An evaluation of four CT–MRI co-registration techniques for radiotherapy treatment planning of prone rectal cancer patients

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Objectives: MRI is the preferred staging modality for rectal carcinoma patients. This work assesses the CT–MRI co-registration accuracy of four commercial rigid-body techniques for external beam radiotherapy treatment planning for patients treated in the prone position without fiducial markers.

Methods: 17 patients with biopsy-proven rectal carcinoma were scanned with CT and MRI in the prone position without the use of fiducial markers. A reference co-registration was performed by consensus of a radiologist and two physicists. This was compared with two automated and two manual techniques on two separate treatment planning systems. Accuracy and reproducibility were analysed using a measure of target registration error (TRE) that was based on the average distance of the mis-registration between vertices of the clinically relevant gross tumour volume as delineated on the CT image.

Results: An automated technique achieved the greatest accuracy, with a TRE of 2.3 mm. Both automated techniques demonstrated perfect reproducibility and were significantly faster than their manual counterparts. There was a significant difference in TRE between registrations performed on the two planning systems, but there were no significant differences between the manual and automated techniques.

Conclusion: For patients with rectal cancer, MRI acquired in the prone treatment position without fiducial markers can be accurately registered with planning CT. An automated registration technique offered a fast and accurate solution with associated uncertainties within acceptable treatment planning limits.

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Randomised trials have demonstrated that adjuvant radiotherapy (RT) in patients with resectable rectal cancer offers a statistically significant reduction in the risk of local recurrence compared with surgery alone [1]. Two meta-analyses and a systematic review have confirmed this finding [2–4]: cancer-specific survival was found to be improved when RT was delivered with biological equivalent doses of >30 Gy pre-operatively. Two further trials have confirmed similar benefit when short-course pre-operative RT was combined with total mesorectal excision (TME) [5, 6].

Three further randomised trials have evaluated the role of pre-operative adjuvant chemoradiotherapy (CRT) for patients with stage T3–T4 or node-positive disease. Two of these studies demonstrated a reduction in local recurrence when pre-operative adjuvant CRT was used rather than long-course adjuvant RT alone [7, 8]. The third study demonstrated both reduced local recurrence and reduced acute and late toxicity for pre-operative CRT compared with post-operative CRT [9]. The Cochrane review [4] also examined CRT and concluded that CRT provided incremental benefit in local control, irrespective of the

timing of the chemotherapy. These results have led to a significant increase in the use of pre-operative radiation for patients with rectal cancer.

MRI offers increased soft-tissue contrast compared with other radiographic imaging modalities such as CT. This improvement allows the accurate identification of the gross tumour and the mesorectal fascia in at least three planes. A number of studies have recommended using high-resolution MRI as a tool to determine the relationship between the potential circumferential resection margin (CRM) and the tumour [10–15], with one recent large prospective multicentre study demonstrating a specificity of 92% in predicting an involved CRM [16]. These results are supported by a recent meta-analysis of nine studies (529 patients) that revealed an overall sensitivity of 94% and specificity of 85% [17]. The review article by Klessen et al [18] also suggests that MRI is the only imaging modality that enables such accurate evaluation. Consequently, MRI is the reference standard for the clinical assessment of patients with colorectal cancer and is recommended for routine use by the National Institute for Clinical Excellence (NICE) in the UK [19].

Current clinical practice at St James's Institute of Oncology is for patients to be selected for pre-operative CRT if the margins of resection are considered at risk by the colorectal multidisciplinary team. The patient is CT-scanned in the prone treatment position and the

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oncologist defines the gross tumour volume (GTV) on individual transaxial images, leading to the determination of the planning target volume (PTV). To assist in the definition of the GTV, the oncologist is aided by diagnostic CT and/or MRI and other clinical information. Where diagnostic MRI is available, it is usually acquired in a different patient orientation (*e.g.* supine position) or radiographic plane (*e.g.* orthogonal to the long axis of the tumour) and at a different time to the CT study, meaning that the anatomy may differ in appearance. Furthermore, the MRI may be on radiographic film or on a different computer system to the planning CT.

