Multi-modal deformable image registration for quantitative assessment of radiation-induced ventilation and perfusion changes in lung cancer patients

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Background

Medical image registration continues to see much research interest due to its increased use in mono- and multi-modal diagnosis, treatment planning and assessment. The field is largely dominated by methods developed for use on brain images, being easier to register due the lack of motion in the organ being imaged[1]; pulmonary images are not afforded this luxury. The latter often involves free breathing image acquisitions or breath hold images acquired at the extremes of inflation, requiring significantly more computational effort for accurate registration. Nonetheless, research in this field is on the rise due to the development of efficient deformable registration algorithms and increasingly widespread availability of computational resources[1]. In this study, deformable image registration is used to align the dose delivered during radiotherapy (RT) to structural and functional magnetic resonance (MR) images to allow the assessment of regional lung function changes post-RT.

Purpose

The aim of this study was to develop registration algorithms to align:

1. free-breathing computed tomography (CT) (and related dose distributions, tumour volumes) to inspiratory breath-hold CT;
2. inspiratory CT to a proton (^{1}H) MR image acquired in the same breath as a hyperpolarized (HP) helium (^{3}He) ventilation image (with the resulting transforms also applied to the output from point 1);
3. dynamic contrast enhanced perfusion (DCE) MR images to the same-breath ^{1}H MR image from point 2.

This shall facilitate both quantitative and qualitative (outside the scope of this project) analysis of the effects of radiotherapy on the lungs.

Methods

This study utilised inspiratory, expiratory and free breathing CT, HP ^{3}He and ^{1}H MR images and DCE lung perfusion images of 22 patients with non-small cell lung cancer undergoing radiotherapy. Of these 22 patients, 10 had only pre-treatment images and the remaining 12 had pre- and post-treatment images available; not all patients and visits contained every type of CT or MR image, so in some cases specific registrations were not possible. Prior to registration, for the free breathing CT images, initial lung mask segmentations generated from a deep learning algorithm were manually edited using ITK-SNAP. The state-of-the-art image registration toolkit, Advanced Normalization Tools (ANTs)[2] was used for the registration. Each registration comprised three distinct steps; rigid, affine and diffeomorphic (BSplineSyN) that has seen previous effective application in lung registrations[3]. Initially, mono-modal registration was used to align free breathing CT images, dose distributions and segmentations to inspiratory CT and then multi-modal registration was used to align these components to the same-breath ^{1}H magnetic resonance imaging (MRI) spatial domain. In addition, DCE lung perfusion MR images were also registered to the same-breath ^{1}H MRI spatial domain. The registrations carried out are illustrated in Figure 1. Due to the high computational demand for pulmonary deformable registration, bash scripts containing each full registration were run on the INSIGNEO nodes of the Sheffield Advanced Research Computer (ShARC). Each script contained a distinct pre-processing, masking, resampling, registration and evaluation section and was applied to images/segmentations/doses in the domain as necessary. As well as the previously mentioned registrations, multiple other intra-modality visit 2 to visit 1 registrations were carried out. Image registration accuracy was assessed using the Dice similarity coefficient.

Finally, analysis of statistical information, including mean, standard deviation, maximum, minimum, count, volume and extent was carried out for a random subset of 5 patients for the output from registration 2 detailed in the Purpose section. This served as a sanity check to ensure that there was no information loss or undesired fundamental changes made to the images through registration.

Results

Figure 2 shows an example of the registrations carried out to (a) map the dose from free breathing CT domain to same-breath ^{1}H MRI domain and (b) map the DCE perfusion MR image to same-breath ^{1}H MRI domain thus bringing delivered dose and perfusion information into the same domain as ventilation information allowing for quantitative assessment. Figure 4 shows that high Dice scores were achieved using the implemented registrations. Finally, Figure 3 shows an analysis of the percentage difference in means of different image and mask combinations pre and post image mapping, studied in the statistical analyses.

