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Technical Note

An evaluation of systematic errors on marker-based registration of computed tomography and magnetic resonance images of the liver

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ABSTRACT

We demonstrated a general method to evaluate systematic errors related to Magnetic Resonance (MR) imaging sequences in marker-based co-registration of MR and Computed Tomography (CT) images, and investigated the effect of MR image quality in the co-registration process using clinical MR and CT protocols for stereotactic ablative body radiotherapy (SABR) planning of the liver. Small systematic errors (under 1.6 mm) were detected, unlikely to be a clinical risk to liver SABR. The least favourable marker configuration was found to be a co-planar arrangement parallel to the transaxial image plane.

1. Introduction

The fusion of magnetic resonance (MR) and computed tomography (CT) images combines the superior soft tissue contrast of MRI with the CT-based electron density information required for Radiotherapy (RT) planning [1]. MR is the diagnostic imaging modality of choice for liver tumours and aids radiotherapy target delineation, which can be challenging particularly for tumours difficult to visualise on CT such as liver metastases [2,3]. Optimal MR-CT co-registration is therefore essential to the accuracy of MR derived target volume (TV) delineation and the definition of the disease extent. For mobile anatomical structures, metallic markers inserted around the TV may be used for accurate patient set up before treatment and to enable the MR-CT co-registration during RT planning [4,5]. Markers may also be used to track tumour motion in real time during X-Ray guided RT delivery thus mitigating the effects of physiological motion [6–9]. In X-Ray Guided Stereotactic Ablative Body Radiotherapy (SABR) of non-resectable metastatic liver disease, a minimum of three non-colinear markers is used to track tumour motion during RT treatment.

There are practical constraints in placing markers. In livers, access to the tumour is limited by the surrounding organs and ribcage [10]. Liver CT images are acquired relatively rapidly in exhale breath hold. However, there are practical constraints to the spatial resolution of MRI images acquired within a breath-hold. Typical breath-holds for liver examinations last for 10–20 s and require 2D or 3D techniques characterised by thicker slices (at least 4 mm) and data truncation to enable the entire liver volume to be examined; the nominal in-plane spatial resolution is rarely achieved in practice in MRI. In MRI markers are characterised by susceptibility-related signal loss, which depends on the MRI pulse sequence properties and the orientation of the marker in relation to the main magnetic field and to the image plane [11]. Both the receiver bandwidth and the frequency encoding direction have an effect on the depiction of the signal void around the marker and the signal loss pattern is not necessarily symmetric in relation to the marker position [12].

Clinical studies of CT-MR co-registration have considered different error sources, including marker migration and tissue deformations [10,13], and different methods have been proposed to improve registration accuracy [14,15]. A previous multi-institutional study reported considerable uncertainties employing MR-CT deformable registration for liver cancer [16]. Automated and semi-automated segmentation of internal structures may improve registration accuracy and can potentially facilitate tumour delineation in SABR of the liver [17]. In the liver, marker group deformations and rotations have been observed; they can be significant in the vicinity of the tumour, close to high dose gradients and this could compromise target coverage [4]. In contrast, clinical prostate studies have demonstrated smaller discrepancies between marker midpoints [12,18], suggesting greater accuracy with a

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smaller, more rigid organ.

In clinical studies, the compromise between time and spatial resolution in MRI impacts on image quality, but the effect of the latter on the registration accuracy cannot be investigated independently from clinical factors such as motion artifacts and marker migrations. We hypothesise that data truncation artifacts and the low resolution of MRI datasets (compared to CT) are detrimental to the co-registration process. In this work we assess the accuracy of the CT-MR co-registration by implanting markers in gel test objects to be scanned (MR and CT) with clinical liver protocols. By using homogenous gel test objects, the effect of marker image quality on CT-MR registration is assessed separately. This registration is challenging, as it cannot be guided by heterogeneous tissue structure and anatomical borders in the vicinity of the lesion. The methods used in this study therefore aim to evaluate the limitations of breath hold MR sequences used for liver SABR under a variety of scenarios including those which are expected to be least favourable.

2. Materials and methods

Patients scheduled for liver SABR at our institution had at least two pairs of linked fiducial markers (FlexiMarc G/T™, FM-1.0-2-20-GT-18-20, CIVCO) inserted before undertaking MR and CT examinations for RT planning. Each marker's diameter is 1 mm and each pair of markers is separated by a 20 mm titanium rod and was inserted along a different path under local anaesthetic using CT guidance by an interventional radiologist. The proximity and arrangement of the markers with respect to the lesion are determining factors in the accuracy of tumour tracking [4,10]. Radiologists aimed to place the markers proximal to the treatment site in a non-colinear orientation, approximately centred on the tumour, but without contacting the lesion. The latter prevents the deposit of cancerous cells along the needle tract during removal. This resulted in inter-marker separations as low as 20–40 mm for small lesions.