Image co-registration is the process of finding the mathematical transformation that aligns several different radiographic studies [20]. Various rigid-body co-registration techniques are currently offered by commercial RT treatment planning systems (TPSs), including those that employ operator-defined corresponding landmarks, interactive drag-and-drop or full automation.

There are obvious potential advantages of including image registration in the treatment planning process [21], but historically, technical issues associated with MRI distortion, artefacts and lack of electron density information, along with little evidence of its positive effect on patient outcome, are likely to have precluded its universal use in treatment planning [22]. Despite these issues, studies have demonstrated the feasibility of pelvic image registration for RT treatment planning [23–26].

Furthermore, rectal cancer specifically has been identified as a disease for which co-registered MRI could enhance treatment planning [27, 28]. There is considerable interest in RT in which the GTV is defined on MR imaging in the same frame of reference as the planning CT. Increased accuracy in defining the GTV and/or clinical target volume (CTV) would give a more accurate definition of the dose required to those volumes or allow dose escalation to the GTV in patients with locally advanced disease. Acquiring an MRI with the patient in the prone position, however, introduces a new set of potential challenges, including increased respiratory artefacts that affect registration accuracy.

Several studies have investigated the accuracy of image registration in a RT context, but as concluded by Sharpe and Brock [29] in their review of image registration quality assurance, there is no consistent approach. One approach is to image phantoms with objects of known spatial location with both CT and MRI [30–33]. This has the advantage of enabling controlled measurement of errors throughout the entire process of image acquisition and image registration, with a ground truth established through the objects with known spatial location. Such phantoms can also be used to estimate the spatial distortion in the images. However, these studies are all based on the use of MRI to image the head and neck rather than the pelvis. The studies' dependence on physical phantoms means that uncertainties that may arise from natural variations in shape, size and composition in the patient population are not measured. Furthermore, the two studies evaluating the performance of commercial registration algorithms using patient images are both based on the registration of images of the head [32, 34].

Several studies have employed CT-MRI co-registration for pelvic sites [23–26, 35, 36], but few data exist on

measured image registration uncertainties using existing image registration functionality in commercial TPSs. Furthermore, no evidence could be found of image registration for patients imaged in the prone position.

The primary aim of this study is to assess the co-registration accuracy of two fully automated and two hybrid manual-automatic techniques using two commercial TPSs. On the basis of these results, this study aims to determine the most appropriate clinical image registration process and whether manual adjustments after automatic image registration are necessary or even beneficial. It is expected to provide supporting information for RT centres that are considering utilising co-registered prone MRI in treatment planning for rectal cancer.

Materials and methods

Sample population

Between January 2006 and April 2007, patients with biopsy-proven carcinoma of the rectum with an indication for pre-operative CRT because of an involved or threatened CRM (as demonstrated on MRI) were screened for study eligibility. Of those approached, 17 were willing to participate in the study and provided informed written consent. The study was approved by a local research ethics committee. The patients' treatment proceeded as per the standard protocol without the use of the additional MRI study data.

Image acquisition

Patients were positioned prone with their hands under their head on the GE Lightspeed CT scanner (General Electric Healthcare, Milwaukee, WI) having received oral contrast (2% gastrograffin) 1 h prior to their scan. A radio-opaque marker was placed at the anal margin. The superior and inferior limits of the acquired transaxial data (set by the topogram) were the iliac crests and 5 cm inferior to the anal marker, respectively.

Patients then underwent a T_2 weighted turbo spin echo MRI scan using a 1.5T Siemens Magnetom Symphony scanner (Siemens, Erlangen, Germany) within 45 min of the CT scan. Each patient was set up for their MRI as similarly as possible as for their CT by ensuring the same radiographer/technician was present for both scans. The patient lay on the standard flat, firm, thin mattress. An oil capsule was placed at the anal margin and a body matrix coil positioned loosely on the posterior pelvic surface. No MRI contrast or muscle relaxant was administered. Superior-inferior scan limits were set similarly to those for the CT.

