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Towards adaptive radiotherapy for head and neck patients: validation of an in-house deformable registration algorithm

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Abstract. The purpose of this work is to validate an in-house deformable image registration (DIR) algorithm for adaptive radiotherapy for head and neck patients. We aim to use the registrations to estimate the "dose of the day" and assess the need to replan. NiftyReg is an open-source implementation of the B-splines deformable registration algorithm, developed in our institution. We registered a planning CT to a CBCT acquired midway through treatment for 5 HN patients that required replanning. We investigated 16 different parameter settings that previously showed promising results. To assess the registrations, structures delineated in the CT were warped and compared with contours manually drawn by the same clinical expert on the CBCT. This structure set contained vertebral bodies and soft tissue. Dice similarity coefficient (DSC), overlap index (OI), centroid position and distance between structures' surfaces were calculated for every registration, and a set of parameters that produces good results for all datasets was found. We achieve a median value of 0.845 in DSC, 0.889 in OI, error smaller than 2 mm in centroid position and over 90% of the warped surface pixels are distanced less than 2 mm of the manually drawn ones. By using appropriate DIR parameters, we are able to register the planning geometry (pCT) to the daily geometry (CBCT).

1. Introduction

The concept of adaptive radiation therapy (ART) was introduced by Yan *et al* as a closed-loop feedback process, where the variational positioning of the beams and internal motion of the patients are systematically monitored and characterized, and the plan is modified accordingly [1]. Cone-beam computed tomography (CBCT) is an online imaging method that provides valuable 3D information of the patient in treatment position but with incorrect Hounsfield units (HU) for dose calculations [2]. Deformable image registration (DIR) can help resolve the major challenges in ART: planning computed tomography (pCT) scans warped to match the daily cone-beam CT (CBCT) can be used for reliable dose calculations and to facilitate dose summation and automatic recontouring [3]. A fast, accurate, and robust CT-CBCT DIR algorithm is then a fundamental step in ART implementation. While there are a wide variety of studies assessing the quality of CT-CT deformable registration with patient data [4, 5], for CT-CBCT (a quasi-intermodality case) they are scarcer [6, 7]. Particularly, Castadot *et al* (2008) compare 12 CT-CT registration strategies combining different registration algorithms

[8]. However, in our opinion it is as important to carefully tune the registration parameters as it is to choose an appropriate algorithm, as a bad choice of parameters can cause in sub-optimal or even unacceptable registration results.

In this work we investigate a DIR algorithm implemented at University College London (UCL) to register the planning CT and weekly CBCT images taken from head and neck (HN) patients, a cohort known to benefit from ART [9].

2. Methods and Materials

2.1. Patients data acquisition and registration

Data from 5 HN patients treated in our clinic was used in this study. These patients presented considerable anatomical changes throughout their treatment, and were referred for midtreatment re-planning. The CT was acquired on a GE Widebore 16 slice system, while the VARIAN (Palo Alto, USA) OBI (on-board imaging) system integrated in the linear accelerator was used to acquire weekly CBCT images. The resolution was $0.979\times0.979\times2.5$ mm^3 and $0.897\times0.897\times2$ mm^3, for the CT and CBCT images respectively.

NiftyRef is an open-source registration package developed by UCL's Centre for Medical Image Computing, containing a GPU implementation of the B-spline deformable registration algorithm [10]. On a preliminary study we investigated proper registration parameters to be used in CT-CBCT registration in the HN region [11]. The optimal range of parameters found was: bending energy (BE) weight between 2 and 6%, logarithm of the jacobian weight of 1%, a maximum of 1000 iterations, a binning of 32 for the joint histogram calculation, intensities thresholded to the range [-1000 2000] and a control point spacing (CPS) between 5 and 10 voxels. Lower BE allows more liberty for the algorithm to perform larger contractions and expansions, however if its weight is too small the registrations are under-constrained and unrealistic deformations are likely to occur. The logarithm of the jacobian penalty term encourages the registrations to be folding-free. Masking refers to defining the region in the CBCT where the deformation field is optimized, considerably speeding the computation. For a full explanation of the different parameters see [11]. As a follow-up of this study we found evidence that pre-processing the CBCT image with non-linear intensity adjustment (gamma correction) improved the registrations. These conclusions led to the selection of a variety of parameters settings, tested here more extensively. The aim is to find a single set of parameters that performs well over all the datasets available.

