The influence of CT based attenuation correction on PET/CT registration: an evaluation study

Ziv Yaniv, Kenneth H. Wong, Filip Banovac, Elliot Levy, Kevin Cleary

Imaging Science and Information Systems (ISIS) Center, Dept. of Radiology, Georgetown University Medical Center, Washington, DC, USA.

ABSTRACT

We are currently developing a PET/CT based navigation system for guidance of biopsies and radiofrequency ablation (RFA) of early stage hepatic tumors. For these procedures, combined PET/CT data can potentially improve current interventions. The diagnostic efficacy of biopsies can potentially be improved by accurately targeting the region within the tumor that exhibits the highest metabolic activity. For RFA procedures the system can potentially enable treatment of early stage tumors, targeting tumors before structural abnormalities are clearly visible on CT. In both cases target definition is based on the metabolic data (PET), and navigation is based on the spatial data (CT), making the system highly dependent upon accurate spatial alignment between these data sets. In our institute all clinical data sets include three image volumes: one CT, and two PET volumes, with and without CT-based attenuation correction. This paper studies the effect of the CT-based attenuation correction on the registration process. From comparing the pairs of registrations from five data sets we observe that the point motion magnitude difference between registrations is on the same scale as the point motion magnitude in each one of the registrations, and that visual inspection cannot identify this discrepancy. We conclude that using non-rigid registration to align the PET and CT data sets is too variable, and most likely does not provide sufficient accuracy for interventional procedures.

Keywords: Image-Guided Therapy, PET/CT, non-rigid registration, PET attenuation correction

1. INTRODUCTION

We are currently developing a PET/CT based navigation system for guidance of biopsies and Radio Frequency Ablation (RFA) of hepatic tumors.[1] For RFA procedures combined PET/CT data can potentially enable treatment of tumors before structural abnormalities appear on CT, or when these abnormalities are not clearly visible. For tumor biopsies this system can potentially improve diagnostic results by accurately targeting regions within the tumor that exhibit the highest metabolic activity. In both cases we use PET data to define a spatial target which is not clearly visible on the CT. The underlying assumption of our approach is that the PET and CT are spatially aligned.

To date, combined Positron Emission Tomography (PET) and Computed Tomography (CT) machines have been primarily used for diagnostic purposes in the oncological setting. They have led to improved diagnostic accuracy,[2] and higher patient throughput. The former is due to the fusion of spatial and functional information, while the later is due to the higher speed of CT-based attenuation correction as compared to PET transmission based correction.

These combined machines facilitate image fusion by providing intrinsically registered data sets, under the assumption that there is a known *rigid* relationship between the PET and CT data. In the regions of the abdomen and thorax this is an approximation as the data sets are related via a non-rigid transformation. This inconsistency is a result of the acquisition protocols. CT images are acquired at breath-hold while PET images are acquired with normal tidal breathing, due to the long acquisition times (several minutes per slice).

The visual quality and quantitative accuracy of PET data is primarily influenced by photon attenuation, necessitating the use of attenuation correction schemes.[3] One possible correction scheme is based on the use of CT data for X-ray based attenuation correction, and is the method used in combined PET/CT scanners.[4]