No additional external fiducial markers were used for either scan, and the CT and MRI parameters were as detailed in Tables 1 and 2, respectively. A high-bandwidth (195 Hz/pixel⁻¹) spin-echo sequence was chosen to reduce the magnitude of magnetic distortion artefact. Other sequence parameters were chosen to optimise image quality, given the relatively large field of view when compared with a diagnostic-type scan, and to mimic the CT protocol as closely as possible. This was a balance between reducing motion artefact (by reducing

Table 1. Nominal scan parameters used for CT imaging on the GE Lightspeed CT scanner (General Electric Healthcare, Milwaukee, WI)

Parameter	
Number of slices	~55
Slice thickness	5 mm
Scan interval	5 mm
Orientation	Axial
In-plane resolution	0.9 × 0.9 mm
Matrix size	512 × 512
Beam energy	120 kV _p
Tube current	150 mA
Collection diameter	120 cm

These values are as per the clinical imaging protocol.

the acquisition time) and increasing signal-to-noise ratio (by increasing the number of concatenations). The MRI scans for some patients exhibited significant patient motion artefact (from both normal respiratory and unpredictable motion) when these parameters were used. For these patients, a similar sequence was used with a poorer resolution and shorter scan time.

Image registration

Two TPSs were used for image co-registration, namely CMS Xio (and specifically its plan review/image fusion software CMS Focal v.4.3.3) and Nucletron Oncentra Masterplan v1.5 (OMP). Each has both manual and automatic modes of rigid-body image registration (*i.e.* using rotation and translation only).

The manual system offered by CMS allows an operator to translate and rotate one study relative to the other interactively using drag-and-drop functionality. The MRI is displayed as a semi-transparent colour overlay on the CT image. With the OMP system, the operator defines corresponding landmarks in each study; once landmarks are selected, the least squares optimisation algorithm determines the transformation that minimises the average distance between all the placed points automatically [37]. In this sense, it is a hybrid manual–automatic technique.

The automated systems offered by OMP and CMS both use mutual information (MI) that seeks solutions with a low joint entropy and high marginal entropies [20]. They are both iterative gradient-based optimisation algorithms in which the rigid body transform between the moving image set and the fixed image set is updated repeatedly until the joint entropy value reaches a minimum value.

In clinical practice, it is recommended that the alignment of the two images after an automated image registration should be inspected visually and adjusted if necessary. The OMP system did not provide a mechanism for making small manual adjustments to the registration. Therefore, the automatic image registration would either have to succeed or the operator would be forced to restart the registration using the landmark technique. The CMS system, however, enabled small adjustments to be made manually as described above after automatic image registration had completed. It was uncertain, however, whether the observer would introduce a greater uncertainty by performing the manual adjustment. Performing

Table 2. Nominal scan parameters used for the turbo spin-echo MRI sequence

Parameter	
Number of slices	~55
Slice thickness	5 mm
Scan interval	5 mm
Orientation	Axial
Nominal in-plane resolution	0.9 × 0.7 mm
Nominal matrix size	269 × 512
TR	8110 ms
TE	89 ms
Phase encoding direction	A P
Averages	2
Receive coil	Body
Turbo factor	11
Concatenation	1
Bandwidth	195 Hz pixel ⁻¹

TE, echo time; TR, relaxation time.

Parameters were chosen to optimise image quality while maintaining a reasonable scan time in order to reduce the possibility of motion artefact. Note that the slice thickness, resolution and field-of-view were chosen to be as close as possible to those for CT imaging.

the manual match after the automatic registration makes this also a hybrid manual–automatic technique.

Hybrid manual–automatic registration techniques

Three trained technical planning staff members (operators 1–3) completed each registration. For each operator, the starting point (initial registration) was identical in each planning system. For the landmark-based OMP system, the initial mathematical registration was inconsequential to the outcome. For the CMS system, however, the initial registration position was the unity matrix using the CMS frame of reference.