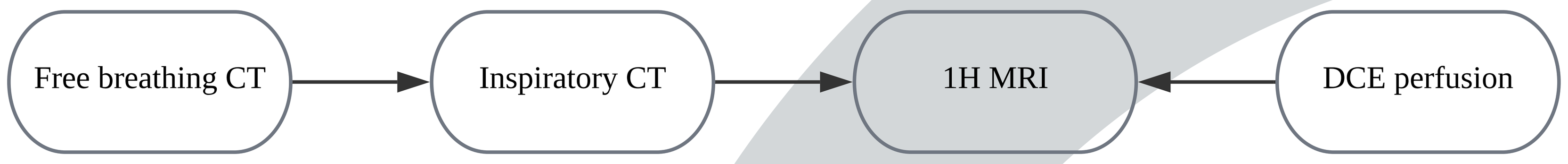
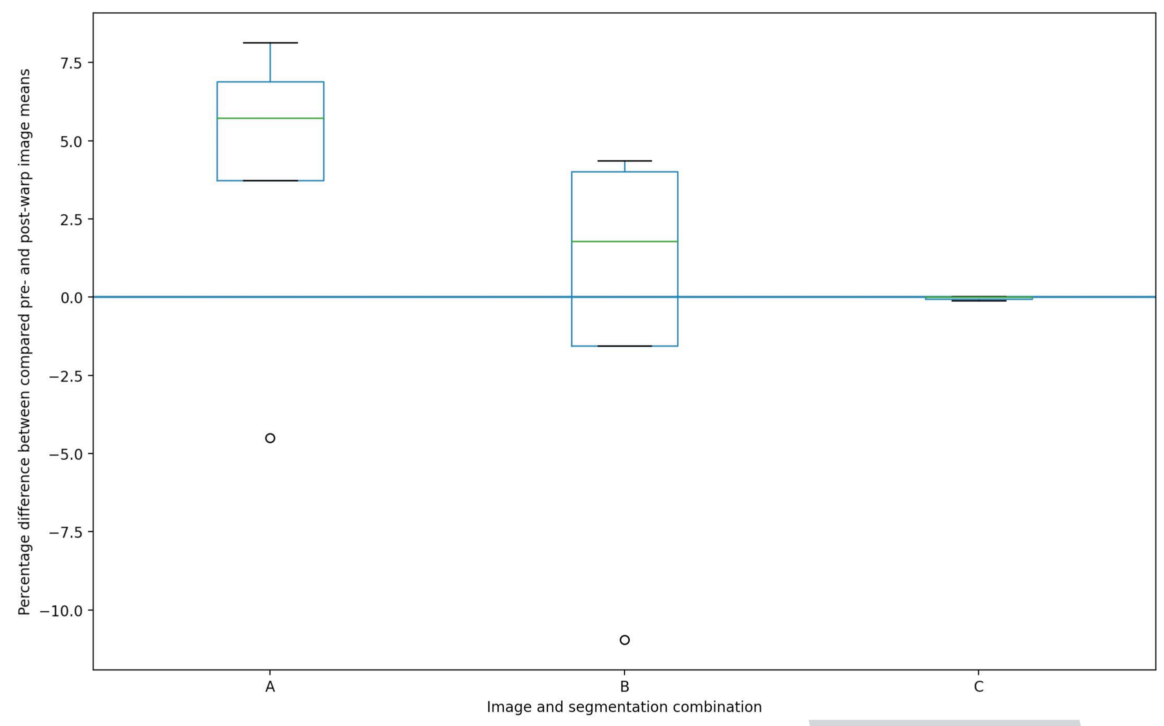


Figure 1 – An illustration of the different registrations applied; each arrow represents a registration.



