Inverse-consistent rigid registration of CT and MR for MR-based planning and adaptive prostate radiation therapy

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Abstract. MRI-alone treatment planning and adaptive MRI-based prostate radiation therapy are two promising techniques that could significantly increase the accuracy of the curative dose delivery processes while reducing the total radiation dose. State-of-the-art methods rely on the registration of a patient MRI with a MR-CT atlas for the estimation of pseudo-CT [5]. This atlas itself is generally created by registering many CT and MRI pairs. Most registration methods are not symmetric, but the order of the images influences the result [8]. The computed transformation is therefore biased, introducing unwanted variability. This work examines how much a symmetric algorithm improves the registration.

Methods: A robust symmetric registration algorithm is proposed that simultaneously optimises a half space transform and its inverse. During the registration process, the two input volumetric images are transformed to a common position in space, therefore minimising any computational bias. An asymmetrical implementation of the same algorithm was used for comparison purposes.

Results: Whole pelvis MRI and CT scans from 15 prostate patients were registered, as in the creation of MR-CT atlases. In each case, two registrations were performed, with different input image orders, and the transformation error quantified. Mean residuals of 0.63±0.26 mm (translation) and (8.7±7.3)×10⁻³ rad (rotation) were found for the asymmetrical implementation with corresponding values of 0.038±0.039 mm and (1.6 ± 1.3) × 10⁻³ rad for the proposed symmetric algorithm, a substantial improvement.

Conclusions: The increased registration precision will enhance the generation of pseudo-CT from MRI for atlas based MR planning methods.

1. Introduction

Medical image registration is a computerised alignment process now well established in many prospective or curative clinical workflows. In particular, in image-guided radiation therapy (IGRT) the planning CT volume is aligned with the portal images of the linear accelerator (linac) in order to ensure the accurate delivery of the radiation dose to the tumour region. One weakness of the classical IGRT approach for the treatment of prostate cancer is that the planning CT might not be an accurate representation of the patient anatomy throughout the whole duration of the treatment, which might consist of around 35 fractions delivered over a span of 7 weeks. As it is not generally considered acceptable in clinical practice to perform multiple CT acquisitions...
during the course of the treatment, adaptive MRI-based prostate radiation therapy has been proposed as a way to adapt the treatment dose planning to a changing patient's anatomy at regular intervals. This approach promises to significantly increase the accuracy of the curative dose delivery processes while reducing overall patient exposure to radiation. With MRI-alone treatment planning, the planning CT itself is replaced by a MRI acquisition that serves as a reference for the calculation of the radiation plan. The main challenge in MRI-alone treatment planning and adaptive MRI-based prostate radiation therapy is to estimate the electron density map from MRI acquisitions.

As it is generally acknowledged, there is no simple mapping between any clinically relevant MRI intensity and the underlying electron density [3]. State-of-the-art methods address this challenge by registering the MR image with a CT volume representing the same anatomy, and then use the spatial mapping between the MRI and the CT to estimate the probable CT intensity, and thus the electron density, at each MRI voxel location. By repeating this process with multiple patients, a CT-MR atlas is built. In turn, a new MR scan, which does not have a corresponding CT, can be registered with this atlas in order to estimate the electron density [5]. With this approach, it is required to accurately register CT and MR scans of the pelvis, which is a hard multi-modal problem. In addition, most registration methods are not symmetric, but instead the order of the images influences the result [8]. The computed transformations are therefore biased, introducing unwanted variability in the process. This phenomenon is usually referred to as the inverse consistency property of an algorithm, and the inverse consistency problem refers to the definition of algorithms that are independent of the input image order.

While the inverse consistency problem was the subject of a certain number of articles [11, 10, 2, 8] in recent years, they were mostly concerned with overall flexible transformations [11, 10, 2]. The inverse consistency issue was largely ignored in the seemingly easier rigid transformation. One notable exception is the work of Reuteur et al [8] who implemented and published an inverse-consistent method as part of the FreeSurfer [1] package. Unfortunately, in our experience, this method is not robust enough to register CT and MR scans of the pelvis. This paper thus presents a new inverse consistent rigid registration method, and examines how much an inverse consistent algorithm improves the registration.

2. Methods
A robust symmetric registration algorithm is proposed that simultaneously optimises a half space transform and its inverse. During the registration process, the two input volumetric images are transformed to a common position in space, therefore minimising any computational bias. An asymmetric implementation of the same algorithm was used for comparison purposes.