For the landmark-based OMP system, operators were asked to place between 8 and 10 well-spread points at suggested bony anatomical landmarks in each modality, based on advice from a consultant radiologist. Points included the inferior tip of coccyx, inferior and anterior symphysis pubis, anterior inferior ilium, superior femoral head, sacro-iliac joint, mid-point of the sacral promontory, and ischia (Figure 1).

For the interactive CMS system, operators were allowed to use MI as an initial attempt at registration, but were instructed to try to improve the bony pelvis registration by subsequently translating and rotating the data sets manually. Automatic image registration prior to manual adjustment was allowed as this would emulate the expected clinical process.

Each registration was performed once per operator per patient. Additionally, for the first 10 patients, an operator was chosen at random to perform 2 further registrations in order to make an assessment of reproducibility.

Automated registration

An independent trained operator performed three repeated registrations using MI only without adjusting the default MI parameters in each system. For each TPS, each attempt began from an identical initial registration, the unity transformation. However, differences in the way in which each TPS interpreted the MRI frame of reference meant that the initial registration differed between TPSs.

Figure 1. CT (left) and MRI (right) identifying some of the bony pelvis anatomical landmarks used for the manual co-registration system in OMP: (a) ischial spine; (b) ischium; and (c) inferior aspect of coccyx.

As MI algorithms rely on the joint and individual probability distributions, it is important that the registration volumes are similar to ensure that these probability distributions do not include anatomy in one modality that is not included in the other. In both TPSs, the entire CT and MRI data sets were included and both encompassed similar volumes of anatomy.

Registrations performed by the manual operators and the automated techniques are termed as 'study registrations' hereafter.

Reference registration

In the absence of a known registration, a best attempt at bony pelvis registration was performed using MI followed by a manual three-dimensional (3D) interactive adjustment in the CMS system by the consensus of a consultant radiologist and two trained physicists. This registration formed the reference standard to which each of the study registrations were compared.

Registration analysis

Transformations between 3D data sets are coded as a (4×4) matrix. The purpose of this mathematical relationship is to convert co-ordinates from one frame of reference to another. Rigid-body transformation consists of three translational and three rotational components; one simple method of comparing two registrations is to compare differences in these individual components.

These data alone are, however, difficult to interpret because the translation and rotation components are inter-linked and the effects of differences on a target transformation depend on the point of rotation. For the purpose of defining a single metric of image registration error per registration, the radiologist defined a clinically relevant GTV on the CT data. This was simplified to a set of eight vertices denoting the extremes of the target volume (a CT-bounding cuboid). Each CT vertex was transformed by the reference transformation matrix to form a reference MRI cuboid.

The same CT cuboid was then transformed using each study registration transformation matrix, thereby creating study cuboids in MRI space. The magnitude of the 3D vector differences between the co-ordinate of a corresponding vertex in the study and those of the reference MRI cuboids was defined as the vertex error. The target registration error (TRE) was defined as the median vertex error per registration. The TRE represented an average measure of the geometric difference in target position between the test and reference registrations. As the eight vertices were chosen on the basis of the GTV, the TRE indicated the effect of registration error near the boundary of the GTV and would be useful when considering the relevance of differences in GTV delineation between the CT and MRI modalities. The time taken to complete the manual registration was noted for each patient for each operator.

In summary of the methodology, CT and MRI scans were acquired for 17 patients in the prone treatment

Table 3. Mean, maximum and range of target registration error for each registration method on CMS and OMP treatment planning systems

		CMS (mm)			OMP (mm)		
		Mean	Max	Range	Mean	Max	Range
Manual	Operator 1	2.8	6.9	1.2	3.3	7.1	1.6
	Operator 2	2.4	6.6	1.9	4.5	8.5	2.5
	Operator 3	2.8	7.6	1.1	4.2	7.2	0.7
	Overall	2.7	7.6	1.2	4.0	8.5	1.3
Automated		2.3	5.9	0.0	4.4	7.9	0.0

position. A clinically relevant GTV was delineated by a radiologist on the CT imaging only. The images were then registered: first by a radiologist and two trained physicists to form the reference registration, and then by a series of operators using the two automated and two hybrid auto-manual systems. The CT GTV was then simplified into a bounding cuboid, which was transformed to the MRI frame of reference by the transformation matrices resulting from the reference registration and from each of the test registrations. The quality of the registration was assessed by comparing the lengths of corresponding MRI cuboid reference and test vertices.

