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WHOLE BODY NONRIGID CT-PET REGISTRATION USING WEIGHTED DEMONS

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Abstract

We present a new registration method for whole-body rat computed tomography (CT) image and positron emission tomography (PET) images using a weighted demons algorithm. The CT and PET images are acquired in separate scanners at different times and the inherent differences in the imaging protocols produced significant nonrigid changes between the two acquisitions in addition to heterogeneous image characteristics. In this situation, we utilized both the transmission-PET and the emission-PET images in the deformable registration process emphasizing particular regions of the moving transmission-PET image using the emission-PET image. We validated our results with nine rat image sets using M-Hausdorff distance similarity measure. We demonstrate improved performance compared to standard methods such as Demons and normalized mutual information-based non-rigid FFD registration.

Index Terms

Whole body PET-CT image fusion

1. INTRODUCTION

Positron emission tomography (PET) can be used to provide three-dimensional information about physiological and functional processes. However, the lack of anatomical detail in PET requires that the images be registered to an anatomical image (e.g. MRI or CT) to place the functional information in context. In the case of abdominal/whole body imaging, the subject has to be moved from scanner to scanner and even small changes in posture/positioning can result in non-rigid deformations in body regions outside the brain. A key part of the PET processing pipeline is attenuation correction. Here transmission-PET scans are used. In transmission scans, a photon source is rotated around the object and the photon attenuation is recorded by the PET scanner, which provides images with sub-optimal quality (called "poor man's CT") for structural information. In order to distinguish from transmission-PET scanning, the PET scan that detects the γ-rays from the radiotracer absorbed in the body is called "emission-PET" scanning.

In the case of whole body registration between PET and CT images, a rigid transform [1] and elastic registration methods [2, 3] were proposed. Previous inter-modal registration methods between PET and CT/MRI were mostly based on the maximization of mutual information (MI) [7, 8]. When registering CT and PET images, usually the CT image is used as the reference image because it has better resolution. The question as to which PET image, i.e. the emission-PET image or the transmission-PET image, should be used as the moving image in a registration process was investigated by Skalski *et al.*[4]. They compared two registration schemes: an indirect fusion scheme and a direct fusion scheme. First, in the indirect fusion scheme, a transmission-PET image was used as a moving image and CT image was used as a reference image for registration process, and then, the transformation between the transmission-PET and the CT images is applied to the corresponding emission-PET image for registration. Second, in the direct fusion scheme, the emission-PET image was directly used as the moving image for the registration process. They [4] report that the indirect scheme has smaller error than that of the direct scheme. In this paper, we propose an automatic, 3-dimensional, fully deformable whole-body registration method between PET and CT images acquired using different scanners. For this purpose, we take advantage of both the transmission-PET and the emission-PET images in the registration process. We emphasize certain parts of the moving transmission-PET image based on the emission-PET image, which amplifies the intensity variation of the low-contrast transmission-PET image. For a registration algorithm, we developed a weighted demons registration method that can give preferences to particular regions of the transmission-PET image using an emission-PET image.

Unlike MI-based registration algorithms that depend on the statistical information of voxel intensities, PDE-based registration algorithms such as demons registration [5] can easily combine the weighting factor with the “gradient” of voxel intensities, which results in the enhanced registration performance for blurry images like the transmission-PET images. This paper does not address the problem of motion correction related to the respiratory process. We validate our results using 9 rat image sets using the M-Hausdorff distance similarity measure with standard methods such as Demons [5] and the MI-based non-rigid registration with free-form deformation (FFD) [6].

2. METHOD

Fig. 1 shows an image set from a single rat that consists of a CT image, a transmission-PET image and an emission-PET image. The CT image was scanned at a different time (using a separate scanner), thus the rat does not have the same posture as in the PET images. Furthermore, since the particular micro-CT scanner is not big enough for the size of our rats, the rat was scanned in three parts and then the images were stitched into one CT image, resulting in artifacts as seen in Fig. 1. An additional challenge is that transmission-PET image is very blurry. Furthermore the co-registered emission-PET image has bright regions of liver, pancreas, stomach, bladder and kidney without clear borderlines among them. Fig. 2 shows the block diagram for the proposed method. This method has three input images: a high-resolution CT reference image, a transmission-PET moving image, and an emission-PET weight image. The final reconstructed images cover 90×90×207 pixels with a pixel size of 1.2 mm for both transmission-PET and emission-PET and the final CT images have 128×128×306 pixels.

