

Cover Page



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The page features two large, stylized orange geometric shapes. The top shape is a jagged, upward-pointing form with a white notch in the center. The bottom shape is a similar jagged, downward-pointing form, also with a white notch in the center. Both shapes are composed of several straight lines of varying lengths and angles, creating a modern, abstract look.

CHAPTER 1

MRI and target volume
delineation of the glandular breast tissue
and the lumpectomy cavity

Registration of MRI and CT for target volume delineation in breast conserving radiotherapy

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Abstract

Background

To assess the optimal method of MRI to CT registration of the glandular breast tissue (GBT) and the lumpectomy cavity (LC).

Materials and methods

After breast conserving surgery 10 breast cancer patients underwent a planning-CT and a MRI (1.5 T, T1 weighted) in supine radiotherapy treatment position. Co-registration of the CT and MR images was performed with five different methods (breast-markers, thoracic-markers, surgical (titanium) clips, normalized mutual information and local correlation). Parameters of the rigid-body transformation (3D translation and 3D rotation) to match the CT and MRI were recorded. Accuracy was evaluated by comparing the misalignment between CT and MR for breast-markers, thoracic-markers, surgical clips and all fiducials. Additionally, an evaluation was performed by delineating the GBT based on CT and MRI by four observers (two radiation oncologists and two radiologists). We determined which registration procedure yields the smallest non-overlapping (rest) volume.

Results

The thoracic-marker-based registration resulted in smallest MRI-CT distances between breast markers. For the surgical clip evaluation, the mean MRI-CT distance for the breast-marker-based registration is the lowest. But the use of surgical clips for MRI-CT registration resulted in large rotations ($> 3^\circ$) for 7 out of 8 patients. Moreover, clips were not always well visible on the MR images. The thoracic-marker-based and breast-marker-based registrations resulted in the smallest MRI-CT displacements between all fiducials.

Co-registration of CT and MR data sets based on breast-markers gave the best result for the GBT delineation in terms of the rest volume.

Conclusions

The use of breast markers for MRI-CT co-registration gives the best results and is recommended not only for delineation of the GBT, but also for delineation of the lumpectomy cavity. For lumpectomy cavity delineation the clip-based registration is an alternative to the breast-marker-based registration.

Introduction

In radiotherapy, target volume delineation is based on computed tomography (CT), while magnetic resonance imaging (MRI) is able to complement the CT data for its superior soft tissue visualisation. The added value of co-registration of CT together with MR images was clearly assessed for various tumour sites such as brain, head-and-neck and prostate [1-3]. However, this added value was not studied in detail for breast cancer radiotherapy [4]. There are some published data available about registration of MR images with mammography and ultrasound [5]. Kirby et al. [6] and Jolicoeur et al. [7] described co-registration of CT to MR images (in prone position and supine position, respectively) for breast cancer radiotherapy. These two studies focussed on co-registration of CT/MRI for surgical bed volumes. For patients in supine position, comparison of CT and MRI remains difficult due to the limited bore size of conventional closed MRI scanners (for example, 60 cm in diameter for a Siemens Magnetom Symphony MRI scanner), respiratory motion artifacts, and distortion of breast tissue by overlying MR receiver coils. In our previous studies [8,9], a first attempt to find an added value of MRI was described for delineation of the glandular breast tissue (GBT) and lumpectomy cavity, respectively. In these studies non-registered CT and MR scans were used. To investigate whether MRI indeed improves GBT and lumpectomy cavity delineation, a method has to be developed for accurate rigid registration of MR and CT in breast cancer.

The majority of registration algorithms in medical imaging can be classified as being either frame based [10], point based [11] or voxel based [12]. Stereotactic frame-based registration is very accurate, but not suitable for breast imaging. The anatomical point-based registration methods are labour-intensive and their accuracy depends on the accurate identification of corresponding landmarks in all modalities. Voxel-based registration methods [12] optimize the similarity of all geometrically corresponding voxel pairs for some features. The overall registration accuracy should be within an acceptable tolerance for 3D treatment planning (2–5 mm) [13]. According to Fraass et al. 3D registration results in about 2 mm accuracy, including distortions and transfer of MRI contours to CT dataset [13].

Nowadays rigid image registration has become more accurate [4,14]. According to Devic et al. [4] the MRI to CT image co-registration error is of the order of 1–2 mm, except for deformable methods. However, the magnitude of the co-registration error depends on the co-registration technique and also on the anatomical site. Skerl et al. [14] compared 12 similarity measures for the rigid registration of multi-modal head images. They concluded that the results for the registration of CT to MR images and MR to CT images indicate that such methods as normalized mutual information are the most accurate similarity measures and have the smallest risk of being trapped in a local optimum.

In addition to the clinically used large region of interest (ROI), a registration of multiple ROIs can be used (mROI). Van Kranen et al. [15] proposed to use this method (based on mROI registration of cone beam computed tomography scans and the planning CT) and van Beek et al. [16] reported the first clinical experience with this method for head-and-neck cancer patients.

In our study, CT and MR images of ten breast cancer patients who were candidates for breast conserving therapy were made in supine position after surgery and before starting the radiotherapy treatment. On the breast of these patients breast markers were placed. For these patients co-registration of the CT and MR images was performed with five different methods (breast-markers, thoracic-markers, surgical clips, anatomical markers, normalized mutual information (NMI) [12] and local correlation

[17]. The rigid-body transformation consists of a 3D translation and 3D rotation, and these parameters were recorded for each registration method. Registration accuracy was evaluated by performing a comparison of the misalignment between CT and MR by breast-markers, thoracic-markers, surgical clips and all fiducials (breast-markers, thoracic-markers and surgical clips). Additionally, an evaluation was performed by delineating the GBT on CT and MRI by four observers (two radiation oncologists and two radiologists). Thereafter, we investigated which registration procedure yields the smallest non-overlapping volume (rest volume).

The aim of this manuscript is to describe advantages and disadvantages of each registration method and to find the best possible MRI to CT registration of the GBT and the lumpectomy cavity.

Materials and methods

Patients

Ten patients with early stage breast cancer (clinically T1-2; N0-1) were treated with breast conserving therapy (patients did not undergo en bloc axillary dissection). After referral to the radiotherapy department a planning-CT scan and directly afterwards an MRI scan were performed. Patient and tumour characteristics are presented in Table 1. All patients confirmed participation in our study by signing an informed consent. The study was approved by the regional institutional review board METC Zuidwest Holland [18].

Mean age in years (range)	Menopausal status	Left (L) - or right (R) sided	Breast quadrant	Pathological TN (2002)	Days since surgery (range)	Ductal (D) or lobular (L) carcinoma
57 (44 - 86)	†post: 4x *pre: 6x	L:3x R:7x	upper outer: 3x upper inner: 1x lower outer: 2x sub areolar/ nipple complex: 2x upper 12 o' clock: 1x lower 6 o' clock: 1x	pT1: 6x pT2: 4x pN0: 8x pN1: 2x	27 (12 - 41)	D: 10x

Table 1. Patient and tumour characteristics.

Abbreviations: *pre = premenopausal; †post = postmenopausal.

CT and MR images of patients

Patients underwent planning CT followed by MRI in the same supine radiotherapy treatment position. No intravenous contrast was used. Patients were imaged in supine position with back, shoulders and arms supported by a CT and MRI compatible wedge (Thorawedge, CIVCO Medical Solutions, The Netherlands) at 5° slope angle and with a knee support for comfort. Both arms were in abduction with both hands jointed above the head. CT and MR images were obtained using 3 mm slice thickness from lung apices up to diaphragm. The field of view covered the whole of the patient's chest and both breasts. CT scans (using a 512 x 512 matrix and a 1.07 mm pixel size) were performed using an AcQSim single slice CT scanner (Philips Medical Systems, Cleveland, OH, USA) with a bore size of 85 cm. MR images were taken using a Magnetom Symphony 1.5 T scanner (Syngo MR 2004A MRI, Siemens, The Netherlands) with a bore size of 60 cm. Only MR images in one direction: T1 weighted TSE (Turbo Spin Echo) transverse MRI scans (256 x 204 matrix and voxel size 1.6 x 1.6 x 3 mm³, no slice-gap) were used in this study.