E-mail: zivy@isis.georgetown.edu

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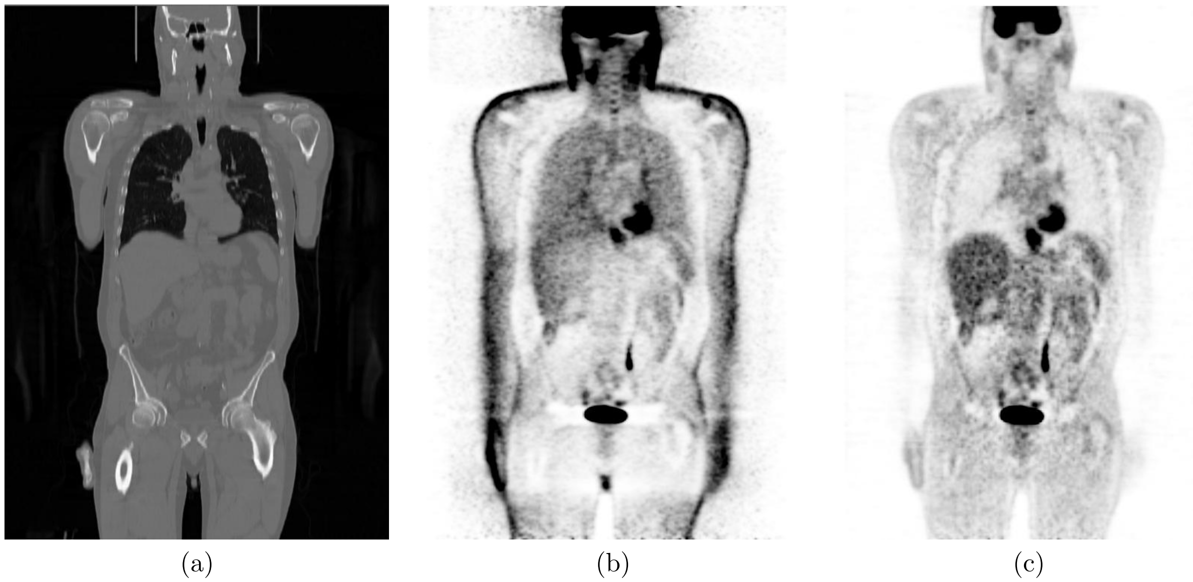


Figure 1. Corresponding coronal slices from a combined PET/CT machine: (a) CT, (b) PET without attenuation correction (c) PET after CT-based attenuation correction. Dark regions in the PET data correspond to high metabolic activity. Note the typical enhanced activity in the region of the lungs prior to attenuation correction.

The primary assumption underlying this scheme is that the spatial relationship between the PET and CT coordinate systems is known (not necessarily rigid). Currently, most PET/CT machines assume that this spatial relationship is both known and rigid. This assumption is invalid in the regions of the abdomen and thorax, resulting in attenuation correction errors. To mitigate the effect of these errors on diagnosis most PET/CT machines output three corresponding data sets: CT, and PET with and without attenuation correction, such as those shown in Figure 1. Evaluating the results is thus deferred to the physicians, relying on their ability to identify imaging artifacts due to respiratory motion.

Thus, combined PET/CT machines produce PET data that is spatially inconsistent with the known CT coordinate system, which in turn leads to erroneous attenuation correction.

A comprehensive solution to these problems is to acquire 4D (3D over time) CT and PET data sets. This approach is based on retrospective or prospective gating. In[5] CT is gated retrospectively and PET is gated prospectively. A respiratory signal is obtained from an optically tracked marker placed on the patient's chest. To acquire 4D CT the respiratory cycle is divided into bins and the CT slices are time-stamped with their respective phases in the respiratory cycle using a signal triggered by the imaging apparatus indicating slice acquisition. The resulting set of binned slices represent the CT volume over time. To acquire a 4D PET data set a prospective gating approach is used with data acquisition triggered by the respiratory signal. In this case the activation events are binned such that each bin represents a single 3D PET volume. A similar approach was used in.[6] In this work both CT and PET data were gated retrospectively, and the respiratory signal was based on the temperature of the patient's breathing airflow.

A possible problem with gated PET reconstruction is the small number of activations per bin. To obtain enough data per bin for a high quality reconstruction longer acquisition times and increased amounts of radioactive tracer material are required, both of which are preferably avoided. A recently proposed solution to this problem is to non-rigidly register all low quality PET volumes to a single phase,[7] resulting in a single high quality volume.