2.1. Preprocessing and rigid transform

In our particular experimental protocol, the rats were placed in cylindrical tubes prior to both the CT and PET imaging which appear as cylindrical rings in the images. The key preprocessing step in Fig. 2 is to eliminate the scanning bed and rings from both images using a semiautomated procedure implemented within our custom software package. We use the emission PET image as weight image which is intensity-normalized and smoothed because the intensity range of the original emission-PET images is very large. We re-scaled the emission-PET image to have range from 0 to 100, and then smoothed it with a median filter. For the rigid transform, we perform 3-dimensional affine transform based on normalized mutual information (NMI). Using the derived rigid transform result between the

CT and transmission-PET images, the emission-PET image is also transformed because those two PET images are acquired during the same session and can be assumed to be co-registered. As the inputs of weighted demons registration method, the CT image and the rigidly-transformed transmission-PET image undergo a histogram matching process (1024 histogram levels) because their intensity scales are different each other.

2.2. Weighted demons registration

Eq. 1 describes the symmetric version [5] of the demons algorithm. Here, $\mathbf{r}(\mathbf{X})$ is the reference CT image, $\mathbf{m}(\mathbf{X})$ is the moving transmission-PET image and $\mathbf{v}(\mathbf{X})$ is the displacement. The local displacement field as a transformation model $\mathbf{T}$ is updated iteratively at each voxel $\mathbf{X}$ by $\mathbf{T}(\mathbf{X}) = \mathbf{X} + \mathbf{v}(\mathbf{X})$.

$$\mathbf{v}(\mathbf{X})=-\frac{2(\mathbf{m}(\mathbf{X})-\mathbf{r}(\mathbf{X}))(\nabla\mathbf{r}(\mathbf{X})+\nabla\mathbf{m}(\mathbf{X}))}{\left\|\nabla\mathbf{r}(\mathbf{X})+\nabla\mathbf{m}(\mathbf{X})\right\|^2+(\mathbf{m}(\mathbf{X})-\mathbf{r}(\mathbf{X}))^2} \quad (1)$$

The demons registration method is commonly utilized in intra-modality registration because this method is based on intensity gradient calculation. In case of inter-modality registration which has a positive-correlation between reference and moving images, the demons registration method also can be used after a preprocessing step such as a histogram-matching. However, as one can see in Fig 3, the intensity variation within the transmission-PET image is too small (even after the histogram-matching) compared to that of the CT image because the transmission-PET image is very blurry. This makes conventional registration methods ineffective in this application. Hence, we propose a weighted demons registration method in which we amplify the intensity gradient of the blurry image using a weight factor to capture minute variations of the intensity. We utilize the emission-PET image co-registered to the moving transmission-PET image for this weight factor. Eq. 2 shows the displacement for the weighted demons registration in which the intensity gradient of the moving transmission-PET image was amplified by the weight factor $\mathbf{K}(\mathbf{X})$. This weight factor affects the displacement calculation of each voxel only when the intensity difference between the corresponding points in reference and moving image is bigger than a threshold (Eq. 3), which means that the weight factors are not imposed in order to avoid over-deformation when the registration alignments are approximately achieved. When $K(x) = 1$ for some point x, this method is equivalent to the original demons registration method for that point.

$$\mathbf{v}(\mathbf{X})=-\frac{2(\mathbf{m}(\mathbf{X})-\mathbf{r}(\mathbf{X}))(\nabla\mathbf{r}(\mathbf{X})+\nabla(\mathbf{m}(\mathbf{X})\mathbf{K}(\mathbf{X})))}{\left\|\nabla\mathbf{r}(\mathbf{X})+\nabla\mathbf{m}(\mathbf{X})\mathbf{K}(\mathbf{X}))\right\|^2+(\mathbf{m}(\mathbf{X})-\mathbf{r}(\mathbf{X}))^2} \quad (2)$$

$$K(x)=1 \text{ if } |m(x)-r(x)|<thr \text{ or } W(x) \text{ otherwise.} \quad (3)$$

where $W(x)$ is the intensity value of the corresponding voxels in the normalized/smoothed emission-PET image. Our weighted demons registration method utilized three levels of resolution to search the displacement in the 3D data set from coarse to fine resolutions (100, 100 and 50 iterations, respectively). For the threshold value in Eq. 3, we used a value 10. We used a Gaussian model with $\sigma = 2$ for smoothing displacement field. Note that the weighting method in this paper does not deal with the matching problem of images with different distributions of different modalities. Instead it aims to ensure that the registration in more important areas is more accurate, in the same way that weighted-least squares fits aims to fit the more reliable/important information preferentially. In the case of PET/CT the important regions are those were we have high counts (in the emission PET) hence we derive our weights from the emission PET.