Statistical analysis

TRE difference data between operators or techniques that did not prove significantly dissimilar to a normal-type distribution (using the Lilliefors [38] test, $\alpha=0.05$) were analysed using the paired *t*-test; otherwise, the non-parametric Wilcoxon [39] signed-rank test was used. The Lilliefors and Wilcoxon tests were performed in MATLAB v2007a (The Mathworks, Natick, MA) and confidence intervals for mean differences calculated in SPSS v15.0 (SPSS Inc., Chicago, IL).

Results

Summary TRE data including the mean, maximum and range for each technique and operator are shown in Table 3; range is the median range of TRE for 3 repeated attempts per operator (for the first 10 subjects). Overall values include all operators.

Table 4. Differences in target registration error (TRE) that are significant at the 95% level according to the paired *t*-test. Mean TRE is quoted along with the 95% confidence interval and its corresponding *p*-value. Note that all values are negative, meaning that the TRE of the variable stated second is the larger

Data pair	Mean TRE difference (mm)	95% confidence interval (mm)		<i>p</i> -value
		Lower	Upper	
CMS op2 – OMP op2	–2.0	–3.2	–0.9	0.004
CMS op3 – OMP op3	–1.4	–2.3	–0.5	0.008
CMS mean op – OMP mean op	–1.3	–2.0	–0.6	0.006
CMS auto – OMP auto	–2.1	–3.1	–1.1	0.001
CMS auto – OMP mean op	–1.7	–2.5	–0.8	0.002
CMS auto – OMP op2	–2.2	–3.3	–1.1	0.002
CMS auto – OMP op3	–1.9	–3.0	–0.8	0.005
CMS mean op – OMP auto	–1.8	–2.7	–0.8	0.003
CMS op1 – OMP auto	–1.6	–2.9	–0.3	0.021
CMS op2 – OMP auto	–2.0	–2.8	–1.2	<0.001
CMS op3 – OMP auto	–1.6	–2.6	–0.6	0.004

auto, automated method; op, operator; TRE, target registration error.

The single non-parametric comparison was not significantly different from zero, but the paired *t*-tests revealed some significant differences (Table 4). The mean difference between the two automated methods was 2.1 mm [95% confidence interval (CI): 1.1–3.1 mm] in favour of CMS. This order of difference was also seen between the CMS automated and OMP manual methods. There were no significant differences between the manual and automated techniques in each TPS.

A mean increase in accuracy of 1.3 mm (CI: 0.6–2.0 mm) was achieved by registering data using the CMS manual method rather than the OMP manual method. In absolute terms, this means reducing the average TRE from 4.0 mm to 2.7 mm. This is echoed in the maximum TRE results, which show a difference of 0.9 mm between the manual methods in favour of CMS. Although maximum TRE differences were not statistically analysed, it is worth noting that the lowest maximum TRE was for the CMS automated system at 5.9 mm.

The reproducibility of the manual methods was similar for the two systems, with variations of 1.2 mm and 1.3 mm for CMS and OMP, respectively. The automated methods, by comparison, had zero variation.

Registration times are shown in Table 5. A small significant difference was detected between operators 2 and 3 on the CMS system. Larger differences were seen for the OMP system between operators 1 and 3, with a mean of 6 min (CI: 3–10 min), and between operators 2 and 3, with a mean of 11 min (CI: 6–16 min). Operators 1 and 2 completed the registration on average 8 min (CI: 4–11 min) and 13 min (CI: 10–16 min) faster on the CMS system, respectively. Operator 3 showed no difference in mean registration time between the manual methods. Maximum times were all smaller for the CMS system than for the OMP system.

