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Original article

Automated, reference-free local error assessment of multimodal deformable image registration for radiotherapy in the head and neck

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ABSTRACT

Background: Head and neck MR-CT deformable image registration (DIR) for radiotherapy planning is hindered by the lack of both ground-truth and per-patient accuracy assessment methods. This study assesses novel post-registration reference-free error assessment algorithms, based on local rigid re-registration of native and pseudomodality images.

Methods: Head and neck MR obtained in and out of the treatment position underwent DIR to planning CT. Block-wise mutual information (b-MI) and pseudomodality mutual information (b-pmMI) algorithms were validated against applied rotations and translations. Inherent registration error detection was compared across 14 patient datasets.

Results: Using radiotherapy position MR-CT DIR, quantitative comparison of applied rotations and translations revealed that errors between 1 and 4 mm were accurately determined by both algorithms. Using diagnostic position MR-CT DIR, translations of up to 5 mm were accurately detected within the gross tumour volume by both methods. In 14 patient datasets, b-MI and b-pmMI detected similar errors with improved stability in regions of low contrast or CT artefact and a 10-fold speedup for b-pmMI.

Conclusions: b-MI and b-pmMI algorithms have been validated as providing accurate reference-free quantitative assessment of DIR accuracy on a per-patient basis. b-pmMI is faster and more robust in the presence of modality-specific information.

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Target volume and organ at risk (OAR) delineation error is important in head and neck (H&N) radiotherapy [1] planning with computed tomography (CT). Limited soft tissue contrast and dental artefact [2] cause high inter-observer variability in GTV definition [3], whilst OARs (brainstem, spinal cord and optic chiasm) are often poorly demonstrated on CT [4]. Magnetic resonance (MR) imaging exhibits improved soft tissue contrast and is less prone to dental artefact, potentially improving GTV and OAR delineation [5].

Accurate multimodal image co-registration is required to combine the advantages of MR and CT. Although rigid image registration (RIR) of treatment-position MR and CT data is possible [6], positional variability, internal motion and geometric distortion [7] in MR often cause non-rigid deformations [8]. Multi-modality deformable image registration (DIR) enhances registration accuracy even with patient immobilisation [9]. Treatment position MR is often unavailable clinically, and MM-DIR of diagnostic position MR has been shown to improve GTV propagation accuracy [10]. DIR is also fundamental to atlas and model based synthetic CT generation and auto-contouring, which are of increasing importance for MR-only planning and adaptive radiotherapy.

Per-patient DIR accuracy assessment is clinically desirable. However, absolute verification of DIR is unachievable due to lack of ground-truth availability. AAPM report TG132 [11] discusses process validation and commissioning of DIR, including contour [10,12,13], landmark comparison [14,15] or phantom work [16], but does not consider local, per-patient, registration errors beyond the current standard of visual assessment [17]. Automated, local, reference-free, registration assessment would increase confidence in DIR contour propagation.

Translation-only re-registration, using image sub-blocks, can provide local error estimates, as non-rigid deformations are approximated by a sufficiently fine grid of local translations, without regularisation and block edge-matching requirements. We have implemented and validated two such methods. Firstly, block-wise mutual information (b-MI), based on the well-understood MI similarity metric [18], commonly utilised by MM-DIR algorithms. However, multimodal MI can become unreliable for small blocks [19], in regions of low CT soft-tissue contrast or CT artefact, where local maxima affect the metric. A second approach, using joint histogram variance-minimisation greyscale

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remapping, as originally described by Andronache [20], to create a common reduced-contrast pseudomodality image pair for each block, with subsequent MI (b-pmMI), offers potential improvements in convergence and speed. Validation of both methods was performed via applied rotational and translational co-registration errors, with further cross-validation of b-pmMI against b-MI on 14 patient datasets.

Materials and methods

Patient data and imaging methods

MR and CT images from a previous prospective single centre pilot imaging study of MR and PET-CT in the H&N [10,21,22], approved by Research Ethics Committee (11/YH/0212), ISRCTN Registry: ISRCTN34165059, were used. 14 patients (11, 2 and 1 with oropharyngeal, hypopharyngeal and laryngeal carcinoma, respectively) underwent pre-treatment diagnostic position MR (MR-D) and treatment position MR (MR-RT), immobilised with a 5-point thermoplastic mask. Patient details are shown in Table 1. MR and CT were acquired as previously described [10,22]. In brief, T1w TSE axial post-contrast (Dotarem) MR images were acquired on a 1.5T Siemens Magnetom Avanto (Siemens Healthcare, Erlangen, Germany) with voxel size = 0.9 × 0.9 × 2.0 mm. CT was acquired with 1.36 × 1.36 × 2.5 mm voxels.

MR-D and MR-RT datasets underwent DIR to CT (Mirada RTx v1.6 – Mirada Medical, Oxford UK), using a workflow of automated RIR, manual optimisation at the C1-C2 region and subsequent automated MM-DIR. Optionally, artificial shifts (or rotations) were then applied and the resulting MR images were resampled into the CT frame of reference for residual registration error analysis.