3. RESULTS

We present experimental results demonstrating the performance of our proposed method. Following rigid transformation (which was performed identically in all cases), we compared the registration result of the proposed method against two standard methods, namely the FFD-based method of Ruckert [6] which uses a mutual information metric that is suitable for multimodality registration and the Demons method, which uses the same deformation model as our method. Both competing methods follow the indirect scheme of Skalski *et al.* [4] described in section 1. We first describe qualitative results followed by a description of our accuracy validation experiments.

3.1. Comparison of registered images

Although the visual evaluation for whole body PET/CT registration is not easy, we can visually evaluate some distinctive features such as upper borderlines of liver and bladder boundaries. Fig. 4(a) shows the reference CT image of a rat, and Fig. 4(b) shows the transmission-PET (above) and emission-PET (below) images after a rigid transform. This rigidly-transformed transmission-PET image is used as an input moving image for all competing deformable registration methods. The cross-hairs indicate an arbitrary point on the rat's liver boundary in CT image. Fig. 4(c) shows the PET results of our proposed weighted demons method. The cross-hairs in both PET images correspond to those of the reference CT image. The liver boundaries of the emission-PET image in Fig. 4(c) (Blue arrow) are well aligned to those of the CT image while both the results of Demons (Fig. 4(d)) and NMI-base FFD method (Fig. 4(e)) are not aligned. In case of NMI-based FFD, we can observe that only small deformation occurs from the rigidly-transformed input image because the small variation of intensity in transmission-PET image cannot contribute much to the broad histogram bins.

3.2. M-Hausdorff distance similarity measure

For a quantitative comparison of our weighted demons method with other competing methods, we measured a maximum-likelihood Hausdorff distance (M-HD) [9] after edge-detection (Canny edge-detector with a Gaussian $\sigma = 2.0$) in both the CT image and the deformed emission-PET image. In the transmission-PET image, we cannot generate suitable edges except skin boundaries due to the severe blurriness. For two sets of edge positions in 3-dimensional binary images, $P=\{(p_1^x, p_1^y, p_1^z), \dots, (p_I^x, p_I^y, p_I^z)\}$ and $Q=\{(q_1^x, q_1^y, q_1^z), \dots, (q_J^x, q_J^y, q_J^z)\}$ of which sizes are I and J, respectively, the directed distance $h_M(P; Q)$ of the M-HD based on M-estimation is defined as

$$h_M(P;Q)=\frac{1}{I}\sum_{(p^x,p^y,p^z)\in P}\rho(D_Q(p^x,p^y,p^z)) \quad (4)$$

where $D_Q(p^x, p^y, p^z)$ is the minimum correspondent distance at point (p^x, p^y, p^z) to the set Q and the cost function $\rho(\cdot)$ has a threshold of distance to eliminate outliers as below.

$$\rho(x)=\begin{cases} |x|, & |x| \le OSP \\ |OSP|, & otherwise \end{cases} \quad (5)$$

The outlier-suppression parameter (OSP) is a threshold to eliminate outliers, so the outliers yielding large distance errors are discarded. Because the M-HD similarity measure is robust in the presence of outliers and occlusions, the M-HD measure can be used to compare the similarity of PET-CT images even though the edges are not fully generated from the PET images due to vague contours. Table 1 shows the M-HD similarity measures of our weighted demons method with other competing methods. The “Rigid Transform” in Table 1 means the rigidly-transformed emission-PET image which is used as an input to competing deformable registration methods. Over the 9 rat sets, the M-HD measure shows our proposed method’s superior performance over other methods with statistical significance ($p < 0.05$). In Table 1, we performed a paired-T test between the result of the rigidly-transformed emission-PET image and the results of non-rigidly registered emission-PET images. With larger OSP (10 and 20), the quantitative performance difference between our weighted demons and other methods become bigger, which means that our proposed method shows stable performance independent of edge detection.