2.1. Symmetric formulation of the registration problem
Let $I_1$ and $I_2$ be the two volumetric images to be registered. Classic registration methods usually involve finding the transformation $T$ that minimise an energy function of the form

$$E_C = \sum_{\forall x \in \Omega} M(I_1(x), I_2(T(x))),$$

where $M$ is a certain metric characterising the difference between two image intensities, and where $x \in \Omega$ represent a spatial coordinate inside the domain of interest. Such energy function is minimal when the rigid transformation $T$ reduces the overall distance between $I_1$ and $I_2$, as computed by the metric $M$, as much as possible. In practice, however, the transformation of a spatial coordinate $T(x)$ will generally not fall on the image grid, so some interpolation method must be used when computing image intensities $I_2(T(x))$. In contrast, this is not the case with image intensities $I_1(x)$, which bias the result toward $I_1$. Hence, registering $I_1$ with $I_2$ is not
equivalent to registering $I_2$ with $I_1$, and significant differences can be observed in practice, as is demonstrated in section 3.

The inverse consistency of the method can be improved by adopting a fully symmetrical formulation, as follows:

$$E_{\text{Sym}} = \sum_{\forall \mathbf{x} \in \Omega} M(I_1(T^{-1/2}(\mathbf{x})), I_2(T^{1/2}(\mathbf{x}))).$$  \hspace{1cm} (2)

In this case, the transformation $T$ is split in two parts using a matrix square root transform such as $T = T^{1/2} \times T^{-1/2}$, where $T^{-1/2}$ denotes the matrix inverse of $T^{1/2}$. With this formulation, a spatial coordinate $\mathbf{x}$ is transformed before sampling either $I_1$ or $I_2$. Therefore, the two images are given an equivalent treatment, and the formulation is perfectly symmetric and mostly unaffected by a switch in the input image order. The classic and the inverse-consistent registration schemes are represented in Fig. 1.

2.2. Robust image registration via block matching

The algorithm presented in this paper is based on a robust block matching approach that has been demonstrated as being effective at aligning difficult datasets [7]. The algorithm performs a local minimization of the image comparison metric, and iteratively updates a global rigid transformation. It is composed of three main steps:

(i) **Image resampling.** In the first step, the two input images are resampled in a way such that they share a common image grid (see discussion in section 2.3). Tri-linear interpolation is used for both images.

(ii) **Block matching.** After the images have been resampled, the image domain is divided into an $N_1 \times N_2 \times N_3$ grid of $N$ cubic blocks of size $B^3$. Then, a block from the grid covering $I_1$ and centred at $\mathbf{x}$ is matched against the blocks from $I_2$ that are centred at $\mathbf{x} + \epsilon$, where $\epsilon = [i, j, k], i, j, k \in \{-L, \ldots, -l, 0, l, \ldots, L\} \subset \mathbb{Z}$. The position $\mathbf{x}^* = \mathbf{x} + \epsilon^*$ maximizing the block matching metric is kept if and only if: a) the matching score is higher than a small numerical epsilon, and b) the best matching score is significantly higher than the second best. In that case the pair $\{\mathbf{x}, \mathbf{x}^*\}$ is stored in the set $C_1$. This process is repeated independently for all blocks of the grid covering $I_1$, resulting in a set $C_1$ of at most $N$ matches. The whole block matching process is also repeated for all the blocks from the grid covering $I_2$, storing the correspondences in the set $C_2$. At the end of the block matching process, we thus have two sets of correspondences, $C_1$ and $C_2$. In this study, we used $B = 9$, $L = 28$, $l = 3$, and the block matching metric was normalized cross-correlation [7].

(iii) **Updating the rigid transformation.** In the last step, the rigid transformation $T$ is updated by using a quaternion representation and a robust process: a) create the set of all correspondences $C = C_1 \cup C_2^-$, where $C_2^-$ correspond to set $C_2$ but with the $\mathbf{x}$ and $\mathbf{x}^*$ swapped; b) compute the rigid transformation that best aligns the set of all $\mathbf{x} \in C$ with

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**Figure 1.** Left: classic registration scheme corresponding to (1), Right: inverse-consistent registration scheme corresponding to (2).
Figure 2. Evaluation of the consistency of the classic and inverse-consistent implementation of the presented registration algorithm. The graphs show the residual between the registration transformations computed using the forward (MRI→CT) and backward (CT→MRI) scheme.

the set of all $x^* \in C$ [6]; c) create $C^*$, a subset of $C$, by computing the distance between the points of all pairs $\{x, T \cdot x^*\} \in C$ and keeping the size$(C)/2$ points with the smallest distance; and d) iterate steps b) and c) until convergence, but using $C^*$ in place of $C$.