No fat suppression was used as the entire GBT including the lumpectomy cavity was intended to be visualized. The MRI body coil was set at a bandwidth of 150.0 Hz/pixel with a signal-to-noise ratio of 1. An additional phased-array coil was positioned over the affected breast supported by foam blocks aside to the breast to prevent changes of the original breast shape and to keep the breast in radiotherapy treatment position. The border of palpable GBT was marked with a thin plastic tube by the radiation oncologist (HS) just prior to CT scanning. The position of the tube remained the same during both CT and MR scanning. For CT and MR imaging the tube was filled with either a copper wire or lipiodol, respectively. During CT and MR scans multimodality hydrogel filled markers (MedCaT B.V., Erica, The Netherlands) were used to evaluate MR-CT matching possibilities. The donut shaped markers were 15 mm in diameter and had a thickness of 3.5 mm with a hole in the middle with a diameter of 5 mm. Four markers were placed along the laser lines on the thorax and four markers were placed on the breast (see Figure 1) of each patient. Surgical (titanium) clips (Teleflex Medical, Morrisville, NC, USA) within the breast, applied by surgeons to mark the borders of the lumpectomy cavity, were no contra-indication for MRI. In two of the remaining ten patients no surgical clips were placed in the lumpectomy cavity.

CT and MR image registration

CT and MR images were registered using Syntegra software of the Pinnacle3 treatment planning system (version 8.0, Philips Medical Systems, The Netherlands). Syntegra provides manual and point-based image registration, and three automated methods of gray value voxel-based image registration.

NMI registration is nowadays the state of the art for many clinical sites. For ten breast patients, the registration of the MR with CT images was performed with five different methods: four point-based (breast-markers, thoracic-markers, and surgical clips) and two automated voxel-based (NMI and local correlation) methods.

Multimodality markers (thoracic-markers or breast-markers) matching was achieved by using the midpoint of each marker by one observer (ALP). The midpoints were manually identified on each of the CT and MR scans. Misalignment between CT and MR markers was calculated in terms of the distance, defined as the mean of the distances between all point pairs. Syntegra software allows for automatic minimization of this distance between two sets.

The centre of gravity of the hole of each donut was manually determined on the axial slices of the CT and MR scans, sagittally and coronally reconstructed images were used for verification. For each clip, an identical procedure of identification of the centre of gravity was manually performed. Impaired visibility of the surgical clips on the MR images of some patients [9] made registration on the surgical clips difficult. Moreover, the surgical clips were often located close to each other (see e.g. Figure 2).

NMI and local correlation are two automated image registration algorithms in Pinnacle³. They are based on maximizing of similarity measures: NMI is based on probability distributions of the gray values in each image set [12], whereas local correlation assumes a local linear relationship between gray values. Local correlation is the default option in Syntegra for registration of CT and MR images because it works best for different image sets in which equivalent features can easily be seen. After a preliminary study for NMI and local correlation the complete set of CT and MR scans were used. Alternatively, a bounding box was used to limit the image set to a rectangular box defined by the user. An attempt to define the bounding box around the breast of each patient has failed probably because of the absence of high-contrast structures such as bones in the breast. Likewise, the use of a ROI to limit the existing image set was not preferred because this method is time consuming and subjective since the results strongly depend on the ROI delineation.

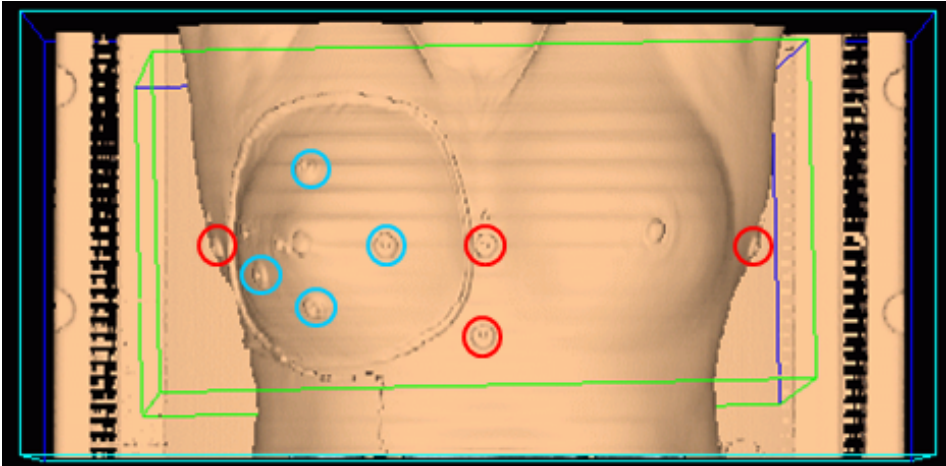


Figure 1. Patient 1 lying in the supine radiotherapy position on a Thorawedge with 5° slope angle. Four multimodality markers were placed along the laser lines on the thorax (red circles) and four markers were placed on the breast (aqua circles). The border of palpable GBT was marked with a thin copper wire. Thin blue and green lines indicate the CT and MR scan volumes, respectively.

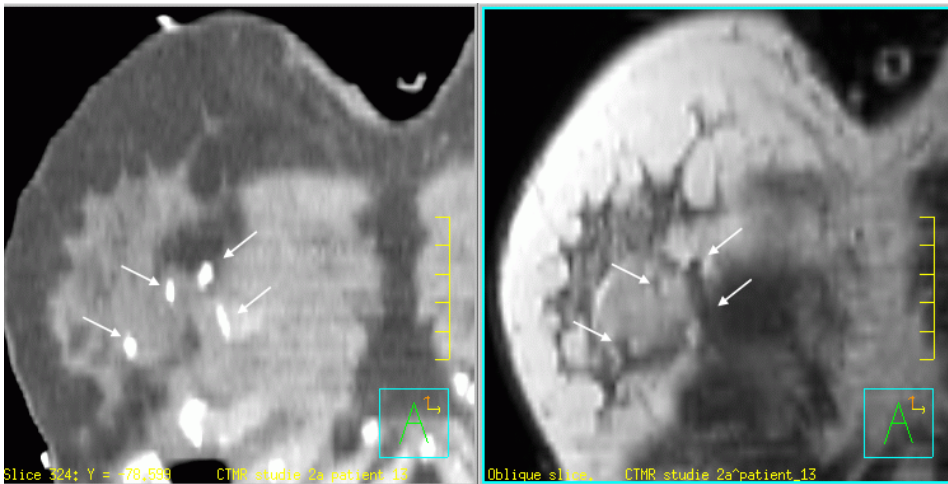


Figure 2. Patient 8 (54 years, premenopausal status) with four surgical clips in the breast: sagittal CT (left) and MR (right) images registered using breast markers. Note that the four clips, which can be seen on these images, are located very close to each other.

Evaluation of the registration accuracy

For each patient and each registration method the rigid-body transformation was recorded, defined as a 3D translation along the x-, y- and z-axis and 3D rotation around the x-, y- and z-axes. Note that according to the patient's CT scans, in all cases the x-axis is directed from patient's right to left, the y-axis is directed from posterior to anterior and the z-axis is directed from cranial to caudal. Although each patient underwent the CT and MR scans in the same treatment position, limited rotations between two scans can occur.

Each registration method started with the movement of the centre of the MR data set to the centre of the CT data set. Consecutively the translations and rotations were adjusted according to the applied registration method. For each evaluation method the fiducials (breast-markers or thoracic-markers or the clips) remained on the same place during the CT and MR. For each patient the registration accuracy of each method was evaluated (post-registration) by comparison of the average MR-CT displacement of the breast-markers or the surgical clips, the thoracic-markers or all fiducials.

In addition to the other registration method evaluations, target delineations (Clinical Target Volume) of the GBT by four observers (two radiation oncologists and two radiologists) [8] were used. The GBTs were delineated blind to the viewing contours of others and using written delineation instructions according to Giezen et al. [8]. For each individual patient, the mean, range and standard deviation values of the GBT delineation were calculated to evaluate the inter-observer variability in GBT delineation. For each registration method an averaged rest volume over the four observers on CT and MR images was determined according to Rasch et al. [19]. The rest volume (CT, MRI) was determined for each observer and consisted of specific parts of the GBT volumes, which were delineated on CT but not on MRI.