4. DISCUSSION AND CONCLUSION

We have presented a new three-dimensional whole body rat inter-modal nonrigid registration method between CT and PET images using a weighted demons algorithm. We utilized both the transmission-PET and the emission-PET images in the registration process by emphasizing particular regions of the transmission-PET image using an emission-PET image. Experiments with nine rats demonstrate encouraging performance of our method over competitive techniques. We note that the evaluation of the results of nonrigid inter-modal registration between PET and CT images are challenging because of the lack of easily available gold-standards. Hence, as a second best, we utilized the M-HD metric. The proposed method would be applicable to other multimodal imaging studies acquired in separate scanners.

Acknowledgments

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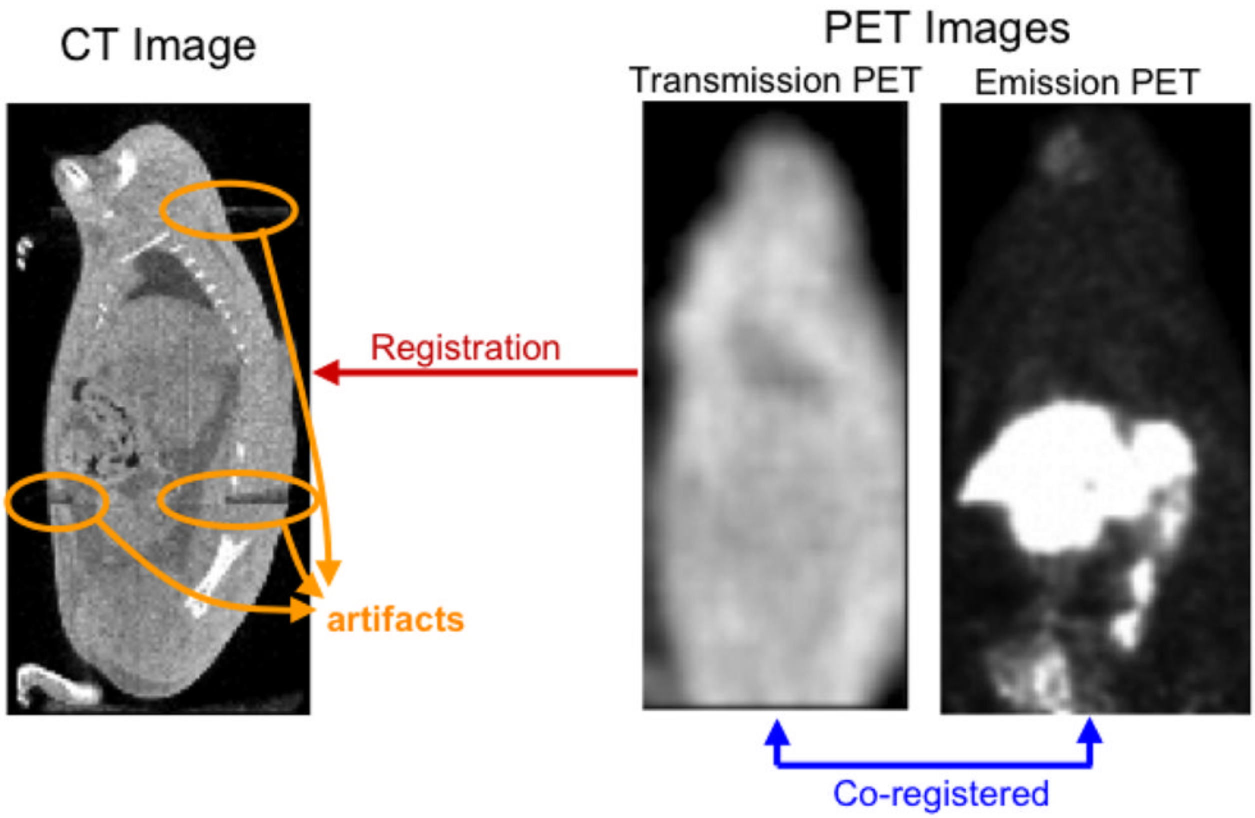

Fig. 1.
Registration between CT images and the pair of transmission and emission-PET images. There are a number of challenges here including (i) the multimodal nature of the registration, (ii) the relatively low resolution of the PET images and (iii) the artifacts in the CT images due to their being acquired in three parts.