While these are comprehensive solutions they require interaction with the imaging apparatus, either to trigger acquisition or to receive a signal that data has been acquired. These hardware interfaces are not always available which has lead researchers to make the following implicit assumption: CT and PET data sets are correct representations of the underlying anatomical structures for two different points in the respiratory cycle, and can thus be aligned using non-rigid registration.[8,9]

Currently we do not have access to the internal workings of the imaging apparatus . As our navigation system assumes that PET and CT data are spatially aligned we turn to a registration-based approach, which in many cases is a sufficiently accurate approximation.

In our institute all clinical data sets include three image volumes, CT, and two PET data sets, before and after CT-based attenuation correction. As both PET data sets are spatially equivalent the transformation obtained by non-rigid PET/CT registration should be approximately the same for both PET data sets. The purpose of the work reported here is to assess the effect of the CT-based attenuation correction on non-rigid registration, and to evaluate the reliability of visual inspection as a qualitative method for evaluating non-rigid PET/CT registration when ground truth is not available.

2. METHODS

Non-rigid PET/CT registration has been previously addressed using a variety of approaches including the use of free-form deformations[9] and hierarchical piecewise rigid registration.[8,10] It has been demonstrated that deformable registration of CT-based attenuation corrected PET and CT can potentially improve the alignment between the two data sets.[10]

We chose to use the Free Form Deformation (FFD) based registration method described in[9] and implemented in the Insight Toolkit (ITK).[11] Registration is cast as an optimization task with the objective function defined by image similarity. In our case images are related via a stochastic process and mutual information serves as the similarity measure. To deform the image volume it is embedded inside a grid of node points that control a set of approximating B-splines. The volume is then deformed by changing the position of the node points. Our choice of the FFD based registration method is due to its successful record in registering various anatomical structures including the liver[12] and its previous use for PET/CT registration of the chest region.[9]

All data was acquired using a Siemens Biograph 6 PET/CT machine. The original data are whole-body scans with the following image resolutions: $512 \times 512 \times 244$, for CT, with a voxel size of $1.3 \times 1.3 \times 4mm^3$, and $168 \times 168 \times 244$, for PET, with a voxel size of $4.1 \times 4.1 \times 4mm^3$. CT data was acquired with the patients holding their breath, while PET was acquired with normal tidal breathing. As these are whole-body scans and we are only interested in the region of the liver, all volumes were manually cropped to include only image slices in the region of the liver.

Five clinical PET/CT data sets were used in our evaluation. For each data set the PET volumes before and after attenuation correction were registered to the CT using the registration method described above. For each data set we obtain three vector fields, two fields describe the mapping from CT coordinates to corresponding PET coordinates, and the third field is the difference between the two mappings. Descriptive statistics were computed on the magnitudes of each of the three fields. The original PET volumes were then deformed and blended with the CT volume to allow for visual assessment of the registration results.

3. RESULTS

Table 1 summarizes the results of our five experiments. In all cases the measures of location (mean, median, max) for the attenuation corrected PET are smaller than for the PET data prior to attenuation correction. That is, the magnitude of the deformations for the PET data after CT-based attenuation correction is consistently smaller than the magnitude of the deformation without attenuation correction. This is not surprising as attenuation correction is based on the CT data, which is expected to bias the registration. In all cases the location measures for the magnitude of the difference vectors are greater than that of the attenuation corrected PET data, suggesting that the deformation obtained when using the PET data without attenuation correction differs considerably from that obtained when using attenuation corrected PET. As both PET data sets are spatially equivalent and a ground truth transformation is not available, it is not clear which deformation is closer to the true one, and hence which data set should be used for registration.