MR image distortion and validation of the methods used

Sources of MRI distortion can be divided into two groups: machine related distortions and object induced (i.e. patient dependant) effects [4]. Machine related distortions could be quantified and subsequently corrected for. Modern MRI scanners compensate for the majority of machine-derived distortions [4]. Object induced distortions arise from magnetic susceptibility effects, which modify the local magnetic field and tend to be most pronounced at air/tissue boundaries. The other major source of object induced distortions is chemical shift. Protons in fatty tissues resonate at slightly lower frequencies than those in water. The difference in frequency is called chemical shift [20] and water-fat shift (WFS) for the specific case of body fat. Susceptibility-induced distortions of the markers were minor. The markers are used for evaluation of registration accuracy without any correction for shift. Motion is an additional problem in MR imaging which can result in blurring, misregistration and artifacts within the scanned images. Both cardiac as well as respiratory movements affect the thorax.

Statistics

For the statistical analysis SPSS version 17 (SPSS Inc. Chicago, IL, USA) was used. To analyze the differences between the different registration methods a Wilcoxon signed-rank test was used to compare the differences of the average values between both imaging modalities. The level of statistical significance was considered $p < 0.05$ (two-sided) for all calculations.

Results

CT and MR images registration

The translations of MRI relative to CT images along the x-, y-, and z-axes, as determined with five registration algorithms, are presented in Table 2.

Differences between various registration methods for the translation along the same axis are limited within a few millimetres. The angles of rotations of the MR image data sets along the x-, y-, and z-axes after completing MRI/CT fusion with the five registration algorithms are shown in Table 3. Figure 3 shows an example of the breast-marker-based and clip-based registrations for patient 4. For the clip-based registration a rotation of the MR image along the z-axis relative to the CT image can be seen clearly.

Translations and distance d (cm)																				
Pa- tient	Breast-markers				Thoracic-markers				Surgical clips				Local Correlation				Normalized Mutual Information			
	#	x	y	z	d	x	y	z	d	x	y	z	d	x	y	z	d	x	y	z
1	-0.4	-48.0	2.1	48.0	0.2	-47.8	2.1	47.9	-0.3	-47.7	2.2	47.7	-0.4	-47.7	2.1	47.7	-0.4	-47.7	2.3	47.7
2	0.7	-48.2	0.3	48.2	0.1	-47.5	0.7	47.5	0.7	-49.1	1.4	49.1	0.1	-47.4	0.7	47.4	0.0	-47.3	0.6	47.3
3	0.2	-46.3	3.0	46.4	0.0	-46.4	3.1	46.5	-0.2	-47.3	4.2	47.5	-0.2	-46.4	3.5	46.6	-0.2	-46.4	3.6	46.6
4	-0.3	-50.5	1.7	50.5	-0.1	-50.4	1.7	50.4	-1.6	-51.1	2.1	51.2	-0.5	-50.4	2.1	50.5	-0.5	-50.4	2.2	50.4
5	-1.8	-46.7	-2.3	46.8	-2.2	-46.8	-2.0	46.9	-2.2	-46.9	-3.2	47.1	-2.3	-46.8	-2.2	46.9	-2.3	-46.8	-2.1	46.9
6	0.5	-47.2	-8.4	47.9	0.6	-47.0	-8.2	47.7	n.a.*	n.a.*	n.a.*	n.a.*	0.4	-47.2	-8.3	48.0	0.4	-47.2	-8.4	47.9
7	1.3	-47.5	-7.4	48.1	1.4	-47.0	-7.5	47.6	n.a.*	n.a.*	n.a.*	n.a.*	1.0	-47.2	-7.2	47.7	1.0	-47.1	-7.1	47.7
8	-0.1	-50.9	-8.1	51.5	0.0	-50.9	-7.9	51.5	-0.4	-50.9	-7.4	51.5	-0.2	-50.8	-7.8	51.4	-0.2	-50.8	-7.8	51.4
9	-2.3	-47.1	-1.9	47.2	-2.0	-47.1	-1.4	47.2	-2.2	-47.0	-0.9	47.0	-1.9	-47.1	-1.2	47.1	-1.9	-47.1	-1.1	47.1
10	3.1	-48.8	-6.4	49.3	2.8	-48.9	-6.5	49.4	3.1	-49.0	-6.0	49.4	2.7	-48.7	-6.6	49.2	2.6	-48.8	-6.4	49.2

Table 2. CT and MR image registration parameters found for breast-marker, thoracic-marker, surgical-clip-based registration, local correlation and normalized mutual information (NMI). The Table shows the translation of MR images along the x-, y-, and z-axes and the distance (d) between the two imaging modalities.

Rotations (degree)																
Patient	Breast-markers			Thoracic-markers			Surgical clips			Local Correlation			Normalized Mutual Information			
	#	x	y	z	x	y	z	x	y	z	x	y	z	x	y	z
1	-2.1	1.2	-3.1	-2.0	0.6	-1.3	1.0	-1.0	-1.1	-0.9	0.3	-1.1	-0.9	0.5	-0.9	
2	-3.6	-2.1	7.5	-3.8	-1.3	2.8	-3.0	2.7	10.5	-1.8	-0.6	2.2	-1.4	-0.5	2.0	
3	-3.8	-0.7	-0.1	-2.2	-0.4	-1.1	-10.2	-4.1	-2.8	-2.0	-0.3	-0.2	-1.2	-0.3	-0.4	
4	-2.8	1.6	0.0	-1.8	2.2	2.2	-1.4	-1.6	-6.1	-1.2	2.3	0.3	-1.0	2.0	1.0	
5	-0.1	-1.5	0.0	-2.3	0.3	-0.2	3.1	-4.1	1.1	-1.1	0.7	0.0	-0.8	0.8	-0.3	
6	-0.8	-2.3	0.6	-2.0	-2.2	1.4	n.a.*	n.a.*	n.a.*	-1.4	-2.3	0.4	-1.4	-2.3	0.4	
7	-1.8	-1.2	-2.2	-2.3	-0.3	-0.1	n.a.*	n.a.*	n.a.*	-2.2	0.5	0.4	-1.8	0.2	0.6	
8	-2.8	1.3	-0.3	-3.0	0.6	0.3	-4.3	-1.3	-1.8	-2.3	0.3	-0.4	-2.5	0.4	-0.1	
9	-1.2	0.5	0.9	-1.7	-0.4	1.7	-4.7	-3.2	2.1	-2.0	-1.2	0.2	-1.6	-1.3	0.6	
10	-1.3	0.4	-0.3	-0.5	0.3	0.1	-1.9	3.1	0.6	-0.2	1.4	0.4	-0.2	1.6	0.4	

Table 3. The same as Table 2, but for rotation of MR images around the x-, y-, and z-axes.

Rotations larger than 3° are highlighted by shadowing.

*In patients 6 and 7 no surgical clips were placed in the lumpectomy cavity.

Registration accuracy

The registration accuracy for the five registration methods evaluated using breast-markers; surgical clips, thoracic-markers and all fiducials are presented in Figures 4a, 4b, 4c and 4d, respectively. The various registration methods are given in the Figures in an increasing level of misalignment between the CT and MR scans according to the breast-marker evaluation, shown in Figure 4a. For the other three evaluation methods the same order was used. Note that the smallest MRI-CT distances for the breast markers are achieved for breast-multimodality-marker registration (breast-mmm). This is not surprising, since here the same breast markers are used for matching and evaluation. This result can be considered as an indicator of the best achievable accuracy of the markers themselves.

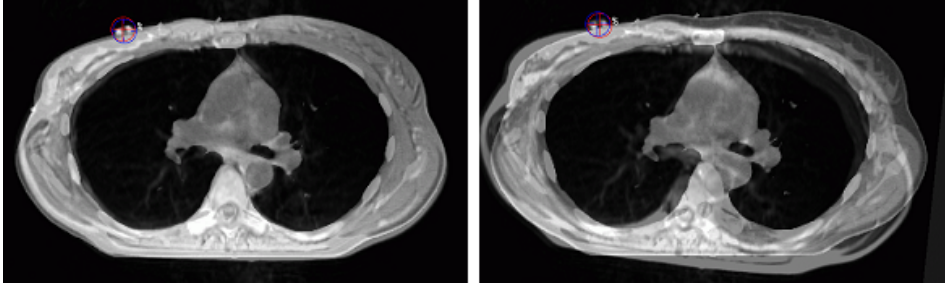


Figure 3. Axial scans of the fused CT and MR images of patient 4 (44 years, premenopausal status) with a breast-marker: the left panel shows the result of breast-marker based registration the right panel shows that for surgical clips based registration. The red and blue circles show the position of the marker on the CT and MR images, respectively.