Algorithms for registration error assessment

b-MI and b-pmMI algorithms were implemented in MATLAB 2014b (The MathWorks, Inc., Natick, Massachusetts, USA). CT and resampled deformably co-registered MR data were decomposed into 3D blocks with 8-bit greyscale depth. Per-block registration errors were determined for each algorithm as follows:

i) Blockwise mutual information (b-MI)

Block pre-selection via greyscale value (mean > 5) and standard deviation thresholding (s.d. > 5) removed blocks outside the patient contour or with insufficient CT contrast (e.g. entirely within brain). Translation-only MI-based re-registration was performed, with evolutionary optimisation to limit trapping in local MI maxima. An error vector field (EVF) was reconstructed by 3D interpolation of missing data (due to excluded blocks).

ii) Pseudomodal block-wise mutual information (b-pmMI)

b-pmMI relies on the variance minimisation pseudomodality generation technique of Andronache et al. [20] For each block, two pseudomodality images (pmCT and pmMR) were generated (Fig. 1a), from CT and MR data respectively, by grayscale re-mapping. CT-pmCT and MR-pmMR mappings were determined iteratively (Fig. 1b), by retaining a grey-value or replacing it with the corresponding mean grey-value of the opposing modality from the joint histogram [20]. Thus, variance minimisation results in pseudomodality block pairs with minimal joint entropy and visually similar appearance. Geometric information from each source image is preserved in the pmCT and pmMR images (Fig. 1a), whilst contrast features unique to a single modality (including CT artefact) are removed. In soft tissue, where CT contrast is low and MR contrast high, MR grey values are typically mapped to the CT contrast space (Fig. 1b – blue circles), resulting in CT-like contrast with removal of MR specific detail. In bone, high CT greyscale values are remapped to low values (Fig. 1b – red squares), resulting in dark (MR-like) bone for both pm-CT and pm-MR images (Fig. 1a). Without modality specific details, b-pmMI block re-registrations converged reliably with steepest descent optimisation, even in the presence of CT artefact. EVFs were constructed from per-block translation vectors as for b-MI.

Validation with known rotations/translations

A high quality MR-RT to CT RIR, with minimal intrinsic error was selected by visual inspection. This 'reference' dataset was modified by applied rotations and translations (ImSimQA v3.1, OSL, Shrewsbury UK). 5° rotations about the cranio-caudal, anterior-posterior and lateral (x, y, z) axes, 1.5 mm translations along the in-plane axes and 2.5 mm (single slice) translations in the (cranio-caudal) axis were applied to create a set of misregistered datasets. The applied error at distance d from the applied rotation axis is given by:

$$E_{prod} = d.\tan(R_z) \quad (1)$$

where R_z is the applied rotation. b-MI and b-pmMI derived EVFs were corrected for underlying RIR errors by subtraction of the original dataset EVFs.

Table 1
Patient demographics and mean GTV and brainstem contour registration errors.

PtID	Tumour Site	TNM Stage	GTV volume	GTV mean mag. error			Brainstem volume	Brainstem mean mag. error		
			/cm^3	b-MI	b-pmMI	Δ	/cm^3	b-MI	b-pmMI	Δ
01	Tonsil	T2N2b	4.49	1.44	2.11	0.68	4.85	4.16	3.58	0.59
02	Supraglottis	T3N2b	14.75	1.85	1.92	0.07	3.78	4.17	3.89	0.29
03	Pyriform fossa	T3N0	3.45	4.97	3.51	1.47	3.50	1.44	3.46	2.02
04	Base of tongue	T3N2c	15.96	1.83	1.29	0.54	4.59	3.12	2.68	0.44
05	Base of tongue	T4aN2b	2.35	1.99	2.12	0.12	4.35	1.56	2.69	1.13
06	Base of tongue	T4aN1	26.95	1.89	2.93	1.03	5.18	2.15	2.43	0.28
07	Base of tongue	T2N1	9.08	2.08	1.69	0.39	4.29	2.53	1.79	0.75
08	Tonsil	T1N2b	1.00	2.07	1.36	0.71	3.63	3.46	2.92	0.54
09	Base of tongue	T2N2b	0.95	1.69	0.94	0.74	4.89	1.98	2.67	0.70
10	Base of tongue	T2N2b	12.40	1.50	1.18	0.32	4.44	3.31	3.57	0.26
11	Soft palate	T4aN1	8.05	1.26	0.89	0.38	3.75	4.74	3.53	1.21
12	Base of tongue	T1N2b	0.93	1.81	3.70	1.88	3.93	3.12	2.23	0.88
13	Soft palate	T4aN2b	14.78	1.38	0.86	0.52	5.90	1.07	2.41	1.34
14	Base of tongue	T2N2b	2.51	2.29	2.45	0.16	3.58	2.15	1.64	0.51
Population mean errors				2.01	1.93			2.78	2.82	

Comparison of b-MI and b-pmMI in series of H&N cancer patients following MM-DIR of MR-D to planning CT. Disease site and staging, with tumour volume and mean errors within the GTV and brainstem consensus contours as determined by b-MI and b-pmMI. Differences (Δ) between the results from the two algorithms are shown.

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