Data Set	Vector Field	mean	median	std	max
1	PET with attenuation	1.9	1.8	1.0	4.9
	PET without attenuation	2.7	2.7	1.2	5.7
	difference	2.5	2.3	1.4	7.9
2	PET with attenuation	1.6	1.1	1.2	4.8
	PET without attenuation	2.7	2.7	1.1	6.0
	difference	3.1	3.0	1.4	6.6
3	PET with attenuation	2.8	2.9	1.2	5.5
	PET without attenuation	4.6	5.0	1.6	7.0
	difference	6.6	6.8	2.2	10.7
4	PET with attenuation	0.0	0.0	0.0	0.0
	PET without attenuation	4.3	4.4	1.6	6.8
	difference	4.3	4.4	1.6	6.8
5	PET with attenuation	2.8	2.7	1.3	5.7
	PET without attenuation	3.2	3.3	1.4	6.8
	difference	3.2	3.0	1.7	8.4

Table 1. Descriptive statistics of the magnitude of the vector fields that align the PET data to the CT. All measurements are in *mm*.

Lacking a ground truth transformation, a surrogate figure of merit for registration is often defined using manually marked pairs of homologous points on PET and CT. After registration, the points on CT are mapped to the PET coordinate system using the computed transformation and the distances between the expert delineated points and the mapped points serve as the figure of merit for the registration results. As this approach relies on visual assessment of both PET and CT data sets by experts it is not directly applicable in our case as we target structures that are visible in PET and not on CT. We thus use visual inspection only as a qualitative measure, inspecting fused PET/CT data before and after registration, as presented in Figure 2 and Figure 3, for the first and third data sets from Table 1. Unfortunately, in all cases visual inspection did not produce a distinction between registration using PET before attenuation correction and after attenuation correction. In both cases the registration seems to improve the alignment in a similar manner, though the deformation fields differ.

4. DISCUSSION AND CONCLUSIONS

We are currently developing a PET/CT based interventional navigation system to enable biopsies and RFA treatments in tumors that are clearly visible on PET and not on CT. A prerequisite of our system is accurate spatial alignment of both data sets. In the diagnostic setting, researchers have shown that the alignment of PET/CT data sets can be improved using non-rigid registration.[10] This improvement is quantified using homologous points that are visually identified across data sets.

In our institute data acquisition results in a CT data set and two PET data sets, with and without CT-based attenuation correction. The goal of this study was to evaluate the effect of the attenuation correction on non-rigid registration. As both PET data sets correspond to the same physical situation the deformations computed by the registration algorithm should be similar. As a ground truth transformation is not available we used visual inspection as an indicator of success.

While visual inspection only provides a qualitative measure, quantitative, physically meaningful, evaluation using clinical data involves developing finite element models. This approach has been previously used to evaluate the FFD based non-rigid registration with MR images of the breast.[13] As we do not have the material properties for the various soft tissue structures in the region of the liver we could not apply this approach. As a quantitative measure we only use the vector magnitudes of each of the two deformation fields.

From the quantitative analysis of the magnitude of the deformations, it is clear that CT-based attenuation correction causes bias in the registration, as the magnitude of the deformation without attenuation correction is higher than with it. This is not surprising, as CT-based attenuation correction modifies the PET intensity values in a manner that increases the correlation between the PET and CT data. Previous studies have not

