Atlas-based attenuation correction for small animal PET/MRI scanners

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Small animal PET/MRI scanners producing anatomically co-registered simultaneously-acquired images of morphology, function and metabolic activity have become available and are expected to have a huge positive impact on the pre-clinical imaging field. Attenuation correction (AC) necessary for accurate quantification of PET signals is challenging in these scanners because the measured anatomical map from MRI is based on proton densities and not on electron densities. We propose a deformable mouse atlas-based registration method for AC in small animal PET/MRI. In this method, we first match the posture of the atlas to the posture of the mouse being imaged using landmark and elasticity constraints. The asymmetric L^2 pseudo-distance between the atlas surface and the extracted mouse surface is then minimized in order to register the two surface data. A Sobolov prior is used to ensure smoothness of the warping field. This warping field is then extended to the entire mouse volume using elastic deformations. The computed transform is then applied to the CT of the mouse atlas. Mutual information-based rigid registration is maximized to spatially normalize the warped atlas CT to the mouse MRI. We evaluated the proposed method for co-registered MRI and CT data acquired for a normal nu/nu mouse. Four organs were manually segmented from the animal MRI. Dice coefficients of organ overlap were measured for these organs between the manually assigned labels and those estimated by the proposed method. Dice coefficients were also measured between the skull and skeleton extracted directly from the animal CT and those estimated using the proposed method. Organ overlap of > 90 % in the head and torso region of the animal and > 60 % in the abdominal region are observed. For the skull and skeleton, the measured overlap was > 90 %. Based on published values, we derive a detailed attenuation map at 511 keV for the mouse using the warping field estimated by the proposed method.

Summary of 'Atlas-based attenuation correction for small animal PET/MRI scanners', Chaudhari et al.

I. Introduction

The magnitude of tissue attenuation for annihilation photons in small animal positron emission tomography (PET) is a fraction of that for humans, however, attenuation correction (AC) should help further improve overall quantitative accuracy of reconstructed PET images, especially in high resolution tomographs [1]. In PET/MRI scanners, direct estimation of the attenuation map is challenging because reconstructed MRI intensities relate to proton densities and not to electron densities [2]. There also are pitfalls in direct mapping of MRI values to absolute CT intensities [3]. Rotating a PET transmission source around the animal in magnetic field may lead to associated MRI artifacts and is not always possible because of space constraints. Thus, researchers have to resort to indirect methods based on image processing techniques for estimating the attenuation map from the acquired MR images [3]–[6]. Deformable mouse atlas-based AC approaches show great promise for AC in small animal PET/MR imaging as they can allow estimation of a detailed attenuation map. However, general purpose robust mouse registration techniques need to be developed in order to warp the atlas accurately to the animal being imaged.

In this paper, we propose a mouse atlas-based approach for AC of small animal PET images that can be summarized in three steps:

1) surface-based volumetric elastic warping of a deformable mouse atlas to the animal by posture matching and asymmetric L^2 distance minimization
2) refinement of volumetric registration by maximization of mutual information between the mouse MRI and the atlas CT
3) generation of a 3D attenuation map at 511 keV by assigning linear attenuation coefficients to each structure in the atlas according to the values obtained by logarithmic extrapolation of published CT attenuation values [7].

We evaluated the proposed method by warping the Digimouse [8] atlas to co-registered MRI and CT images of a mouse. We show comparisons of volumetric overlap between the warped atlas and those derived directly from the mouse MRI or CT using proposed method and those measured after rigid registration or only surface-based warping. We also derive a atlas-based attenuation map to be used for AC based on the proposed method.

