PET AND CT IMAGE REGISTRATION OF THE RAT BRAIN AND SKULL USING THE AIR ALGORITHM

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Abstract

Spatially registered PET and CT images of the same small animal offer at least three potential advantages over PET alone. First, the CT images should allow accurate, nearly noise-free correction of the PET image data for attenuation. Second, the CT images should permit more certain identification of structures evident in the PET images and third, the CT images provide *a priori* anatomical information that may be of use with resolution-improving image reconstruction algorithms that model the PET imaging process. Thus far, however, image registration algorithms effective in human studies have not been characterized in the small animal setting. Accordingly, we evaluated the ability of the AIR algorithm to accurately register PET F-18 fluoride and F-18 FDG images of the rat skull and brain, respectively, to CT images acquired following each PET imaging session. The AIR algorithm was able to register the bone-to-bone images with a maximum error of less than 1.0 mm. The registration error for the brain-to-brain study, however, was greater (2.4 mm) and required additional steps and user intervention to segment the brain from the head in both data sets before registration. These preliminary results suggest that the AIR algorithm can accurately combine PET and CT images in small animals when the data sets are nearly homologous, but may require additional segmentation steps with increased mis-registration errors when registering disparate, low contrast soft tissue structures.

I. INTRODUCTION

Imaging technologies originally developed for use in human medical diagnosis are rapidly being adapted to imaging small animals such as the mouse and rat [1]. Moreover, it has become increasingly apparent that certain combinations of these method can yield synergistically improved results. The combination of PET and CT, for example, offers the prospect of nearly noise-free attenuation correction of the PET data, improved target identification and the potential for correcting PET data for other confounding effects, e.g. positron range variations. Before these benefits can be realized, however, the PET and CT image data must be in spatial registration. While a number of multi-modality registration algorithms have been devised and validated in human subjects, comparatively little is known about the performance of these algorithms when applied to PET and CT images of small animals. Accordingly, we have begun investigating already validated human registration algorithms to establish their accuracy in this setting. As an initial test, we elected to evaluate the automated image registration, or "AIR" algorithm [2] in two extreme cases, high contrast bone-to-bone registration of CT and F-18 fluoride PET images of the rat head and low contrast brain-to-brain registration of F-18 FDG and CT images of the rat head.

II. MATERIALS AND METHODS

Both experiments were carried out in a similar manner using the rat head as the imaging target. In each study the rat was injected intravenously with the PET tracer (1.3 mCi of F-18 fluoride and 2.8 mCi of F-18 FDG) and uptake allowed to occur with the animal awake. At the end of the uptake period (2 hours for F-18 fluoride and 1 hour for F-18 FDG) the animal was sacrificed and the head removed intact. Each head was packed snugly into a plastic tube having almost exactly the head diameter. After adding extra gauze to immobilize the head within the tube, the tube was sealed. Three glass capillary tubes partially filled with an F-18 solution were then taped to the sides of the tube. These partial line sources were oriented axially along the tube and were spaced at roughly equal angular intervals around the tube circumference with a fourth, shorter tube placed midway along the tube length. These tubes with attached line sources were then affixed to the mechanical rotation stage of the "PiPET" small animal PET scanner [3] and imaged for several hours in order to acquire large numbers of counts (16 M counts for F-18 fluoride and 44 M counts for F-18 FDG). These data were then reconstructed with FBP and ramp filter into forty-three 64 x 64 tomographic images that spanned the axial field-of-view. Spatial resolution in these images is approximately 1.8 mm (isotropic).

Following each PET study, the tubes were transported to a GE High Speed CT/i human CT scanner where the entire head was again imaged using the same CT settings (80 kVp, 100 mA, 1 mm thick slices, 96 mm x 96 mm in-plane FOV, 512x512 acquisition matrix).

After removing extraneous markers, the PET and CT volumetric data sets obtained in each study were registered with the AIR algorithm [2] using an implementation previously validated in human clinical studies [4]. Registrations were done using a rigid geometric transformation (six parameters) and no smoothing of either data set. For the case of F-18 fluoride and CT, the studies were treated as an intramodality registration since the CT and PET images showed a strong correlation between their intensity distributions. In contrast, The F-18 FDG and CT studies required manual intervention to segment the brain in both studies prior to registration. The algorithm in this case was applied not to the original greyshade images but to the homogeneous regions obtained from the segmentation masks. This semi-automated, user-validated segmentation process was needed, in part, because high FDG uptake structures are present in the FDG-labeled rat head that are not present in FDG images of the human head, e.g. the Harderian glands.