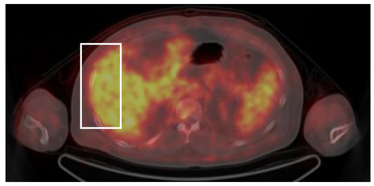
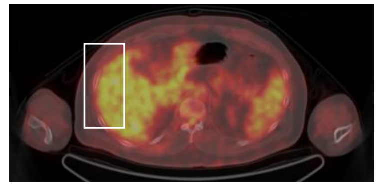
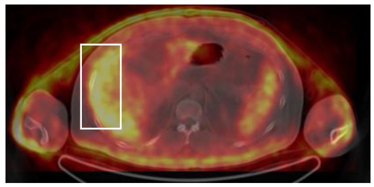
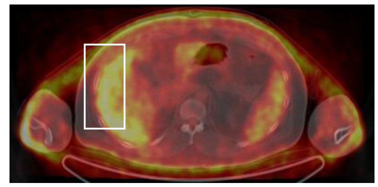
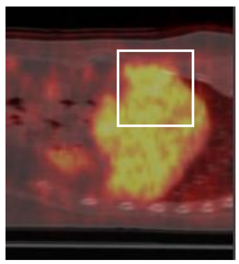
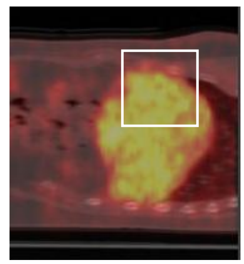
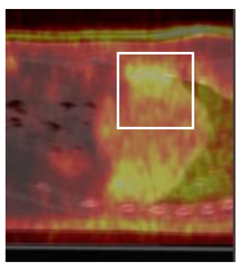
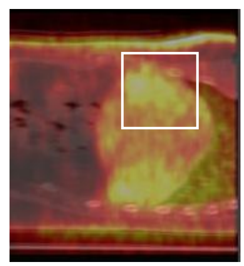
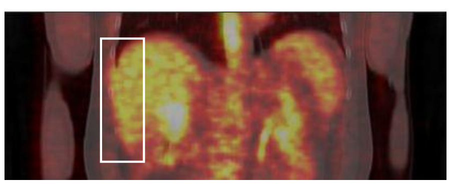
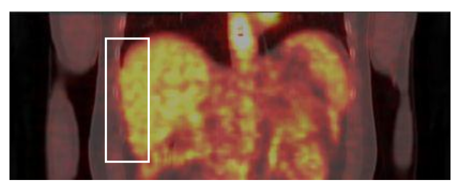
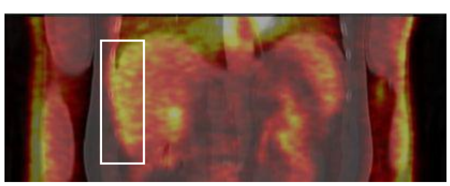
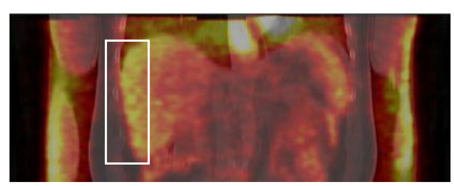
Blended PET/CT	Before Registration	After Registration
PET with CT-based attenuation correction		
PET without CT-based attenuation correction		
PET with CT-based attenuation correction		
PET without CT-based attenuation correction		
PET with CT-based attenuation correction		
PET without CT-based attenuation correction		

Figure 2. Image overlay of PET and CT, displaying the same axial, sagittal, and coronal slices with and without attenuation correction, before and after registration. Images are from the first data set in Table 1. Color figure appears in electronic version.