The time taken for the automated techniques was not measured but was in the order of 1 min for both systems, which was significantly different to all of the results for manual systems.

Discussion

This study has shown that MRI acquisition with the patient in the prone treatment position is well tolerated and is both practical and technically feasible.

Table 5. Summarised results of the time taken to perform manual registrations for each system and operator

		CMS (min)		OMP (min)	
		Mean	Max	Mean	Max
Manual	Operator 1	8	15	16	30
	Operator 2	7	10	20	34
	Operator 3	9	15	9	20
	Overall	8	15	15	34

Furthermore, although the image quality is reduced in comparison with diagnostic MRI, the data collected are of adequate image quality for image co-registration with planning CT.

Automated and manual techniques were both faster and more accurate when the interactive CMS system was used rather than the landmark-based manual OMP system. In terms of reproducibility, the manual systems were acceptable and comparable, whereas the automated methods produced identical registrations when the same process was repeated from an identical starting point. The two automated systems were similar in terms of registration time and significantly faster than the manual techniques.

One reason for the improved accuracy and speed of the hybrid manual-automated CMS system over the manual OMP system is likely to be that the operator has constant visual feedback during the registration process, allowing them to visually assess the quality of the registration in three dimensions after each intervention. The OMP system offers no graphical feedback, and it is only once all of the landmark points have been identified and the registration is complete that the registration becomes available to review.

Automated registration yielded identical results on repetition with an identical initial registration and the same algorithm, indicating that the optimisation of both MI algorithms was deterministic. Differences in accuracy between the two planning systems are likely to be due to a combination of the use of different algorithm parameters and different data initialisation positions. No significant difference in accuracy was detected between the automated and manual methods within each planning system. This was unexpected for the OMP system in which the manual and automated methods are totally independent, unlike in the CMS system where the user was allowed to start by using the MI as a first attempt.

This study has shown that the differences between these four methods of image registration are small yet measurable with the largest difference in accuracy between methods being in the order of 2 mm at the extremes of the GTV.

We recognise that there are a number of limitations to this study. The most significant is the potential bias introduced by the definition of the reference standard. The reference standard was MI followed by manual adjustment by a consultant radiologist and two physicists. In the absence of a known transform, this was deemed a best effort at registration using the tools available. However, because both CMS techniques incorporated the use of MI, one might have predicted that this would perform better than OMP. Several factors should be considered in defence of this. First, given that the MI

technique produces a reasonable registration, it would be sensible for an operator to use MI as a first attempt in order to improve efficiency in clinical practice. Second, operators in the hybrid manual-automated group were instructed to attempt an improvement if they deemed it possible using the MI starting point. Finally, different operators worked independently to perform the reference standard registration, hybrid manual-automated registrations and automated registrations. It is clear from the individual transformations that the CMS hybrid manual-automated registrations were not identical to the CMS automated transformations, indicating that the operators did indeed attempt improvement. However, no statistically significant difference was detected between the outcome of the two methods, indicating that intervention generally produced no added value.

Other authors have used external fiducial markers to improve patient set-up and to infer a reference standard; however, such markers were not used in this study for both practical and technical reasons. Lack of fiducial markers meant that patients could be set up quickly for both CT and MRI, and as a consequence the imaging was well tolerated. In addition, markers at the patient surface are likely to move in a non-rigid manner in relation to the internal pelvic anatomy; hence they suffer more from MRI distortion towards the edge of the field-of-view, compromising their value.