II. Materials and Methods

A. Atlas registration

The Digimouse atlas was used as the anatomical template. Seventeen anatomical structures have been labeled in the Digimouse. The corresponding co-registered CT and volumetric tetrahedral mesh are also available. We register the Digimouse to the mouse that was imaged in four steps:

1) Creation of an elastically deformable Digimouse: We model the mouse atlas body as an elastic volume and therefore, deformations to it will be governed by the elastic equilibrium equation, i.e. at equilibrium, the elastic energy $L(u)$ corresponding to deformation u equals the external forces f applied on the body [9]:

$$L(u) = -\text{div}\left[(I + \nabla u)\,\hat{S}\right] = f \quad \hat{S} : \Omega \rightarrow \mathbb{R}^3, \qquad (1)$$

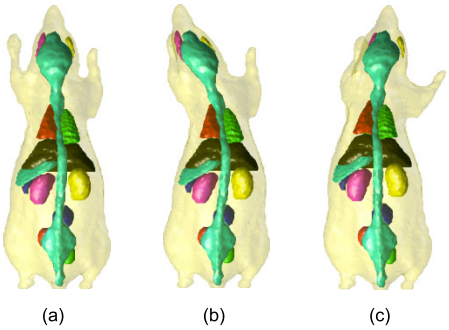

Fig. 1. The Digimouse atlas, (a) true posture, (b) and (c) different postures generated by choosing five landmarks on each animal surface. Also shown is the corresponding 3D animal volume deformation

where $\hat{S}$ denotes the second Piola-Kirchoff stress tensor defined by $\hat{S} = \lambda \text{Tr}(\hat{G})I + 2\mu\hat{G}$ and $\hat{G} = \frac{1}{2}\left(\nabla u^T + \nabla u + \nabla u^T \nabla u\right)$ represents the Green-St. Venant strain tensor. The coefficients λ and μ are Lamés elasticity constants. We discretized the elasticity operator L using a finite element method. Let $U = [U_1, U_2..., U_N]^T$ be the vector of displacements at N nodes in the tetrahedral mesh and K be the matrix that discretizes the elastic energy operator. When external forces are applied at the surface points such that the surface points $U_i, \{i \in \partial\Omega\}$ transform to their new locations V_i, the elastic energy becomes

$$E_{elastic}(U) = U^T K U + \alpha \sum_{i \in \partial\Omega} \|U_i - V_i\|^2 \qquad (2)$$

where $\alpha > 0$ is a mismatch penalty parameter. As a result, the whole mouse atlas volume deforms elastically when displacements are applied on only the surface nodes of its mesh.

2) Posture matching: In this step, the top surface of the mouse is extracted from the MRI scan. We select five landmarks on its surface, $(p_i, i = 1...5)$; one each at the ends of four limbs and one at the center of the two ears. The corresponding landmarks a_i are also selected on the deformable atlas. This gives five displacement vectors $W_i = (p_i - a_i)$ at the atlas surface points a_i. The displacement vector field is then extrapolated to the whole mouse surface $\partial\Omega$ by minimizing the Sobolov energy. Once the new surface points are determined, the displacement field is extrapolated to the whole volume using (2).

3) Asymmetric L^2-distance minimization based volumetric warping: In order to be able to register the surface topographies of the animals, the matching problem is formulated as an asymmetric L^2 pseudo-distance minimization, where the distance is computed from the mouse surface to the atlas surface. Smoothness of the displacement field is achieved by a Laplacian regularizer. The minimization of this pseudo-distance is performed by a searching strategy over the point-set and results in a displacement vector. This displacement vector on the surface is extrapolated to the volume using the deformable elastic model presented in (2).

4) CT-MRI volumetric warping: Once the volumetric deformation field that registers the atlas to the mouse based on surface-matching alone is determined, it is applied to the CT of the atlas. Rigid registration based on maximization of mutual information (MI) is then used to register this warped atlas CT to the mouse MRI directly.

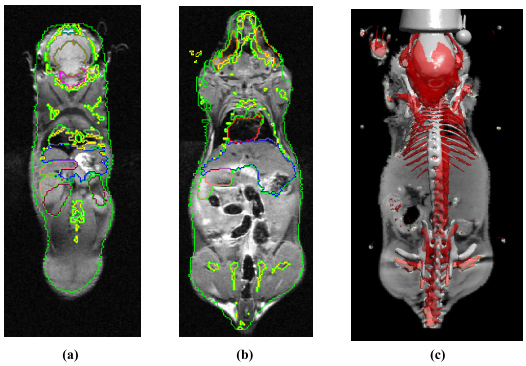

Fig. 2. Warping results using the proposed method, (a) and (b) horizontal sections from the mouse MRI with contours representing organ locations estimated by the proposed method, (c) overlay of the true skull and skeleton estimated from CT (red) and that estimated by the proposed method (gray).