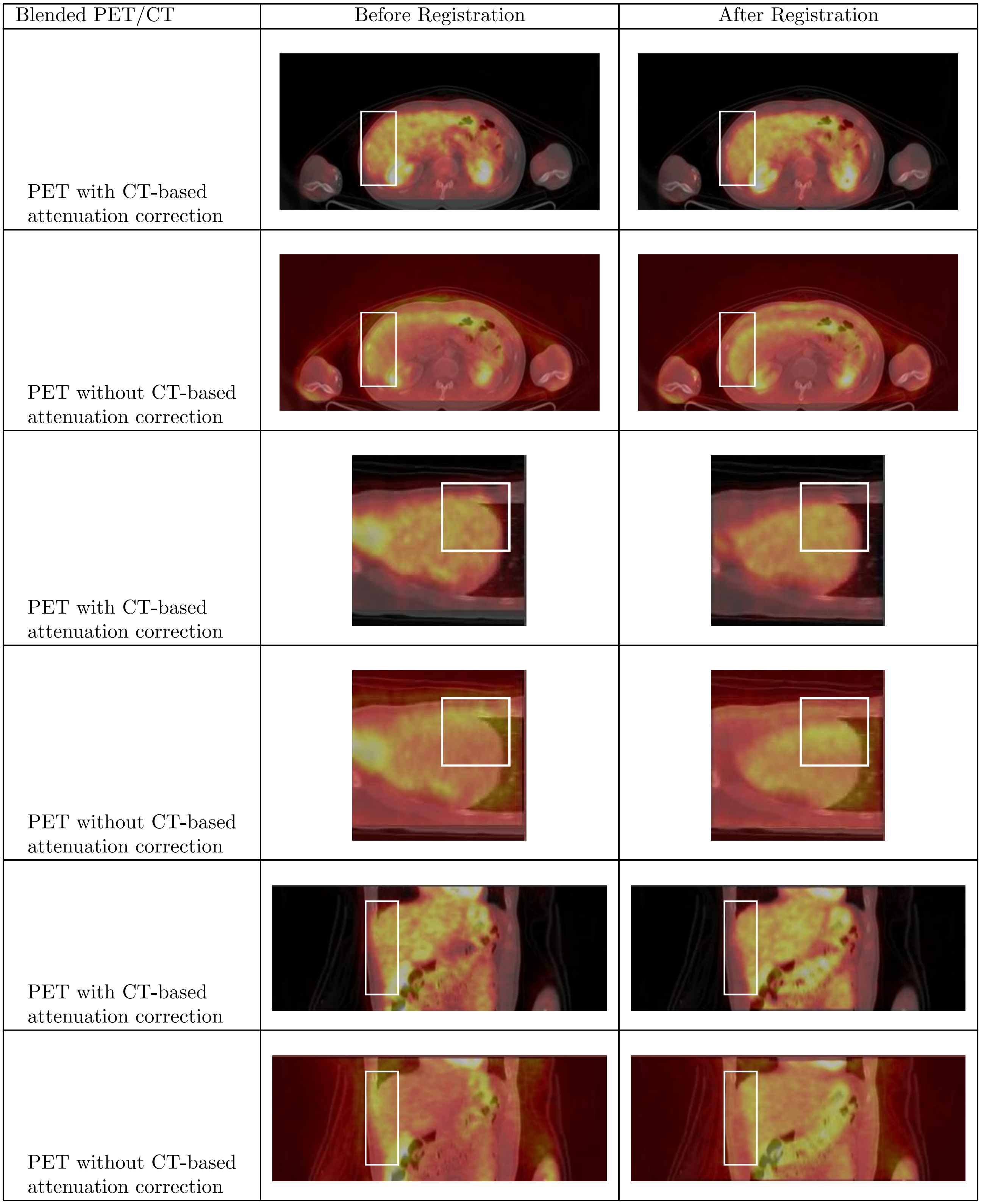


Figure 3. Image overlay of PET and CT, displaying the same axial, sagittal, and coronal slices with and without attenuation correction, before and after registration. Images are from the third data set in Table 1. Color figure appears in electronic version.

made this distinction, and in all likelihood they have used the attenuation corrected data which is usually the data set used for diagnostic purposes.

The interesting observation is that the difference in magnitude cannot be detected visually, as in all cases registration was judged as successful. This brings into question the use of PET/CT non-rigid registration as a method for accurately localizing regions of high metabolic activity on CT data. We have shown that the registration is dependent on the attenuation correction, and that visual inspection cannot distinguish between differing registration results, as it is only affected by object overlap and not by the variations within the objects. More importantly, this casts doubt on the use of visually identified homologous points as a quantitative measure of success, as these are usually identified on the surface of anatomical structures and not within them.

Our results concur with a recently published simulation study comparing the performance of multiple non-rigid registration algorithms.[14] This study has shown that widely differing deformations will result in similar overlaps which cannot be distinguished visually as the deformation differences are within the structures.

We conclude that the accuracy required by our system cannot be obtained using non-rigid registration of the PET/CT data sets currently available in our institute. To pursue the development of our navigation system we will need to interact with the imaging apparatus with the goal of acquiring 4D PET/CT data, as this will ensure that the PET and CT are spatially aligned.

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