Geometric distortion in MRI arises from inherent magnetic susceptibility differences in both the MRI scanner and the patient [40]. Such distortion was minimised in this study by using a high bandwidth turbo spin-echo sequence and by ensuring that the volume of interest was close to the centre of the magnet bore. Various authors have attempted to characterise and/or correct this distortion [41–45] so that MRI could be used to aid computerised RT treatment planning. Some have gone further and promoted the use of planning without a corresponding CT scan [46], with one study using a 3D T_1 FLASH (fast low angle shot) sequence for prostate imaging and quoting a mean distortion of 2 mm in the centre of the pelvis [47]. In the region of the patient surface, geometric distortion increases to between 5 mm and 10 mm [45, 47], depending on the specific scan parameters and size of the patient. However, this study is aimed at evaluating bony anatomy co-registration between CT and MRI and thus the region of interest required to be distortion-free is from the centre of the GTV out to the bony pelvis, where the registration is based. From the available literature, the degree of distortion in this region was likely to be in the order 2 mm. This was confirmed using a phantom similar to that used by Schnabel et al [45].

Distortion of the MRI may have introduced small systematic registration errors between the CT and MRI modalities to all of the registration techniques, including the reference standard. With distortion within the region of interest less than 2 mm, any systematic registration errors due to this distortion were likely to be diluted to less than 1 mm for both manual and hybrid manual-automatic techniques. The systematic error was likely to have been different for the MI techniques than for the hybrid manual-automatic techniques because the MI techniques included all image data, from both inside and outside the patient surface, whereas the hybrid manual-automatic techniques were registered on the bony

anatomy alone. To reduce the effect of local soft-tissue deformations, such as those attributable to the bladder and/or rectal filling, between CT and MRI, the interscan time was minimised (maximum 45 min).

Like most voxel intensity-based image registration algorithms, MI will be affected most by structures that have strong contrast differences. Hence, there would have been a natural weighting towards registration of the bony anatomy in preference to the soft tissues. Despite this potential for bias against the automated methods, the registration errors were found to be on average less than 2.5 mm for the CMS MI method, which also gave the best agreement with the reference registrations of all the registration methods in this study. It should be noted that no obvious distortion was detectable when the reference registrations were performed.

The registration accuracy would have been limited by the relatively coarse slice separation of both the CT and the MRI data sets. Sykes et al [48] showed that systematic errors for CT to cone beam CT registration increased from approximately 0.1 mm to 0.8 mm when the CT slice separation was increased from 0.6 mm to 5 mm in a skull phantom [48]. Since both the CT and MRI were acquired with a 5 mm slice separation, registration errors of the order of 1 mm should be expected from this source.

This study found that the best-performing technique results in an average TRE of 2 mm. This equates to the average GTV placement uncertainty as a result of the registration procedure itself and is small compared with other uncertainties in the treatment planning process. Further, these uncertainties are likely to be insignificant when offset against the potential improvement in target and normal tissue delineation arising from the registration procedure.

This is a relatively small study, which may affect the applicability of the data to a general population. Nevertheless, there was an acceptable case mix within study eligibility criteria. There were also two unusual subjects: patient 6 had previously implanted pins in one hip following trauma and patient 2 was tense for their CT scan. Both scenarios were likely to increase the difficulty of registration, especially by MI. For patient 2, two out of three operators were more accurate than the automated methods; for patient 6, the manual and automated performances were similar.

The literature on CT-MRI registration for rectal carcinoma is sparse, but additional information is available for other pelvic disease sites, *e.g.* the prostate [49], with some studies showing significantly larger target volumes delineated on CT compared with MRI [50]. This may indicate a general overestimation of target size using CT because of a lack of clinical confidence in the extent as a result of relatively poor soft-tissue contrast.

Conclusion

Although we saw some variation in CT-MRI co-registration uncertainty between the commercial techniques examined in this study, a fully automated technique provided a fast and accurate solution with registration uncertainties in the order 2 mm. For patients with resectable rectal cancer, MRI acquired in the prone treatment

position without the use of fiducial markers can be accurately co-registered with planning CT. This offers potential improvement in the accuracy of GTV definition, which, in the pre-operative setting, could reduce the risks of inadequate margins and excessive normal tissue toxicity.

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