2.2. Assessment of the quality of the registrations

Registrations were compared by visual inspection, computation time and similarity of warped structures with a gold standard. The resulting deformation field can be used to map points and regions of interest delineated in the pCT dataset to the CBCT dataset. Structures delineated in the pCT were warped and compared with contours manually drawn by the same physician on the CBCT. Due to the noise and low contrast inherent to CBCT imaging, it is difficult to define points or delineate structures with confidence and consistency. We chose a set of structures that can be seen unequivocally on the CT and CBCT, even though it may not contain some of the typical organs-at-risk (OAR) of the HN region. The set contains a mixture of soft tissue and bones, and was representative of the patient daily positioning and weight loss process. Vertebras C1, C4 and C7 were considered as bone landmarks for different regions, while external body and sternocleidomastoid muscles were chosen as surrogates for soft tissue.

Structures manually drawn in the CBCT and deformed from the pCT were compared using Dice similarity coefficient (DSC) [8], Overlap index (OI) [5], Distance transformation (DT) [4] and centroid position error (CoM) [4]. Dose comparisons, considering dose-differences (DD) and gamma analysis (γ), were performed to assess whether reduced accuracy but faster registrations had a noticeable effect on dosimetry. Dose calculations for the same IMRT plan were performed using VARIAN Eclipse analytical anisotropic algorithm.

Table 1. Mean values of DSC, OI, DT_{2mm} and CoM, grouped by varying parameter.

Parameter	Value	DSC	OI	DT_{2mm} (%)	CoM (mm)
Bending Energy weight (BE)	3%	0.843	0.867	7.7	1.42
	5%	0.837	0.861	8.4	1.43
Control Point Spacing (CPS)	5	0.851	0.877	6.8	1.46
	10	0.828	0.852	9.2	1.39
Masking the reference image	Yes	0.839	0.862	8.3	1.44
	No	0.841	0.867	8.1	1.39
Pre-processing the reference image	Yes	0.842	0.864	7.7	1.39
	No	0.837	0.866	8.8	1.46

3. Results

A total of 16 registrations per dataset were performed by varying 4 different inputs: (i) different BE (3% and 5%), (ii) different CPS (5 and 10 voxels), (iii) pre-processing of the CBCT and, (iv) masking. We compared the results obtained for the different quantities averaged over all structures and datasets (Table 1). The DIR was initialized with a rigid-only alignment. Separating individual structures and datasets we found improvement in 66%, 59%, 70% and 44% of the cases when using lower BE, smaller CPS, pre-processing and masking, respectively. Our findings suggest that combining pre-processing, CPS=5 and BE=3% leads to better registrations. Masking had an unpredictable effect on the registrations accuracy. This assessment considered that the effect of a parameter on the registration was independent of the other parameters, which is not the case. To confirm that the chosen parameters do stand out compared with the rest, we looked at mean DSC, OI, DT_{2mm} and CoM for each registration separately. Figure 1 shows how the registrations in the light blue region (CPS=5 and pre-processing) with odd number (BE=3%) give the best results in general.

Dose distributions were calculated using the same IMRT plan on the registrations that do and do not use a mask. The goal was to assess if accuracy for speed tradeoff has a big impact in the dose calculated. The two dose distributions obtained were very similar (Figure 2). DD was smaller than 2% of the prescribed dose (pD) on 96.2% of the voxels, with a mean value of 0.25 Gy (0.4% pD). The comparison passed a γ-test on 99.4% of the voxels (mean γ of 0.082).

4. Discussion and conclusions

Properly choosing the registration parameters is crucial in using DIR on clinical data as the parameters determine the actual deformations produced. The parameters should be tuned for different sites, imaging modalities, image size and quality, etc. Often default parameters which work well on a wide range of different images will be sub-optimum for a particular task. Non-linear intensity adjustment changes the CBCT contrast map, which had a positive impact in bin size and distribution of the histograms (Figure 1). Masking has an unpredictable effect on the registrations accuracy, depending on the particular dataset. The reduction of computation time is good reasoning for always masking the registrations and we confirmed that this has a small effect on dose calculations, particularly in OARs (Figure 2).