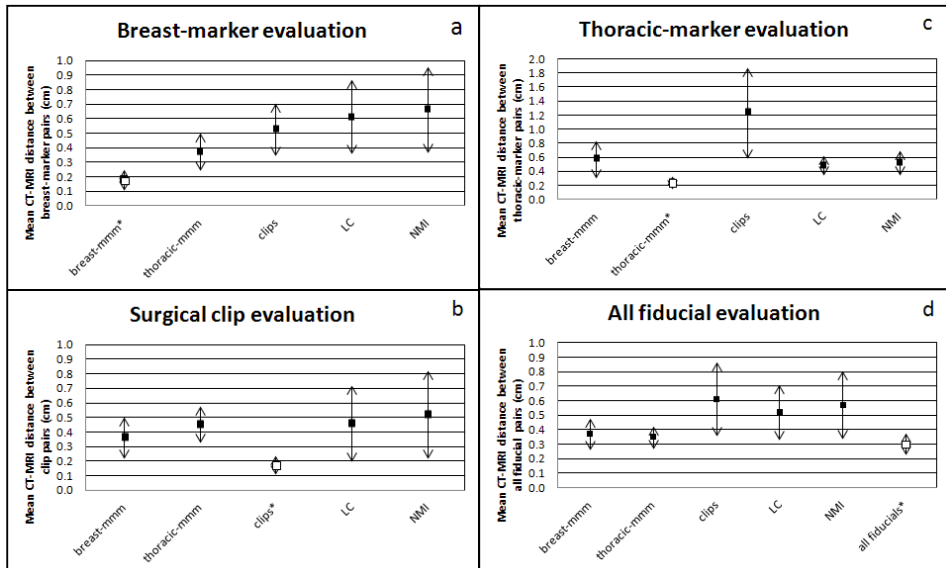


Figure 4. Analysis of CT/MRI fusion accuracy for five registration methods: breast-multimodality-markers (breast-mmm), thoracic-multimodality-markers (thoracic-mmm), surgical clips (clips), local correlation (LC) and normalized mutual information (NMI). Evaluation of each registration is performed using the breast-markers (a), surgical clips (b) or thoracic-markers (c) or all fiducials (d). Each registration result is presented as the mean value with the arrows for ± 1 SD. Note that the y-scale is twice as large for evaluation based on thoracic-markers compared to breast-markers, surgical clips and all fiducials. The (biased) method used for the evaluation is marked with a star (*) and an open symbol. In Figure 4d registration method based on fusion of all fiducials is added.

The thoracic-marker-based registration resulted in smallest MRI-CT distances between breast markers (see Figure 4a). If measured using the breast marker MRI-CT distance, the difference between the thoracic-marker-based and the clip-based ($p=0.05$) or local correlation based ($p \leq 0.01$) registration was significant, whereas the local correlation based and NMI based registration methods showed worse results than the thoracic-marker-based and the clip-based methods.

For the surgical clip evaluation, the mean MRI-CT distance for the breast-marker-based

registration is the lowest (see Figure 4b). The mean value of the clip MRI-CT distance for breast-marker-based registration is not significantly lower ($p=0.09$) than that for the thoracic-marker-based registration.

Evaluation by delineating the GBT on MRI and CT

Figure 5 shows the glandular breast tissue delineations by 4 observers on CT and MRI for patient 7. For each patient in this study, a mean rest volume as percentage of the mean GBT volume is presented in Table 4 for each of the five registration methods. The mean rest volume is the smallest on CT and on MRI for the breast marker registration (followed by the local correlation registration).

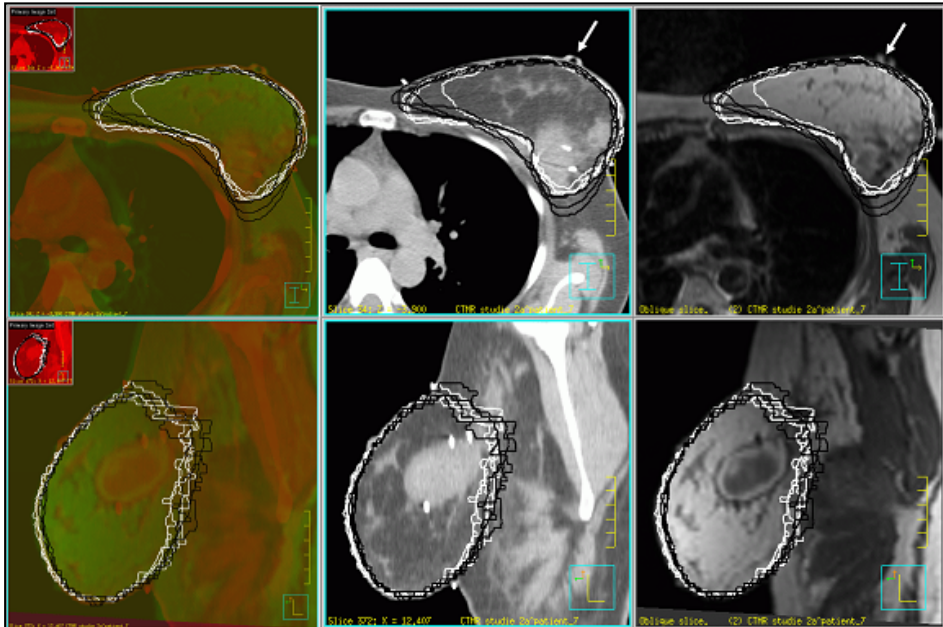


Figure 5. Axial scans (top panels) and sagittally reconstructed scans (bottom panels) of the fused CT and MR images of patient 2 (49 years, premenopausal status) for breast-marker-based registration: the glandular breast tissue delineations by 4 observers on fused CT and MRI (left, CT in red and MRI in green), CT (middle) and MRI (right). The GBT delineations on CT and MRI are shown in black and white, respectively. The arrow in the top panels points to a breast marker. On the axial and sagittally reconstructed scans respectively two and three markers around the seroma, are visible. Note that the GBT volume is well fused with breast marker registration, although a rotation up to 7.5 degrees between CT and MRI took place.

(a)

patient #	Mean GBT (CT)	Mean rest volumes* (CT, MRI) (%)				
	(cm ³) Mean (range, SD)	Breast- markers	Thoracic- markers	Surgical clips	LC	NMI
1	643 (592-675, 37)	12.5	15.5	12.8	12.9	12.4
2	919 (865-977, 46)	10.7	10.6	13.7	10.5	10.4
3	863 (826-902, 40)	7.7	7.0	14.5	6.8	7.9
4	326 (309-360, 23)	16.9	19.4	35.0	17.9	18.6
5	364 (343-413, 33)	15.0	17.6	24.3	14.7	18.5
6	672 (595-767, 81)	15.8	16.3	n.a.#	15.7	15.8
7	408 (366-487, 54)	16.1	17.7	n.a.#	16.4	16.7
8	495 (430-594,76)	13.3	15.8	12.9	12.6	13.1
9	808 (727-1008, 142)	11.7	12.8	11.6	14.3	14.2
10	410 (366-524, 77)	22.8	21.7	22.6	22.6	22.1
Mean	591	14.2	15.4	18.4	14.4	15.0
SD	220	4.1	4.3	8.2	4.3	4.3

(b)

patient #	Mean GBT (MRI)	Mean rest volumes* (MRI, CT) (%)				
	(cm ³) Mean (range, SD)	Breast- markers	Thoracic- markers	Surgical clips	LC	NMI
1	614 (549-667, 59)	8.3	11.5	8.6	8.7	8.2
2	893 (752-974, 100)	8.0	8.0	11.2	7.9	7.7
3	951 (804-1038, 115)	16.1	15.5	22.3	15.3	16.3
4	347 (290-388, 41)	21.9	24.2	38.9	22.9	23.5
5	361 (271-410, 63)	14.2	16.8	23.7	13.9	17.8
6	621 (495-733, 99)	8.8	9.4	n.a. #	8.7	8.9
7	392 (296-441, 66)	12.9	14.6	n.a. #	13.2	13.5
8	497 (361-558, 92)	13.6	16.1	13.2	12.9	13.4
9	808 (653-971, 130)	11.7	12.8	11.6	14.3	14.2
10	354 (307-421, 49)	10.5	9.3	10.4	10.3	9.8
Mean	584	12.6	13.8	17.5	12.8	13.3
SD	232	4.2	4.8	10.3	4.4	5.0

*defined as the average volume delineated by the same observer on MRI, but not on CT.