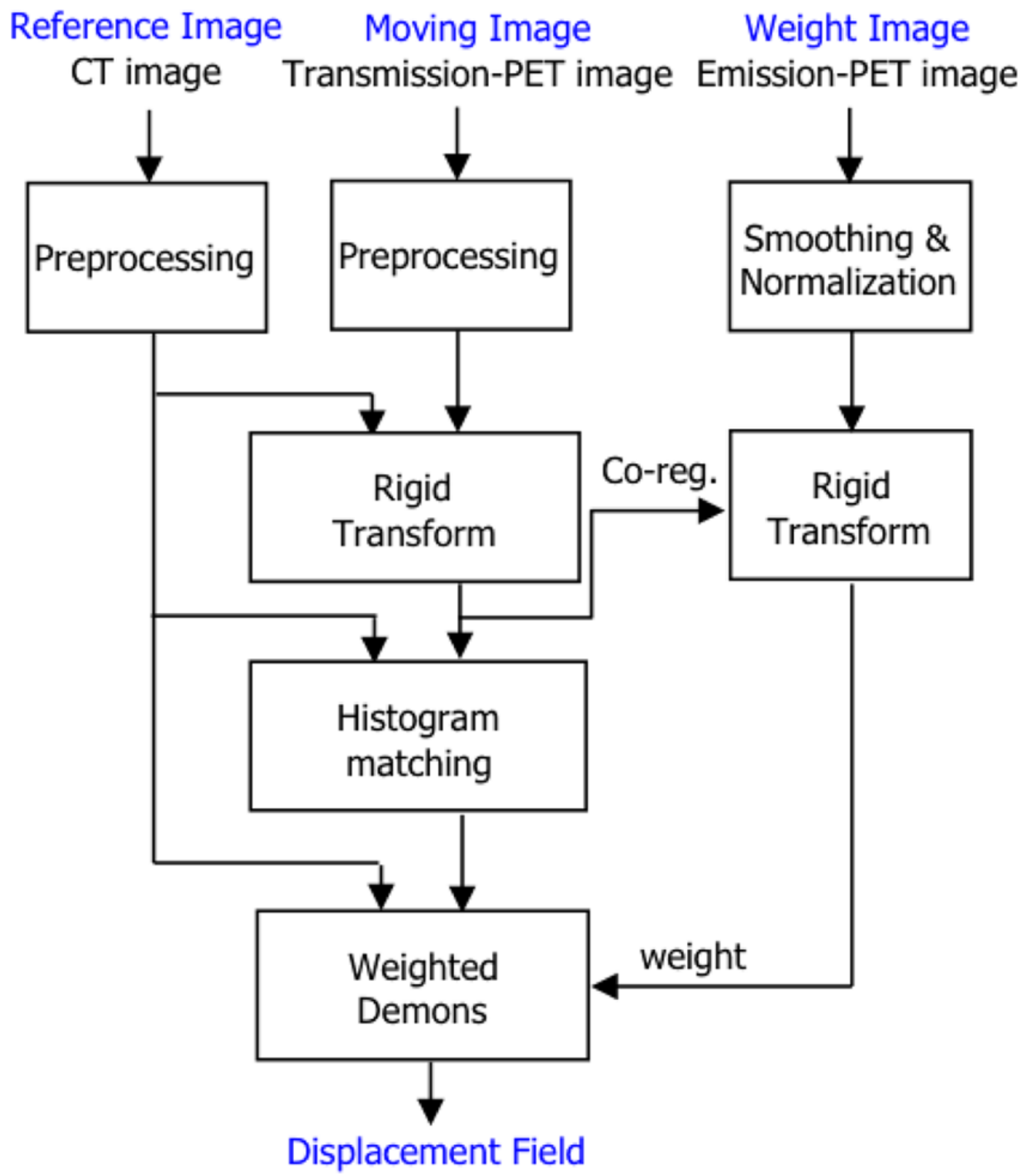

Fig. 2.
Block diagram for our weighted registration between CT and PET images.