Our study aimed at tuning our B-Spline based deformable registration algorithm for excellent performance at CT-CBCT registrations in the head and neck site, for images obtained in our clinic. The optimal parameters found for the deformable registration were: BE of 3%, logarithm of the jacobian weight of 1%, a maximum number of 1000 iterations, a binning of 32 for the joint histogram calculation, thresholding the intensities to the range [-1000 2000], CPS of 5 voxels, non-linear intensity adjustment of the CBCT and masking. We achieved a median value of 0.845 in DSC, 0.889 in OI, error smaller than 2 mm in centroid position and over 90% of the warped

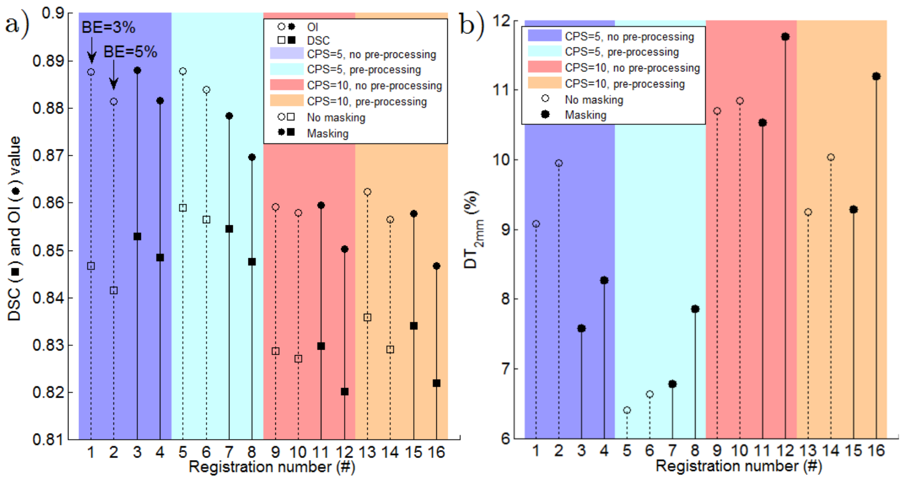

Figure 1. Variation of a) DSC (squares) and OI (circles) and b) DT_{2mm} for different combinations of parameters: BE=3% (#1,3,5,7,9,11,13,15) and BE=5% (#2,4,6,8,10,12,14,16); CPS=5 (#1-8) and CP=10 (#9-16); mask (#3,4,7,8,11,12,15,16) and no mask (#1,2,5,6,9,10,13,14); pre-processing (#5-8,13-16) and no-preprocessing (#1-4,9-12). Smaller control point spacing translated in larger values of DSC and OI. Pre-processing the CBCT improved DSC and DT_{2mm} values.

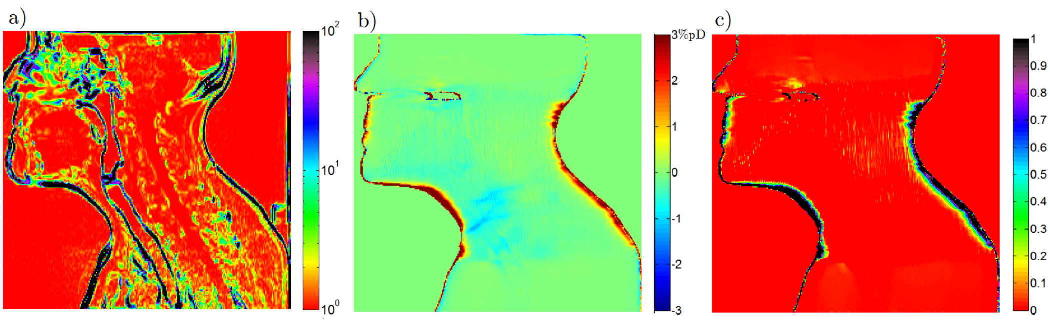

Figure 2. For the two registration approaches: a) difference in pixel intensity, b) DD and c) γ-value. The similarity between the images is high, with most of the differences smaller than 10HU. The regions where the differences in dose are higher are outside the CBCT field of view, in the skin, immobilization mask and airways, and these have little effect on the dosimetry of the OARs.

surface pixels are distanced less than 2 mm of the manually drawn ones. Future work will focus on further validation on a larger cohort to further support the effectiveness and efficiency of the proposed method in clinical applications.

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