In both of these registration tasks, the "gold standard" was taken to be the position of 12 to 15 pairs of homologous points identified manually along the fiducial lines attached to the tubes. An estimate of the registration error after applying the

AIR algorithm was obtained following the methodology described by West et al. [5]. Differences found between the gold standard and the AIR algorithm in translation are the same throughout the registered images whereas the rotational error increases away from the center. As a result, we calculated the maximum registration error and the mean registration error over the entire brain volume.

III RESULTS

F-18 fluoride vs. CT. In this case, the automatic algorithm was robust and relatively insensitive to algorithm settings. The maximum registration error within the brain volume was less than 1.0 mm. Images illustrating this bone-to-bone registration are shown in Figure 1.

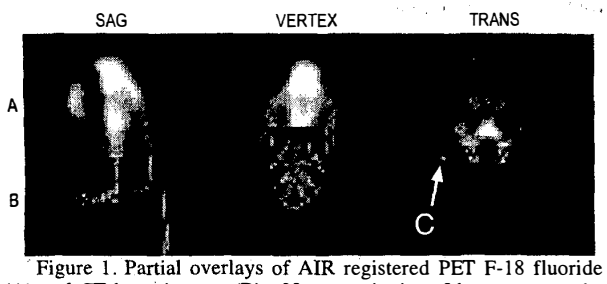

Figure 1. Partial overlays of AIR registered PET F-18 fluoride (A) and CT bone images (B). Note continuity of bones across the PET and CT image boundaries. C=capillary tube.

F-18 FDG vs. CT. In this case, the algorithm was unstable and could not be used until all non-brain structures were removed from both studies. Maximum mis-registration in this case was 2.4 mm with an average mis-registration of 2.1 mm. Images illustrating this brain-to-brain registration are shown in Figure 2.

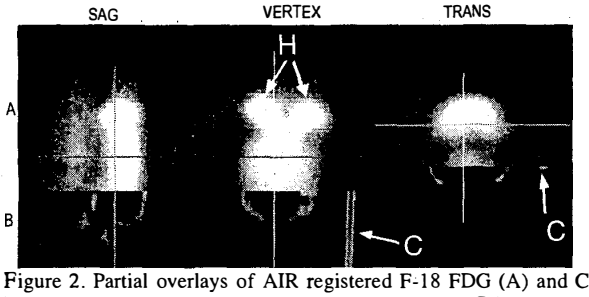

Figure 2. Partial overlays of AIR registered F-18 FDG (A) and CT brain images (B). Note the placement of the PET FDG brain within the CT skull. H=Harderian glands, C=capillary tube.

IV. DISCUSSION

The combination of PET and CT images of the same animal should improve PET target identification, attenuation correction and provide additional information that may be useful in improving PET study quality. In some circumstances it may be necessary to register these data spatially without external fiducial markers, a situation in which alignment might depend strongly on image content. The two cases studied here represent extreme versions of this situation, one in which homology between the sequences is nearly total (bone-to-bone) and the other a situation (brain-to-brain) where only the surface shapes of the structures to be registered are similar. As might be expected, registration errors were larger for the latter case than for the former by more than a factor of two. Given the great variability in the appearance of PET images of the brain for different tracers, it seems likely that registrations errors will also be variably large and, in all probability, tracer-dependent.

The failure of the automated features of the AIR algorithm in the brain-brain registration case is also noteworthy. The AIR algorithm was developed for multi-modality imaging in human subjects and contains default settings tailored to this application. In the present case, the rat head contains structures not present in humans, but which concentrate FDG more strongly than the brain. Unless these structures are removed by segmentation, the AIR algorithm cannot successfully register the PET and CT brain images. Thus, it may be that additional segmentation steps will have to be devised on a tracer-by-tracer basis to eliminate extreme anatomical and/or functional differences that exist between human and small animal studies.

Despite these complications, the present study does suggest that the AIR algorithm can register PET images of the skull and brain to CT images of the head with reasonable accuracy. Further studies, using improved fiducial markers to better assess registration accuracy and lower kVp to improve CT soft tissue contrast, will be required to determine to what degree this finding can be generalized to other tracers and organs.

V. CONCLUSIONS

The AIR registration algorithm, developed for use in multi-modality image registration in human subjects, can be used to automatically register CT with F-18 fluoride bone images of the rat head. PET FDG images of the brain can also be registered with CT but only after modifications that require user-intervention and that yield larger registration errors. Further studies are required to establish the generality of this approach for different tracers and for variations in each imaging procedure.

VI. ACKNOWLEDGEMENT

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VII. REFERENCES

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