In patients 6 and 7 no surgical clips were placed in the lumpectomy cavity.

Table 4. GBT volume delineation on CT (a) and MR (b) images and rest volumes for CT (a) and MRI (b) found for breast-marker, thoracic-marker, surgical-clip-based registration, local correlation (LC) and normalized mutual information (NMI). For each patient the rest volume is given as the percentage of the corresponding mean GBT volume.

Discussion

Comparison of five different registration methods (breast-markers, thoracic-markers, surgical clips, normalized mutual information and local correlation) was performed for the GBT and the lumpectomy cavity. The use of breast markers for MRI-CT co-registration gives the best results and is recommended not only for delineation of the GBT, but also for delineation of the lumpectomy cavity. For lumpectomy cavity delineation the clip-based registration is an alternative to the breast-marker-based registration.

CT and MR images registration

We have chosen, because of the absence of the established gold standard in assessment of the registration accuracy of retrospective intermodality image registration [21], for the comparison of five different registration methods for the GBT and the lumpectomy cavity. The performance of the methods was evaluated by the agreement between delineations [8,9] and by the size of the standard deviation of registration parameters. A rigid transformation was chosen based on our previous results [8]. In this article, Giezen et al. showed that the GBT volumes were comparable on CT and MR scans (mean [SD] ratio MRI to CT GBT volumes, 1.04 [0.06]). In the present study, the mean [SD] ratio MRI to CT GBT volumes was 0.98 [0.07]. In literature breast deformation was observed for MRI in prone position and for CT in supine position [22]. Further investigation of non-rigid transformation is beyond the scope of this study.

MRI-CT translation parameters were comparable for different registration methods (see Table 2), while the rotations were for some registration methods larger than 3°. For the registration using surgical clips, rotations larger than 3° were found for 7 out of 8 patients. We believe that these rotations occur due to small distances between the clips rather than a rotation of the clips relative to patient anatomy.

Results for GBT

Delineation of the CTV of GBT based on CT scans remains a challenge in spite of relatively low interobserver variability [23,24], because of the difficulty of differentiating between fatty (involved) breast tissue and fatty non-breast tissue. Struikmans et al. [23] found a mean conformity index (CI), calculated as an average of the ratios between the common volume and encompassing volume for all possible pairs of delineations, on CT scans of 0.87 (range, 0.75–0.92) for five observers (two radiation oncologists, two radiation oncologist trainees, and one radiologist) averaged over 18 patients. Hurkmans et al. [24] reported the interobserver variability of GBT delineations by four radiation oncologists in seven breast cancer patients ($C_{\text{common}} = 0.43$, where C_{common} was calculated as a ratio of the volume commonly delineated by all observers to the encompassing volume). According to Giezen et al. [8] interobserver variability of the delineation of the CTV of GBT on CT and MRI is comparable.

As can be seen in Table 4, the mean rest volume was the smallest for the breast marker registration and the largest for the clip registration but the differences between various registration methods were small and not statistically significant because of the interobserver variability.

For the breast-marker evaluation, the misalignment between CT and MRI was the smallest for the thoracic-marker registration (except for the breast-marker registration). The breast- and thoracic-marker-based registration resulted in the smallest MRI-CT distances between all fiducials.

In our study the mean MRI-CT distance between the breast marker pairs averaged over 10 patients was 1.8 mm [SD = 0.7 mm] for the breast-marker-based registration. The last results are comparable with the mean clip misalignment described below. Note, that the matching region is larger for the breast-markers (GBT) than for the clips (lumpecto-

my cavity). The local correlation and NMI methods use a larger region than the breast to match. This probably results in additional misalignment, for instance due to distortion of the contra lateral breast by overlying MR receiver coils.

The thoracic-marker evaluation requires a significantly larger region to match. A larger matching region can make registration more difficult due to machine-related and patient-induced image distortions and cardiac and respiratory movements. The mean misalignment between CT and MR across 10 patients was found to be 2.4 mm [SD = 0.9 mm] for the registration based on the same fiducials, which is only slightly larger than the result for breast markers. For thoracic-marker-based evaluation the local correlation showed lowest misalignment between CT and MR scans, followed by the NMI. To our knowledge, CT and MR images co-registration for the GBT was not discussed in literature so far. We therefore cannot compare our results with other studies.

Results for lumpectomy cavity

Delineation of the lumpectomy cavity is based on surgical titanium clips attached to the cavity wall by the surgeon [6]. The interobserver variability in the delineation of the lumpectomy cavity on CT scans is high even in the presence of delineation guidelines: Struikmans et al. [23] reported the mean CI of 0.56 (range 0.39 – 0.74), according to van Mourik et al. [25] considerable delineation variation was present (mean CI = 0.42, range 0.19 - 0.59); partially because of the relatively small volume of the cavity. Addition of MR images to CT/clip data can probably improve interobserver variability [6,9]. Further investigation based on delineation of lumpectomy cavity on MR-CT co-registered images is needed.

For the surgical clip evaluation, which is a reasonable approach for the lumpectomy cavity, the mean CT-MR distance for the breast-marker-based registration was the lowest (except for the clips themselves) 3.6 mm [SD=1.4 mm].

If the thoracic markers were used for registration, the mean misalignment between CT and MR for the clips was 4.5 mm [SD=1.3 mm]. However, if the clips were used for registration the mean misalignment of thoracic markers was larger by more than a factor of two, 12 mm [SD=6 mm]. This large difference can be related to the fact that the clips were close to each other while the thoracic markers were much further away. As a result, small uncertainties in the registration using clips will be greatly enhanced when the thoracic markers were used for the evaluation. The situation is distinctly different when the thoracic markers were used in the registration while clips are exploited for the evaluation.

Kirby et al. [6] used surgical clips to register MRI with CT images of 30 patients in prone position. As a matching structure, clips have the advantage over the chest wall to overcome the problem of accurately identifying bony boundaries on MR images. Moreover, according to Kirby et al. the use of the clips for registration led to a smaller field of view and, therefore, reduced machine-related image distortion. They registered a mean clip misalignment between CT and MRI across all 30 cases of 0.8 mm (medial-lateral), 0.6 mm (superior-inferior), and 1.0 mm (anterior-posterior), yielding a mean misalignment distance of 1.4 mm.

This result is in good agreement with the MRI-CT distance of 1.7 mm [SD = 0.6 mm] averaged over 8 patients for the registration based on the surgical clips in our study.

Surgical-clip-based registration resulted in large rotations (see Table 3 and Figure 3) for 7 out of 8 patients in the present study. This effect is not described by Kirby et al. [6], probably because of smaller rotations in their study due to larger number of the surgical clips (6 to 12 versus 4 to 6 in our case). Moreover, not all the patients have surgical clips for various reasons. In our case 2 out of 10 patients did not have any surgical clips. Jolicoeur et al. [7] used the predefined fusion points (the nipple, the tip of scapula, the sternal notch and the carina) for MRI-CT registration. A qualitative evaluation was

then performed using the skin surface markers on the surgical scar and the nipple. They reported a mean MRI-CT distance of 5.6 mm (range: 1.9–11.6 mm). For the breast-marker-based evaluation and clip registration, the mean MRI-CT distance was 5.3 mm [SD=1.8 mm] (range: 2.8–7.7 mm). These results are difficult to compare because of absence of clips in the study by Jolicoeur et al. [7].

Conclusions

For the breast-marker evaluation, the misalignment between CT and MRI was the smallest for the thoracic-marker registration. For the surgical clips evaluation, the misalignment between CT and MRI was the smallest for the breast-marker registration. The use of surgical clips for MRI-CT registration resulted in large rotations ($> 3^\circ$) for 7 out of 8 patients. Moreover, the clips were not always clearly visible on MR images. The thoracic-marker-based and breast-marker-based registrations resulted in the smallest MRI-CT displacements between all fiducials. Co-registration of CT and MR data sets based on breast-markers gave the best result for the glandular breast tissue delineation in terms of the rest volume.

Considering all observed results, we recommend breast markers for MRI-CT co-registration for both glandular breast tissue and lumpectomy cavity delineation in radiotherapy. For lumpectomy cavity delineation the clip-based registration is an alternative to the breast marker registration. Further work is required to optimize registration methods using deformable registration.

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Target volume delineation in breast conserving radiotherapy:
are co-registered CT and MR images of added value?