The registration algorithm iterates through steps (i), (ii), and (iii) until the computed transformation changes little or until a certain number of iterations have been performed.

2.3. Implementation details

The algorithm described above was implemented within a multiresolution approach. Given the two input images, the software automatically computes three levels of resolution: the first level is defined as the minimum size along each dimension of $I_1$ and $I_2$, and subsequent levels are defined by halving the image dimensions of the precedent level that have the highest value (if two dimensions have the same size, both are halved). The algorithm starts from the lowest resolution level (level 3), and then progressively refines the registration transformation at the higher resolution levels. The algorithm was implemented in C++, and the block matching step was parallelized on the CPU. Registering a CT with an MR scan took around 90 sec on a 6 core Intel® Xeon® W3670 at 3.20GHz desktop computer.

3. Experiments and results

Ethics approval for the study protocol was obtained from the local area health ethic committee, and informed consent was obtained from all patients. CT scans were acquired as part of the normal patient radiation therapy process with either a GE LightSpeed radiotherapy large bore scanner with 2.0 mm slices or a Toshiba Acquilion scanner with 2.5 mm slices. MRI scans were T2 scans of type FSE-x1 with a field of view encompassing the entire pelvis. TE was 15ms, TR was 675ms, and the slice thickness was 3.00 mm [5]. For the purpose of this evaluation, 15 CT-MRI scans pairs were randomly selected in the collected dataset.

The presented inverse-consistent registration algorithm (implementing (2)) was evaluated and compared to a classic formulation of the same algorithm (implementing (1)). The two versions of the software were rigorously identical in what concern the multiresolution approach, the image resampling techniques, and the block matching method used, and differed only in the management of the rigid registration transformation, as described in section 2.
Figure 3. Example of CT–MR multimodal registration for patient 11. Top: results obtained with the classic implementation. Bottom: results obtained with the inverse-consistent implementation. Annotations indicate some areas of interest. The MR images are displayed for visual reference. The CT images have been resampled into the MR space using either the forward transform or the inverse of the backward transform. The difference images present the result of the subtract of the two CT images; black indicate a value $\leq -50$, white a value $\geq 50$, and grayscale are linearly interpolated between those two extreme. In the case of the inverse-consistent implementation, the all gray images indicate very small differences.

We evaluated the inverse consistency of the classic and inverse-consistent implementation of the algorithm by conducting two registrations for each dataset, for each implementation: 1) the registration of each MRI scan with the corresponding CT scan from the same patient (forward registration), and 2) the registration of each CT scan with the corresponding MRI scan (backward registration — the order is inverted). The result of the registration processes is a $4 \times 4$ rotation matrix in homogeneous coordinates [4], so the quantification of the difference between the forward and backward registration results need to be split in two parts. The translation component of the two rigid transformations can be compared directly, so that we have

$$\Delta_t = \| t_b - t_f \|,$$

where $t_f$ and $t_b$ are the translation component of the forward and backward rigid registration transformation, respectively. The rotation component of the rigid registration matrices are not linear and thus cannot be compared directly [4]. We thus converted the rotational part of the rigid transformation matrices into the forward and backward rotation vectors $r_f$ and $r_b$ [9]. The difference in rotation is then quantified as

$$\Delta_r = \| r_b - r_f \|.$$
Residuals (Mean±StdDev) of $\Delta_t = 0.63 \pm 0.26$ mm and $\Delta_r = (8.7 \pm 7.3) \times 10^{-3}$ rad were found for the classic implementation with corresponding values of $\Delta_t = 0.038 \pm 0.039$ mm and $(1.6 \pm 1.3) \times 10^{-3}$ rad for the proposed inverse-consistent algorithm, a substantial improvement. Detailed results on a per-patient basis can be seen on Fig. 2, sample qualitative results are presented in Fig. 3.

4. Conclusion
The proposed inverse-consistent algorithm improved the consistency of the rigid registration algorithm by an order of magnitude. However, the results indicate that even the inverse consistent formulation does not lead to totally consistent results at high accuracy. After further investigation in the software, it appears that this limitation is the result of the accumulation of very small numerical errors due to the limited precision of the computer platform used. Nonetheless, we believe that the precision currently achieved is suitable for most clinical applications, especially in those concerning difficult multimodal registration problems, such as in the creation of CT-MR atlases for MRI-alone treatment planning and adaptive MRI-based prostate radiation therapy. The increased registration precision will enhance the generation of pseudo-CT from MRI for atlas based MR planning methods.

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