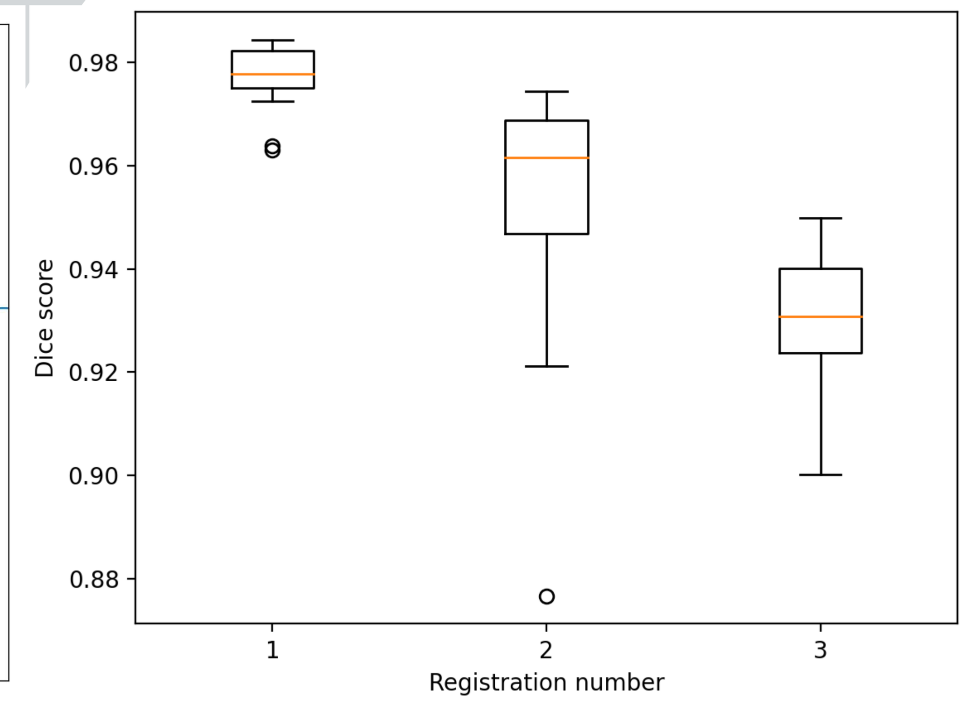


Figure 3 shows the percentage difference in the means of (A) the absolute dose and inspiratory mask to the warped absolute dose and warped inspiratory mask, (B) the absolute dose and inspiratory mask and the warped absolute dose and ^{1}H MRI mask and finally (C) the absolute dose and given treatment volume (GTV) and the warped absolute dose and warped GTV.

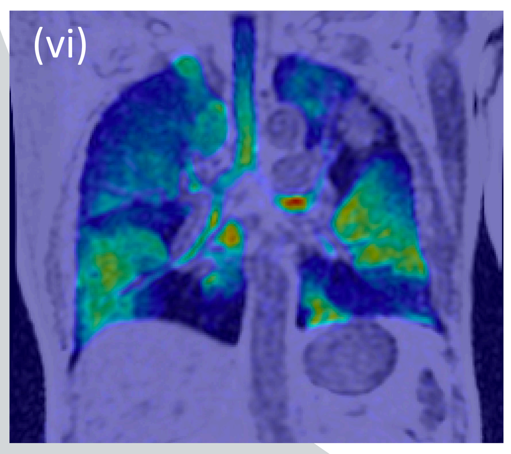
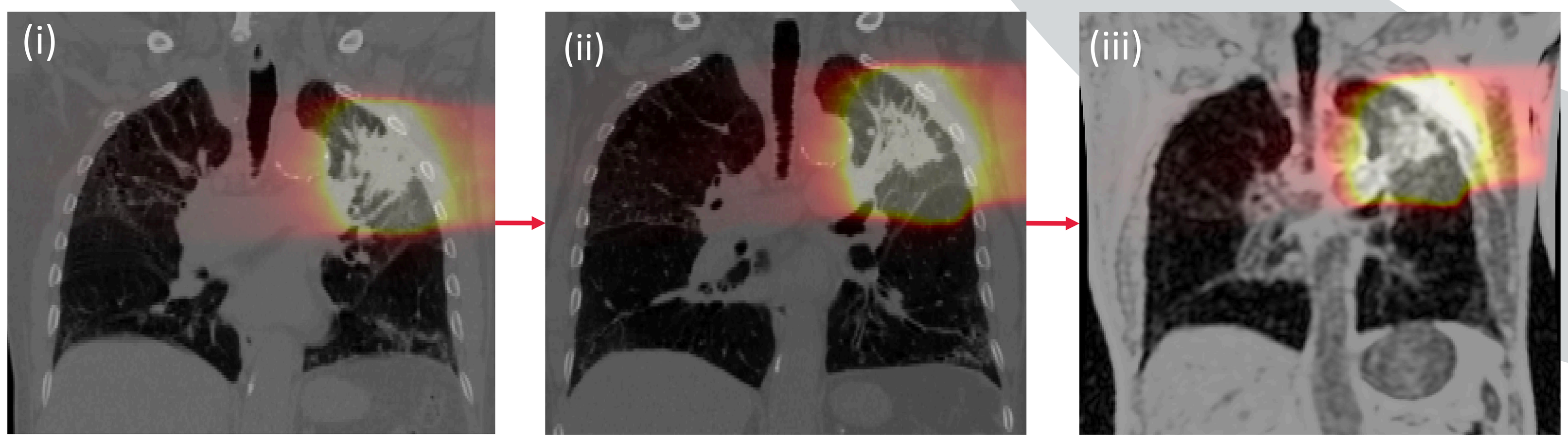