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Abstract

Introduction

In breast conserving radiotherapy differences of target volume delineations between observers do occur. We evaluated whether delineations based on co-registered computed tomography (CT) and magnetic resonance (MR) imaging may result in an improved consistency between observers. We used the delineation conformity index (CI) to compare clinical target volumes of glandular breast tissue (CTV breast) and lumpectomy cavity (LC) on both imaging modalities.

Materials and methods

Four observers delineated CTV breast and LC on co-registered CTMR images in ten breast cancer patients. CIs were determined for CT and CTMR. Furthermore, the Cavity Visualization Score (CVS) of LC was taken into account.

Results

The mean CI for CTV breast ($CI_{CT;CTV}$: 0.82 and $CI_{CT-CTMR;CTV}$: 0.80) and LC ($CI_{CT;LC}$: 0.52 and $CI_{CT-CTMR;LC}$: 0.48) did not differ significantly ($p = 0.07$ and $p = 0.33$, respectively). Taking CVS into account for the LC, with a $CVS \geq 4$ the mean CI was 0.62 for both $CI_{CT;LC}$ and $CI_{CT-CTMR;LC}$.

Conclusion

The mean volume of the delineated glandular breast tissue based on CT was significantly larger compared to the volume based on CTMR. For patients with a $CVS \geq 4$, the mean CIs of the LC were higher compared to $CVS < 4$ for volumes delineated on both CT as well as CTMR images. In our study cohort no significant differences between the CIs of the CTV breast and the LC delineated on CTMR co-registered images were found compared to the CIs on CT images only. Adding MR images does not seem to improve consistency of the delineation of the CTV breast and the LC, even though the volumes were copied from CT images. Since we included only ten patients, caution should be taken with regard to the results of our study.

Background

There can be substantial differences in identification of the target volumes among radiation oncologists specialized in breast cancer radiotherapy [1]; even when written delineation guidelines are used [2-4]. Compared to computed tomography (CT) magnetic resonance imaging (MRI) may reveal more relevant details [5]. And, according to Jolicoeur et al., the use of MRI improved the level of agreement between observers delineating the lumpectomy cavity compared to CT [6]. In our former study, published in 2011, we noted that the concordance for delineation of the volumes on CT differed only slightly from the concordance based on magnetic resonance (MR) images [7]. Whether the use of a co-registration of the two imaging modalities could lead to an improvement of the agreement between observers remained unclear.

Therefore, we analyzed the delineation conformity, when based on CT as well as on CTMR co-registered images. In our study, we have evaluated the delineated clinical target volumes of the glandular breast tissue (CTV breast) and the lumpectomy cavity (LC) in ten patients referred for radiation therapy after breast conserving surgery.

Materials and methods

Between July 2007 and August 2008, fifteen patients with early stage breast cancer (clinically T1-2; N0-1) and treated with breast conserving surgery were included in our study. The mean age was 57 years; 8 patients had right-sided and 7 patients had left-sided breast cancer; the tumor was mostly situated in the upper outer quadrant of the breast. Patient and tumor characteristics were described in detail earlier [7]. Since the rigid co-registration was performed on breast markers which were used only in patients 6–15, we included only these ten patients in the present study [8]. After referral for whole breast radiotherapy, a planning-CT scan and directly afterwards a MRI scan were performed, both in supine treatment position. The procedure was described in detail by Giezen et al. [7].

The study was approved by the regional institutional review board METC Zuidwest Holland. All patients agreed to participate in our study by signing an informed consent. Four observers, i.e. two radiation oncologists and two radiologists, participated in the study and delineated the glandular breast tissue (CTV breast) [7] as well as the lumpectomy cavity (LC) [9]. The four observers delineated CTV breast and LC according to the determined delineation instructions, Table 1 [9].

For all ten patients this resulted in the, for each observer, delineated CTV breast and LC, based on CT images only. After ten weeks, the observers re-evaluated these CTV breast and LC delineations copied on the co-registered CTMR images, and made adaptations when judged necessary. By choosing an interval time of ten weeks it was likely that the observers had forgotten specific details of their CT-based delineations of each specific case. By doing so a more reliable comparison (and eventually an adaptation) between the CT based images and the CTMR images may be achieved. The alternative method of delineating the co-registered CTMR images was not used because this would imply an intra-observer variability.

After defining all CTV breast volumes, a scripting tool was applied to trim all CTV breast volumes up to 5 mm below the skin surface.

To quantify the variability of one delineation compared to another we used the Conformity Index (CI). A CI of 0 indicates no overlap is present between delineations; a CI of 1 indicates completely identical delineations. A method for calculating the CI was used, that is unbiased by the number of observers delineating a target volume [10]. We determined two types of CI of the CTV breast and LC enabling us to assess the influ-

ence of imaging modality on delineation variability, and the inter-observer variation, respectively. Firstly, for each observer, the delineated volumes on CT were compared to CTMR, indicated with the symbols $CI_{CT-CTMR;CTV}$ and $CI_{CT-CTMR;LC}$. The resulting CIs were thereafter averaged over the patient population. Secondly, for every delineated target volume we determined the CIs for CT based and CTMR based delineations separately, by comparing the delineations of the different observers to each other.

	CTV Breast	Lumpectomy Cavity
Window/Level (WL); Window Width (WW)	<ul style="list-style-type: none"> - Fixed: WL 0 Hounsfield Unit (HU) and WW of 500 HU for CT and variable WL and WW for MRI; - Change of WL and WW during delineation permitted for CT and MRI. 	<ul style="list-style-type: none"> - Fixed: WL 0 Hounsfield Unit (HU) and WW of 500 HU for CT and variable WL and WW for MRI; - Change of WL and WW during delineation permitted for CT and MRI.
Appearance	<ul style="list-style-type: none"> - The location of the marking wire, positioned around the palpable Glandular Breast Tissue (GBT), will be used as an aid for CTV Breast delineation; - The clinical target volume (CTV) breast was defined to comprise all GBT including fatty (involved) lobes - Margin of the GBT is (ventrally) assumed to be situated 5 mm below the skin surface; in case of MRI the visible GBT fat is (ventrally) delineated as GBT margin; - Delineation is performed on all CT or MRI slices that are judged to contain GBT; - Appearance of the contralateral breast (by comparing with the ipsilateral breast) on CT or MR images; - The preoperative mammographies and location of the palpable GBT marking wire, visible on CT or MRI, all will serve as an aid for GBT delineation. 	Appearance of contralateral breast (comparing with ipsilateral breast) serves as aid for LC delineation.
Clips	Surgical clips (if applicable) should all be included within the delineated GBT.	All surgical clips (if applicable) should be included within delineated LC.
Seroma	Postoperative seroma/hematoma present in LC should be included within delineated GBT.	Postoperative seroma/hematoma present in LC should be included within delineated LC.

Table 1. Delineation instructions for CTV Breast and the lumpectomy cavity. Abbreviations: LC Lumpectomy Cavity, WL window level, WW window width, HU Hounsfield Units, MRI Magnetic Resonance Imaging, CT computed tomography.

The resulting values are indicated with the symbols $CI_{CT;CTV}$, $CI_{CTMR;CTV}$, $CI_{CT;LC}$ and $CI_{CTMR;LC}$. Again, an average over the patient population was calculated. Furthermore, the earlier assessed ‘‘Cavity Visualization Score’’ (CVS) [9] of the lumpectomy cavity was taken into account in the analysis as well. With the CVS according to Smitt et al. [11] depiction of the lumpectomy cavity is categorized from 1, cavity not visualized, to 5, all cavity margins clearly defined. Finally, a median 3D surface of the CTV breast and LC of all four observers was calculated [12] (local surface variation) in order to analyze and visualize the local inter-observer variation for each patient.

Statistical analysis

Wilcoxon Signed Rank Test was performed to compare all data, CT versus CTMR, since the number of eligible data was less than 30. For analysis we used SPSS Statistics version 17.0. The level of statistical significance was considered $p < 0.05$ (two sided) for all tests.

Results

Glandular breast tissue (CTV breast)

Delineated volumes

The mean volume of the delineated glandular breast tissue based on CT (mean 576 cc; range 303–900) was significantly larger compared to the volume based on CTMR (mean 557 cc; range 287–892) ($p < 0.01$).