TABLE I

DICE COEFFICIENTS FOR ORGANS WARPED ATLAS LABELS AND MANUALLY ASSIGNED LABELS

Organ name	Rigid registration	Surface-based warping	Surface + MI
Brain	0.16	0.83	0.87
Heart	0.64	0.80	0.81
Kidneys	0.11	0.32	0.41
Bladder	0.29	0.62	0.63
Whole body	0.41	0.96	0.97

B. Animal MRI and CT scanning and manual segmentation

A 25 gm nu/nu mouse was anesthetized and first imaged using the MicroCAT II CT scanner. The animal was transported MRI facility and was imaged using the Bruker 7T Biospec small-animal MR scanner equipped with the Bruker B-GA12 gradient coil set. We prevented any animal movement during the transfer between scanners. The brain, heart, kidneys and bladder were manually segmented from the MRI image and labels were assigned to these regions.

III. RESULTS

A. Examination of volumetric overlap

The labeled atlas was warped to the mouse MRI based on the steps outlined above. An overlay of warped labels and the mouse MRI is shown in Fig. 2(a) and (b). Assuming that the mouse CT and MRI are co-registered, the skull and skeleton were directly extracted from CT. Using the proposed method, the CT of the atlas was warped and the skull and skeleton were extracted from this warped CT. Fig 2(c) shows a 3D rendering of the true skull and skeleton of the mouse and that derived from the warped atlas.

We measured Dice coefficients of overlap for four organs between the warped atlas and those manually delineated directly from MRI. Table I shows the measured values. We compare our results against those obtained by direct rigid registration of the Digimouse CT to the mouse MRI, and those obtained after surface-based warping alone. Our results indicate that in regions such as the head and thorax regions, excellent organ overlap is observed. In spite of large inter-species variability in the abdominal region, overlap of $>60\%$ ($\sqrt{\text{Dice coefficient}}$) was measured. In a seperate study measuring overlap between both the skull and skeleton from the mouse CT and the warped atlas CT, a Dice coefficient of 0.86 was measured.

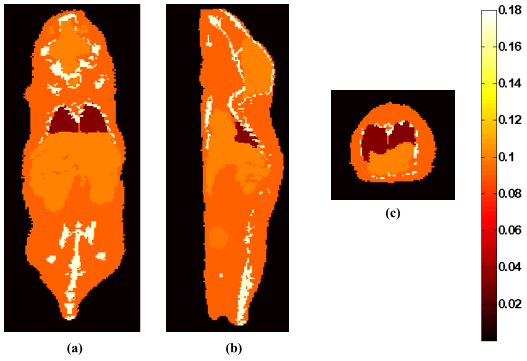

Fig. 3. Three orthogonal sections from the 3D atlas-based attenuation map at 511 keV. The units are cm^{-1}. The map has not been blurred to match the PET spatial resolution and noise has not been added.

B. Generation of the PET attenuation map

For generating an attenuation map from our method, we assigned linear attenuation coefficients to each structure in the warped atlas based on the corresponding organ labels. These values were obtained by logarithmic interpolation of published values [7] to compute specific coefficients at 511 keV. Our results are shown in Fig. 3, where three orthogonal sections from the 3D PET attenuation map are shown. A detailed attenuation map becomes available by our proposed method. We are in the process of evaluating the impact this has on quantitative accuracy of the corresponding PET images compared to using a CT-based two-tissue (bone and soft tissue) attenuation map.

IV. DISCUSSION AND CONCLUSIONS

We present a deformable atlas-based registration algorithm for generation of a detailed attenuation map for PET/MRI studies in small animals. A comparison based on Dice coefficient showed the proposed method resulted in a reasonably accurate alignment of the anatomical organs even though only surface matching and rigid volumetric registration are used. Organ overlap could further be improved by using a non-rigid mutual information-based registration for refinement of the warping of the warped atlas CT to the mouse MRI. Additionally, quasi-rigid priors could be included for registration that would allow only rigid movement of bones and joints, while still allowing soft tissue to deform in a non-rigid manner. We currently are implementing this approach. We will quantify PET signal accuracy by comparing conventional and the proposed method for AC in animal studies in the future.

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