Figure 4 shows the Dice scores of registrations 1, 2, and 3 outlined in the Purpose section. These Dice scores were calculated between the fixed image mask and the warped moving image masks in each case



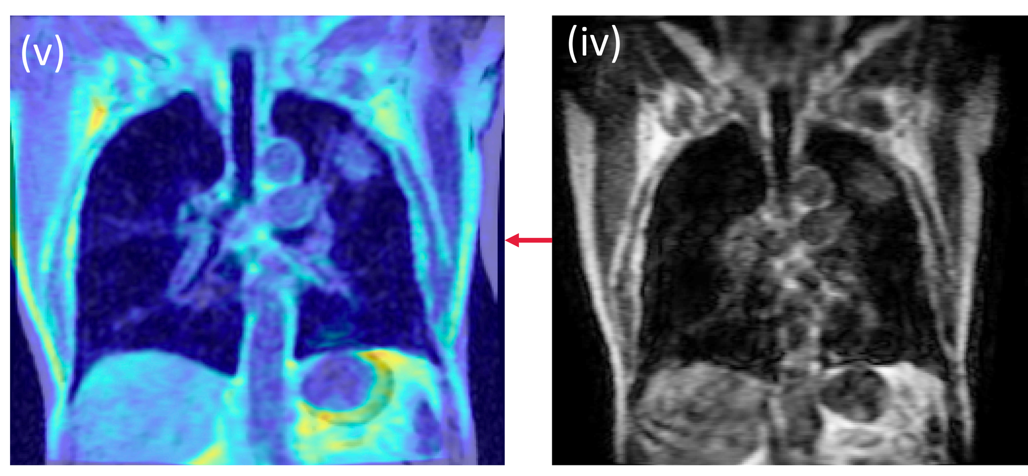


Figure 2(i-vi) – Images of the registrations for a representative patient. (i) depicts the free breathing CT fused with the RT dose. This was then sequentially registered to the inspiratory CT image (ii) and same breath ^{1}H MR image (iii). The RT dose shown in a 'hot' overlay in images (ii and iii) is the transformed dose according to the registrations output transform fields at each step. (iv) is the DCE lung perfusion MR image and is registered to the same breath ^{1}H MR images where it is shown as a 'jet' overlay in (v). (vi) shows the patient's ^{1}H MRI with the HP ^{3}He MRI as a 'jet' overlay.

Conclusions

In this study, through mono- and multi-modal registration, RT dose distributions, tumour contours and perfusion information for lung cancer patients undergoing radiotherapy was mapped onto same-breath ^{1}H and HP gas MRI domain, facilitating qualitative and quantitative analysis of dose related changes in perfusion and ventilation. Image registration quality was verified by qualitative and quantitative analysis. The image registration methods applied may now be used to plan and evaluate future treatments in patients with lung cancer.

References

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