CT versus CTMR: conformity indices and local surface variation

On the CTMR images few adaptations to the delineated volume were carried out. The range in CIs ($CI_{CT-CTMR,CTV}$) for each observer was 0.89 – 1.00 (mean SD 0.03), Table 2. The mean CI for all observers between $CI_{CT,CTV}$ and $CI_{CTMR,CTV}$ did not differ significantly, Table 3.

The local surface variation in Figure 1 shows again that few adaptations were carried out on the co-registered CTMR images. We found a mean local standard variation between observers of 2.2 mm and 2.6 mm for CT and CTMR, respectively ($p = 0.05$). In seven out of ten patients the local standard variation increased on CTMR. For patient 8, 11, 12, 13 and 15 the differences were mostly present in the medial part of the CTV breast.

	$CI_{CT-CTMR,CTV}$ (SD)	$CI_{CT-CTMR,LC}$ (SD)
Observer_1	0.99 (0.01)	0.84 (0.09)
Observer_2	0.89 (0.05)	0.70 (0.23)
Observer_3	1.00 (0.00)	0.91 (0.17)
Observer_4	0.97 (0.05)	0.85 (0.30)

Table 2. Conformity indices of the CTV Breast and lumpectomy cavity (LC) delineations for each observer, CT compared to CTMR.

	CTV breast; Mean CI_{All} (SD)	LC; Mean CI_{All} (SD)
CI_{CT}	0.82 (0.04)	0.52 (0.20)
CI_{CTMR}	0.80 (0.06)	0.48 (0.21)
p-value $CI_{CT-CTMR}$	0.07	0.33

Table 3. Conformity indices ($CI_{CT,CTMR}$) of the CTV breast and lumpectomy cavity (LC) delineations based on CT and CTMR for all observers.

Inter-observer variability

In considering the variation in the local surface distance, it became apparent that the delineations of the observers varied, on CT as well as CTMR, predominantly in the medial and lateral part of the CTV breast, Figure 1.

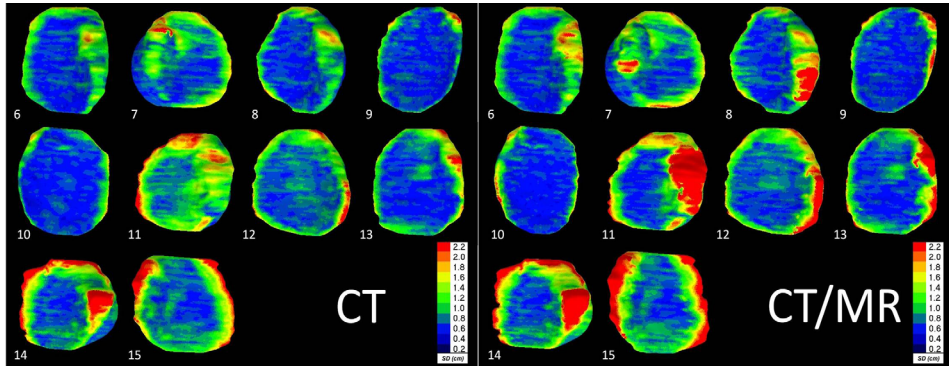


Figure 1. Left: Coronal posterior view of the ten delineated Clinical Target Volume (CTV) breast Computed Tomography (CT) volumes. Right: Coronal view of the ten delineated CTV breast CTMR volumes. The local surface distance variation of the four observers is projected on the median surface of each CTV breast. Colour map: Blue: high agreement between observers; Red: low agreement between observers according to the scale given.

*Lumpectomy cavity (LC)**Delineated volumes*

The mean volumes of the delineated LC based on CT (mean 24 cc; range 4–73) did not differ ($p = 0.2$) compared to those based on CTMR (mean 26 cc; range 7–71), Table 4.

	Mean Lumpectomy Cavity Volume CT	Mean Lumpectomy Cavity Volume CTMR
Patient_6	28	25
Patient_7	73	71
Patient_8	14	13
Patient_9	7	7
Patient_10	11	11
Patient_11	29	32
Patient_12	4	9
Patient_13	30	34
Patient_14	8	13
Patient_15	33	45

Table 4. Mean volumes for all observers of the lumpectomy cavity (LC) delineations based on CT and CTMR.

CT versus CTMR: conformity indices and local surface variation

For LC more adaptations were carried out than for CTV breast, since the range in CIs ($CI_{CT-CTMR;LC}$) for each observer decreased: 0.70 – 0.91 (mean SD 0.20), Table 2. The mean CI for all observers between $CI_{CT;LC}$ and $CI_{CTMR;LC}$, however, did not differ significantly, Table 3.

When taking the CVS into account, we found that, if the CVS was ≥ 4 , the mean CI appeared to increase. An increase of the CI to 0.62 was found for $CI_{CT;LC}$ as well as for $CI_{CTMR;LC}$ delineations in all 5 cases with a CVS of ≥ 4 . In Figure 2 we display the mean CI of both CT and CTMR on the CVS scale from 0 to 5; see Figure 3 as well.

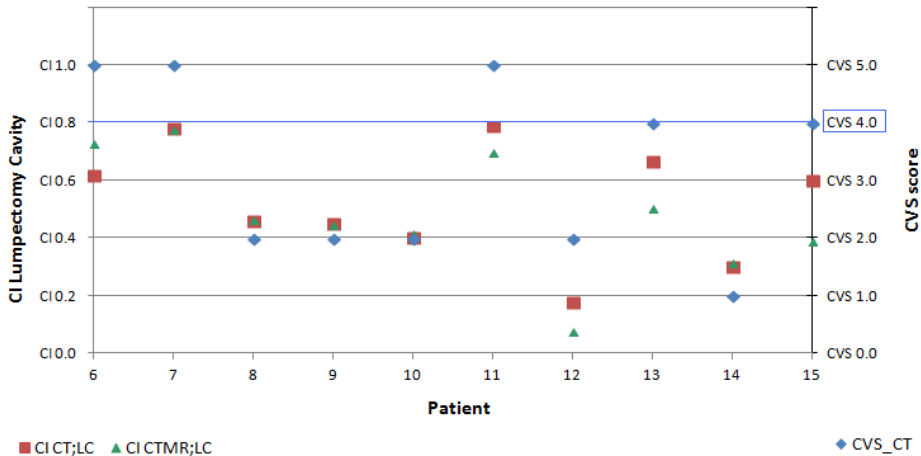


Figure 2. For each patient for the lumpectomy cavity the Conformity Index (CI) on CT, The CI on CTMR and the Cavity Visualization Score (CVS) were determined.

The local surface distance variation showed more variation in the delineation of the LC compared to CTV breast. We found a mean local standard variation between observers of 2.4 mm and 2.8 mm for CT and CTMR, respectively ($p = 0.13$). In five out of ten patients (patient 11, 12, 13, 14 and 15) the degree of variability increased on the co-registered CTMR images and in two patients (patient 6 and 7) the degree of variability was larger on the CT images. For the other two patients, no major variability was noted. As an example, in patient 12, a premenopausal patient, no seroma was found, no clips were placed and the CVS was 2, Figure 4.

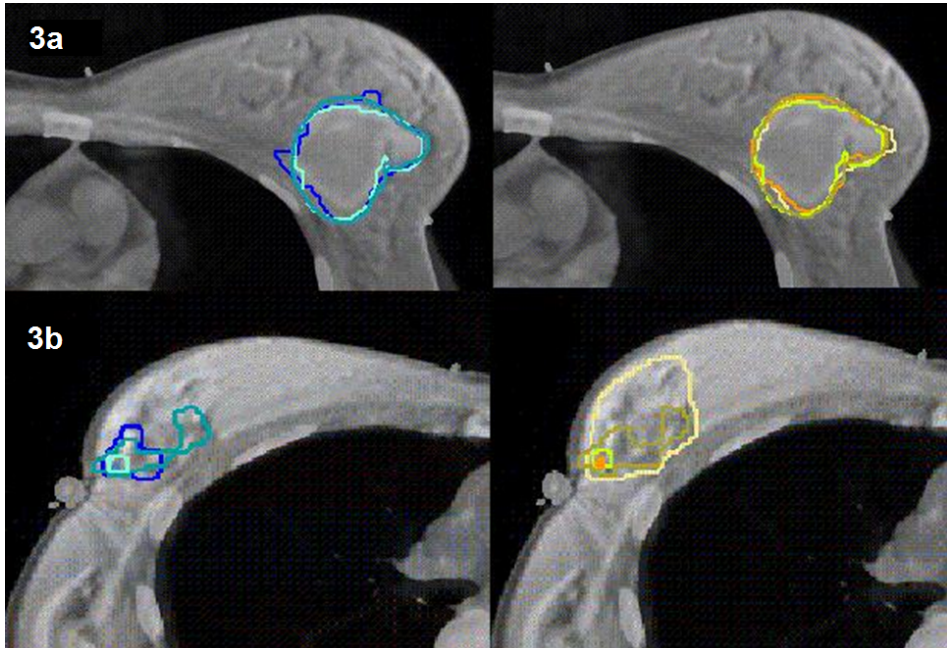


Figure 3. Differences between the 4 observers on co-registered CTMR images; Left: volumes delineated on CT. Right: volumes delineated on CTMR; a. Example of a patient with seroma, a CVS of 5; b. Example of a patient with a CVS of 2.