In a clinical setting, transaxial MR images were acquired during an exhale breath-hold (Skyra 3.0T, Siemens, Erlangen, Germany) and registered to an exhale breath hold CT (LightSpeed RT16, GE Medical Systems). T1-weighted (T1w), T2-weighted (T2w) and T2*-weighted (T2*w) images with 4 mm slice thickness required truncation of the acquisition matrix to be acquired within a breath-hold; MR datasets were thus anisotropic, with higher in-plane resolution in relatively thick slices. Both T1w and T2w images were used for visualisation of tumours, and T2*w images were used to enable visualisation of small markers by emphasising susceptibility-related signal loss. MR sequence parameters are provided in Table 1. Helical exhale breath hold CT examinations had 1.25 mm slice thickness and $1.0 \times 1.0\,mm^2$ in-plane resolution. Rigid MR-CT co-registration was undertaken using automatic and manual rigid-body registration (i.e. rotation and translation only) (Eclipse, Varian Medical Systems, Inc. Palo Alto, CA).

Table 1
MR sequence parameters.

MR sequences	T1w (3D Dixon-VIBE)	T2w (2D fast spin-echo)	T2*w (2D spoiled gradient echo)
TR/TE (ms)	5.87/2.47	1600/96	230/4.92
Voxel size (mm^3)	1.5 × 1.5 × 4	1.2 × 1.2 × 4	1.5 × 1.5 × 4
Reconstruction/ acquisition matrix	256 × 192/ 256 × 144	320 × 240/ 320 × 194	256 × 192/ 256 × 154
% Sampling	75	81	80
Pixel bandwidth (Hz/ px)	1030	710	1395
Readout gradient direction	R/L	R/L	R/L
Parallel imaging factor	2	2	2

2.1. Test object development and imaging

In order to investigate the accuracy of CT-MR co-registration, two test objects were built by suspending two linked pairs of markers in porcine gelatine (100 g/L) inside a 14 cm × 14 cm × 8 cm plastic container. The position of the markers was chosen to represent the most challenging clinical situations. The most unfavourable marker configurations were chosen by limiting the furthest distance between any two markers to the 20–30 mm range. This range represents the typical minimum marker separation in the treatment of metastatic liver tumours using stereotactic radiosurgery at our institution.

In Test Object A, the markers were co-planar; in Test Object B, the markers were non-coplanar (Fig. 1). Both Test Objects were scanned using the clinical liver MR and CT protocols described above, in two different positions (vertical and horizontal). The vertical Test Object orientation places the co-planar arrangement of markers parallel to the image plane (transaxial).

Fully sampled MR datasets were also acquired to obtain a 'gold standard' for the CT-MR registrations (100% sampling in the phase and readout directions). These fully sampled images are not degraded by data truncation artifacts, but cannot be acquired within the duration of a clinical breath-hold scan. All images were transferred to the Treatment Planning System (TPS) for CT-MR co-registration.

2.2. CT-MR co-registration and data analysis

'Gold-standard' CT-MR registrations were performed by a RT expert using the fully sampled MR datasets and were guided by the external shape of the Test Object (Fig. 1A). The same CT datasets were then duplicated and edited to remove any information related to the external Test Object shape which could contribute towards co-registration: a 46 mm diameter spherical volume containing the markers only was defined and the image intensity was assigned to zero elsewhere (Fig. 1A). The edited CT dataset was then registered to the obtained MR Test Object images by a different TPS user. This second registration is based on marker information only. In total 12 registrations were performed independently (Fig. 1B): two different Test Objects (A and B) in two different Test Object orientations (Vertical and Horizontal), and 3 different pulse sequences.

For each registration the transformation coordinates were extracted from the exported DICOM registration object, using in-house software (python, v2.7, and pydicom package v0.9.9). The accuracy of each marker-based registration, $\mathbf{R_{marker}}$, was then quantified by the offset $\mathbf{d}$ in each marker position from the position associated with the gold standard registration, $\mathbf{R_{GoldStd}}$:

$$\mathbf{d} = \mathbf{p}_{\mathrm{GoldStd}} - \mathbf{p}_{\mathrm{Marker}}$$

where $p_{GoldStd}$ and p_{Marker} are the marker coordinate vectors for each registration:

$$\mathbf{p}_{\mathrm{GoldStd}} = \mathbf{R}^{-1}_{\mathbf{GoldStd}}\mathbf{p}_{\mathrm{CT}}$$

$$\mathbf{p}_{\mathrm{Marker}} = \mathbf{R}^{-1}_{\mathbf{Marker}}\mathbf{p}_{\mathrm{CT}}$$

Here p_{CT} is the marker position vector in the original CT image, as found manually by point selection in the TPS.

One sample *t*-tests were performed to test the null hypothesis that the population mean offset is zero on each component of the displacement $\mathbf{d}$ (along the slice selection, readout and phase encoding directions). One-way analysis of variance (ANOVA) was used to find any significance in the difference between the three sequence results. Two sample *t*-tests were performed to test the null hypothesis that the coplanar and non-coplanar test objects share the same mean offset, and that there is no dependence on the test object imaging orientation. A test significance limit of 5% is used for all tests.