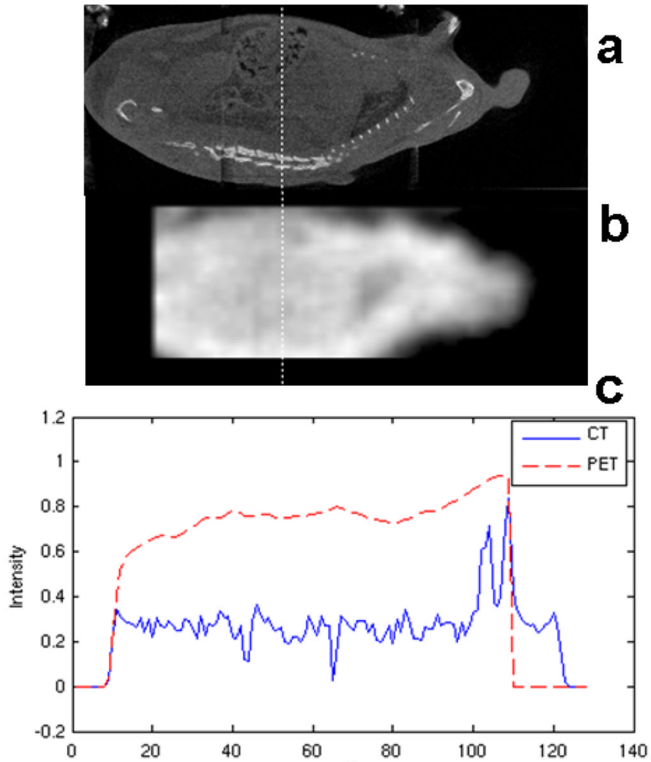

Fig. 3.
Normalized intensity profiles of CT and transmission-PET images. (a) CT image, (b) the transmission-PET image of the same rat, and (c) normalized intensity profiles along the dotted line in (a) & (b).

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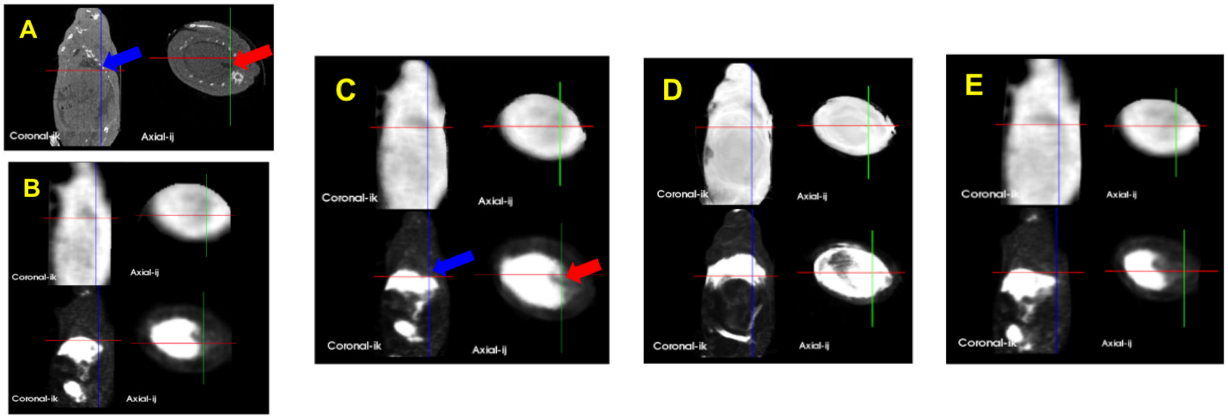

Fig. 4.
Coronal and axial views for (A) reference CT image, (B) rigid transformed PET images (top:transmission, bottom:emission). Panels C–E show the non-linearly warped PET as registered using: (C) the proposed weighted method, (D) Demons and (E) NMI registration. Blue arrows indicate the correctly aligned liver borderline. Red arrows indicate the correctly aligned a small hollow around liver.

Table 1

Comparison of M-Hausdorff distance between edge-detected CT images and edge-detected emission PET images with different outlier-suppression parameters (OSP). (N=9 pairs of images, Unit: Average Hausdorff distance per edge pixel)

Method	*OSP* = 10	T test	*OSP* = 20	T test
Rigid Transform	7.79±1.04		9.05±1.28	
Demons	6.79±0.83	0.07	9.19±2.39	0.84
NMI-based FFD	5.74±1.73	0.02	7.40±7.84	0.08
Proposed	**3.99±1.37**	**2.62E-04**	**5.04±1.59**	**2.79E-04**