Discussion

CT versus CTMR

In this study we investigated the potential merits of CTMR co-registration on the delineation of the CTV breast and the Lumpectomy Cavity (LC). Concerning the study outline, we only focused on the advantages of CTMR co-registration. Therefore, to avoid intra-observer variability, we copied the CTV breast and LC delineated on the CT to the co-registered CTMR images. Thereafter each observer considered to adapt (yes or no) the CTV breast or LC, respectively when based on the CTMR images. Finally, the differences between the CT based and CTMR based delineations were analyzed. This method could have introduced a bias, since the observers did not delineate the CTMR co-registered images. Comparisons and eventually adaptations were, after an interval time of 10 weeks, done directly on the CTMR co-registered images. In doing so the observers could have been distracted by the copied volume. But the alternative method of delineating the co-registered CTMR images had the disadvantage that this would result in an intra-observer variability between the CT based and the CTMR based delineations.

We found that the CT based CTV breast volumes, when compared with CTMR based volumes, were significantly larger. In our study cohort, it became apparent that the CIs for CTMR co-registered images, when compared to those based on CT images only, did not differ significantly from those based on CT images only, neither for CTV breast nor for LC. With respect to LC, in the 5 cases with a CVS \geq 4, the mean CI values increased to 0.62, whereas for the cases with a CVS $<$ 4 a mean CI of 0.50 was found.

Compared to the results of our first investigation [9] the CI for the LC increases from 0.32 for MR to 0.48 for the co-registered CTMR.

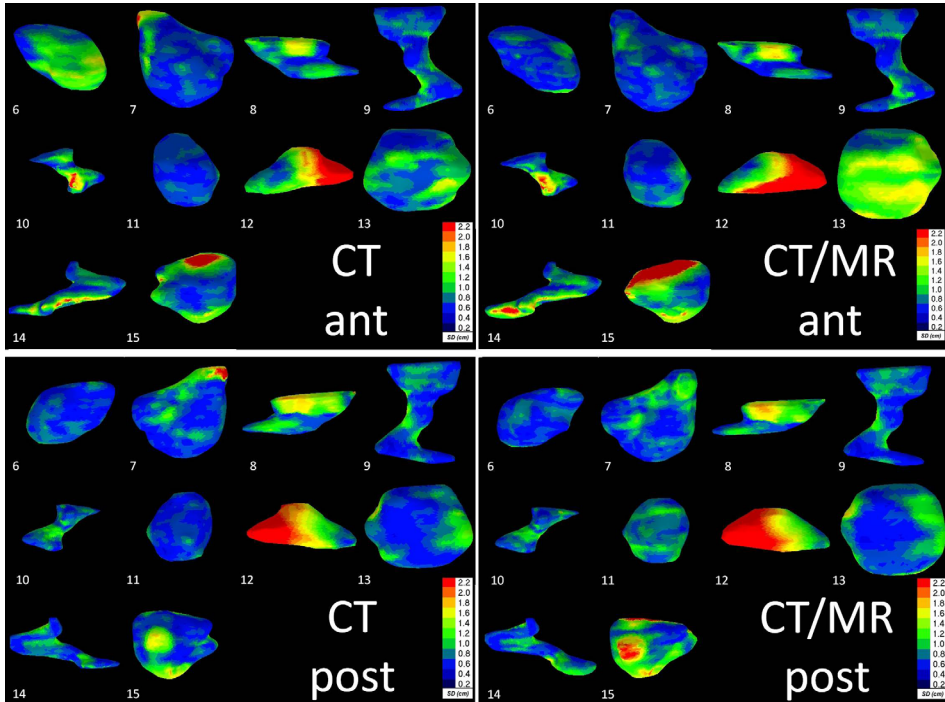


Figure 4. Left: Coronal posterior view of the ten delineated Lumpectomy Cavity (LC) Computed Tomography (CT) volumes in both anterior as well as posterior view. Right: Coronal view of the ten delineated LC CTMR volumes in both anterior as well as posterior view. The local surface distance variation of the four observers is projected on the median surface of each LC. Colour map: Blue: high agreement between observers; Red: low agreement between observers according to the scale given.

Remarkably, we found higher CIs (Lumpectomy Cavity) for both CT and CTMR compared to the results of Boersma et al. although our volumes were smaller and in our study the lumpectomy cavity was defined instead of the CTV boost [4]. The CTV boost in the study of Boersma et al. was defined as the 1.5 cm rim of tissue that had surrounded the primary tumor. Also, manual adaptation of the co-registration by each observer could be a reason for the lower CI in the study of Boersma et al., since this could be a bias in the analysis of the delineated structures. In our study, the co-registration was locked after performing the co-registration. Furthermore, in our study clips were placed directly in several segments in the lumpectomy cavity wall representing the extensions of the primary tumor, whereas in the Boersma study clips only had been placed at the deepest (dorsal) border of the lumpectomy cavity [4].

CTV breast

The major differences in delineation of the target volume between observers were located in the medial and lateral part of the CTV breast. This was confirmed in the study of Li et al. In their study, the effect of these variations on the dose in the organs at risk was studied as well. They concluded, that variations in normal structure dose were found

and that large variations in the medial-lateral borders contributed mostly to the variation in the normal structure dose [13]. Therefore, consistency in delineation of the CTV breast is of great importance. In our study cohort specific guidelines (Table 1) were used and consensus meetings had taken place. The latter could explain the non-significant differences in the CTV breast when MR imaging was added.

Lumpectomy cavity

Delineations of the lumpectomy cavity were done by experienced radiation oncologists and trained radiologists. They used written delineation guidelines (Table 1). All this was in line with the findings of various recent studies. As Wong et al. showed in their study cohort, “trained” oncologists consistently produced smaller target volumes in seroma contouring compared to an “untrained” cohort. The implementation of guidelines reduced the inter-observer variability in volume delineation in their study. These data indicated that improved consistency among radiation oncologists may be achieved by consensus guidelines.[14].

Furthermore, our results reveal that, when the CVS was ≥ 4 , the CI was increased for both CT as well as CTMR defined volumes. This finding was reported before by Landis et al. [1]. This could indicate that, for lumpectomy cavities with a CVS of < 4 , specific landmarks such as surgical clips or gold markers may enable a more precise defined CTV boost [3,15]. According to Topolnjak et al. and Park et al., the position of these clips and markers remain stable throughout the treatment course [16,17]. Nevertheless, it seems important to be aware of interfractional target deformations as reported by Ahunbay et al. [18]. Concerning the use of surgical clips, Jolicoeur et al. did not use clips and found a concordance ratio of 0.66 on CT and 0.96 on MR [6]. Finally, as Van Mourik et al. also suggested [3], we confirm that a multi-disciplinary approach is what should be aimed at in target delineation; especially in the delineation of the LC and when the CVS is lower than 4, since every specialist can contribute to a better understanding. If an inconsistency of the surgical clips and at the edge of the seroma was found, as described by Yang et al., this should be part of the multidisciplinary discussion [19].

Conclusion

The mean volume of the delineated glandular breast tissue based on CT was significantly larger compared to the volume based on CTMR. For patients with a CVS ≥ 4 , the mean CIs of the LC were higher compared to CVS < 4 for volumes delineated on both CT as well as CTMR images. In our study cohort no significant differences between the CIs of the CTV breast and the LC delineated on CTMR co-registered images were found compared to the CIs on CT images only. Adding MR images does not seem to improve consistency of the delineation of the CTV breast and the LC, even though the volumes were copied from CT images. Since we included only ten patients, caution should be taken with regard to the results of our study.

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