Regression based Pseudo-CT Creation from Multimodal Images for PET Attenuation Correction in Hybrid PET-MRI

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Introduction: Inadequate photon attenuation correction in Positron Emission Tomography (PET) has serious implications, such as inaccurate cancer staging or failure to detect tumours [1]. In PET-CT hybrid imaging, a low dose CT image is used to create a tissue-specific attenuation coefficient map (μmap) using a bilinear transform [2]. In hybrid PET-MRI, however, attenuation has to be corrected in the absence of CT. MRI-based attenuation correction (MRAC) is challenging because there is no direct correspondence between tissue attenuation coefficient and image intensity in MRI. Particularly, bone and air exhibit similarly low MRI signal but very different attenuation coefficient. In the majority of existing MRAC methods, image voxels are classified into different tissue types (mainly bone, soft tissue, sinuses, lung and air) with distinct attenuation coefficients. The classes are then assigned with the corresponding attenuation coefficient (an empirical constant) to create a discrete μmap [2, 3]. These methods often suffer from quantisation error, failing to describe the continuously varying attenuation coefficient in a single tissue type, such as lung and sinuses. To address these problems, other MRAC methods employ regression algorithms to calculate a continuous μmap from ultrashort-echo-time (UTE) MRI and/or population-based attenuation correction template [4, 5]. Nevertheless, UTE has not been clinically applicable as its specific absorption rate is too high. Template or atlas based methods are not subject-specific and may fail to represent inter-subject anatomical variation caused by specific pathology (e.g. bone removal).

In clinical settings, different MR images are usually acquired for each patient, particularly oncology patients. These may include structural, diffusion-weighted, and dynamic contrast enhanced (DCE) MR images. In previous studies, we demonstrated that ucPET data was useful in classifying bone, air and soft tissue in MR head images [3, 6]. Similar findings were reported for whole-body PET-MR imaging recently [7]. In this study, we present a regression based, subject specific, MRAC for PET-MRI using clinically available MRI and the raw (uncorrected) PET image (ucPET).

Subjects and Methods: Thirteen patients with confirmed world health organisation grade III and IV brain tumour were scanned. Structural MR images were acquired using MP-RAGE sequence with FOV 24x25.6x17.6 *cm*, TR/TE/TI 2300/2.26/900 *ms*, flip angle of 90, and 1 *mm* isotropic resolution. DCE-MRI were acquired with a 3D fast gradient echo sequence with matrix 256x256, TR 8.1 *ms*, 4 averages, voxel size 1.1x0.9x2 mm^3. A 4-dihydroxy-6-[18F]-fluoro-L-phenylalanine (FDOPA) PET scan with an isotropic image resolution of 2 mm was acquired within 48 hours of the MRI scans. A low dose CT transmission scan (5 seconds) was acquired before administration of an intravenous injection of the tracer (150mSv). The FDOPA images were acquired between 10 and 30 minutes post injection. All MR images were acquired using a 3T Siemens TimTrio (Siemens, Erlangen, Germany) and FDOPA PET scans using a Philips PET/CT GXL scanner (Eindhoven, Netherlands). Intra-subject rigid registration was performed to align all images to the MP-RAGE image and resample to 1 *mm* isotropic voxel size. Inter-subject registration was not attempted. A sample set of images of the nasal slice is shown in Fig. 1.

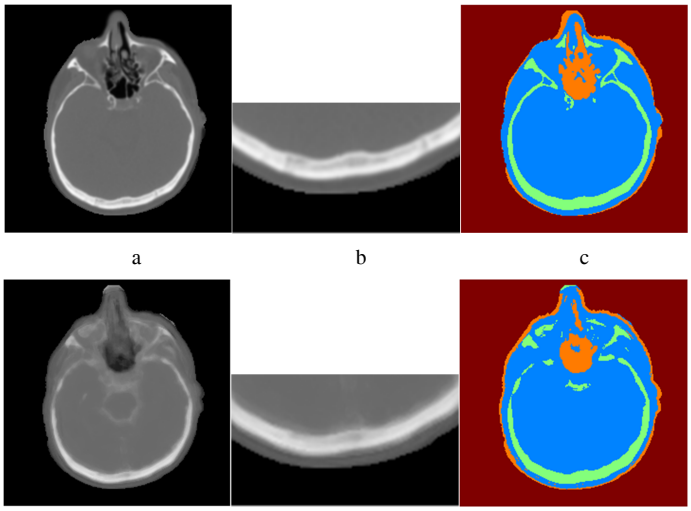

Figure 1: Sample results: (a) original CT image, (b) CT close up view on the cavity in the occipital bone (c) CT-based "ground truth" using thresholding (d) regression result, (e) regression close up view on the cavity in the occipital bone (f) regression-based thresholding.

For each patient, a pseudo-CT image was generated using a voxelwise regression. A total of over 400 features in categories of gradient features, textual features, and contextual features [3] were extracted from MP-RAGE, pre- and post-contrast DCE, and ucPET images. In view of the large number of features, random forest based regression was chosen because of its immunity to 'curse of dimensionality' [3]. An axial slice going through the nasal cavity, which is the most problematic region, was chosen for each patient and used for training the algorithm. 500 voxels per slice were randomly selected from each subject for training the random forest. Leave-one-subject-out cross validation was employed to evaluate the regression performance. For measuring the performance of the method the background from all images was eliminated and two metrics were calculated: (i) the Pearson's correlation between the regression result and the original CT image (inside the head), and (ii) the Dice Similarity Coefficient (DSC) score between the segmentation result and the 'ground truth' obtained by thresholding CT images.

Table I. DSC between CT and regression result.

	Mean	Min	Max
Bone	0.68	0.57	0.77
Air	0.73	0.63	0.82
Soft tissue	0.86	0.81	0.92

Results: The mean correlation between the regression result and the original was 0.82, with a minimum of 0.75 and a maximum of 0.89 ($p<0.01$). The mean DSC of the different tissue classes are summarised in Table 1, while a sample qualitative result is illustrated in Figure 1.

Discussion and Conclusion: We presented a regression based method to generating a subject-specific pseudo-CT image from a set of clinically available images for oncology patients, including structural and DCE MR images, and attenuation uncorrected FDOPA PET image. The proposed method negates the need for tissue segmentation or population-based template construction. The features used are invariant to translation and rotation and therefore no inter-subject spatial alignment is required. Preliminary results exhibit high correlation and DSC between the pseudo-CT and the real CT. These quantitative results suggest that the generated pseudo-CT has the potential to be useful for photon attenuation correction in the absence of CT image, as in the case of hybrid PET-MRI. Qualitative analysis of the results also suggests that regression based attenuation map has the potential to overcome the intensity quantisation limitation of classification based methods. As shown in figure 1, the cavity in the occipital bone can only be reconstructed using regression but is lost when the image is quantised based on tissue classes.

Figure 1 also demonstrates the limitation of this study in the form of biased estimation of bone tissue in the centre of the brain, where the soft tissue is indicated by the CT image. This bias is likely to be the result of the low number of sample points that was used for training of the random forest regression. A larger number of sample points should increase the accuracy of the result but will also dramatically increase calculation times. This aspect will be further explored in the next step of this study.

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