this small magnitude in normal diagnostic imaging is probably negligible. Image size corrections need to be advocated only when a high accuracy is required, such as in image fusion for IMRT planning in the head and neck area.

Several approaches to rigid-body image registration are available. Examples include manual procedures, automatic methods based on mutual information or the iterative closest point algorithm, and landmark-based registration. We used the latter method for our accuracy evaluation, as landmark registration is a robust and accurate technique when reliable landmarks are available [11]. It seems obvious that other rigid-body registration techniques will benefit similarly from the correction of image size differences. Theoretically, when non-rigid transformations are used, there is no need for additional image size corrections.

Multiple approaches may be available to correct the standard image size of PET images. Some PET scanners may allow easy adaptation of the image size on the machine itself, most likely as a parameter in the reconstruction algorithm. Other options include adaptation of the DICOM file that is transported to the fusion software, or adaptation in the fusion software itself. Not all available approaches may support separate adaptation for the transverse and axial directions, as was needed in our specific situation. Otherwise, there are no rational arguments to prefer one approach over another.

As an alternative solution to systematic correction of differences in image size, patient-specific scaling may be advocated as it is relatively easy to perform. Image fusion software generally supports scaling, either manual or automatic. Scaling is even considered as a routine procedure in image fusion with magnetic resonance imaging (MRI), which suffers from spatial distortions and size deviations because of magnetic field inhomogeneities. However, when spatial inhomogeneities are absent, we consider this approach to be suboptimal, as the applied size corrections will be influenced by incidental variations, such as positioning differences. The application of *ad hoc* scaling factors seems to be a less rational procedure, especially when the exact correction values can be derived by relatively simple measurements as discussed in this paper.

It seems unlikely that the correction parameters presented in this article can be transferred to other PET systems in general. Variations may occur between systems, especially when using scanners from different manufacturers. Therefore, the extent of image size differences should be assessed locally.

Hybrid PET/CT systems may also suffer from relative image size differences between PET and CT, as all currently available hybrid systems are dedicated PET and CT scanners placed in-line. Therefore, the adjustment of pixel size may result in a similar benefit in image fusion accuracy when using hybrid PET/CT scanning.

Conclusion

We have demonstrated that a small deviation in PET real image size may occur, as well as a significant difference in PET image size relative to CT. Although a small deviation in PET image size is not clinically relevant in normal diagnostic procedures, correction of such a difference proves to be beneficial with regard to the accuracy of rigid-body software image fusion. Therefore, it is advisable to re-evaluate PET scanner image size relative to CT images before using high-accuracy rigid-body image fusion with CT.

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