Cervix cancer brachytherapy

Applicator reconstruction in MRI 3D image-based dose planning of brachytherapy for cervical cancer

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Background and purpose: To elaborate a method for applicator reconstruction for MRI-based brachytherapy for cervical cancer.

Materials and methods: Custom-made plastic catheters with a copper sulphate solution were made for insertion in the source channels of MR-CT compatible applicators: plastic and titanium tandem ring applicators, and titanium needles. The applicators were CT and MR scanned in a phantom for accurate 3D assessment of applicator visibility and geometry. A reconstruction method was developed and evaluated in 19 patient MR examinations with ring applicator (plastic: 14, titanium: 5). MR applicator reconstruction uncertainties related to inter-observer variation were evaluated.

Results: The catheters were visible in the plastic applicator on T1-weighted images in phantom and in 14/14 clinical applications. On T2-weighted images, the catheters appeared weaker but still visible in phantom and in 13/14 MR clinical applications. In the titanium applicator, the catheters could not be separated from the artifacts from the applicator itself. However, these artifacts could be used to localize both titanium ring applicator (5/5 clinical applications) and needles (6/6 clinical applications). Standard deviations of inter-observer differences were below 2 mm in all directions.

Conclusion: 3D applicator reconstruction based on MR imaging could be performed for plastic and titanium applicators. Plastic applicators proved well to be suited for MRI-based reconstruction. For improved practicability of titanium applicator reconstruction, development of MR applicator markers is essential. Reconstruction of titanium applicator and needles at 1.5 T MR requires geometric evaluations in phantoms before using the applicator in patients.

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Applicator reconstruction is the process of defining the source channels in the images used for brachytherapy dose planning. Traditionally, dose planning in intracavitary brachytherapy treatment of cervical cancer is based on 2D X-rays with dummy wires, and source channels are digitized in these images. However, recent developments in CT- and MRI-based brachytherapy have introduced new challenges for applicator reconstruction [1,2]. CT has the advantage of providing detailed images with high geometric accuracy. The applicator is clearly visible on CT images, and the images are well suited for 3D applicator reconstruction with good accuracy [2]. The disadvantage is that CT is clearly inferior to MRI with respect to defining the target volume [3–5]. The first clinical evidence strongly indicates that 3D image-guided brachytherapy has potential to increase local control in locally advanced cervical cancer without increasing morbidity MRI [6], and MRI is the current method of choice for image-based brachytherapy [7,8]. The challenge in MR images is to localize the source channel, since conventional markers used for X-ray and CT cannot be used in MRI. The introduction of new materials for applicators such as titanium also challenges the use of MRI. By fusing CT or X-ray with MR, the position of the applicator can be transferred to MR images. This approach has been described by Krempien et al. [5] showing that CT and MR image fusion improves target volume definition but also showing that image fusion contains uncertainties due to patient motion and registration errors. The correct identification and localization of the channel are important since reconstruction uncertainties may result in significant uncertainties on DVH parameters [9].

The aim of this study was to elaborate a method for the visualization of applicators used for the treatment of locally advanced cervical cancer, so that both reconstruction and dose planning can be performed in the MR study without requiring fusion with other image modalities.
Methods and materials

Applicators

Two different types of applicators were examined and evaluated for 3D MRI-based reconstruction: A MR-CT compatible plastic tandem ring applicator and a titanium tandem ring applicator (Varian Medical Systems, Charlottesville, VA, USA). The plastic tandem ring system consisted of a tandem (guide tube: polyetheretherketone (PEEK) and probe: fluorinatedethylene-propylene (FEP)) and a ring (outer material: polyetheretherketone (PEEK), inner material: fluorinatedethylene-propylene (FEP)). In the titanium tandem ring system, a cap (acetal) was attached to the ring. Titanium needles (Acrostak Corp., Winterthur, Switzerland) clinically used for combined intracavitary-interstitial applicator according to the principle described by Kirisits et al. [10] and Dimopoulos et al. [11] were also evaluated. In the plastic applicator, a special ring cap produced in the department allowed us to introduce titanium needles through the cap parallel to the tandem [12]. In the titanium applicator, holes for needle insertion were drilled directly in the commercial ring cap.

Construction of copper sulphate catheters and stereotactic brachytherapy phantom

The inner diameter at the entrance of the applicator source channels is 1.3 mm in both plastic and titanium applicators. This allowed the insertion of a plastic tube (Portex polythene tubing, Smiths Industries, Kent) with outer and inner diameters of 1.22 and 0.76 mm, respectively. For contrast media we chose copper sulphate. This is a commonly used material for MRI phantoms since it reduces the relaxation time of water considerably. We produced a copper sulphate (CuSO4) solution (2.08 g/l) with T1 and T2 relaxation times of 325 and 150 ms, respectively. For contrast media we chose copper sulphate. This is a commonly used material for MRI phantoms since it reduces the relaxation time of water considerably. We produced a copper sulphate (CuSO4) solution (2.08 g/l) with T1 and T2 relaxation times of 325 and 150 ms, respectively. The T1 and T2 relaxation times were verified by performing MRI scans of a bottle containing 250 ml of the solution. Catheters were filled with the copper sulphate solution. The catheters were sealed at both ends by heating and it was visually verified that the catheters did not contain any air bubbles.

A stereotactic brachytherapy phantom was designed with an internal coordinate system consisting of oblique and longitudinal acrylic rods with a diameter of 4 mm surrounding the applicator ring and tandem (Fig. 1). The coordinate system allowed determination of the longitudinal position of transversal images according to the same principle as used by De Brabandere et al. [13]. The phantom was filled with agarose gel (3%) with CuSO4 (1 g/L) added to adjust the relaxation times of the gel to resemble human tissue [14].

MR and CT imaging in stereotactic phantom

Visualization of the applicators was at first tested in phantom scans: one with the titanium tandem ring applicator without needles and one with the plastic tandem ring applicator and four titanium needles inserted at different depths parallel to the tandem. The applicator containing the catheters with copper sulphate was fixated in the brachytherapy phantom. The MR images were produced using a 1.5 T Magnetom Symphony MR scanner (Siemens Medical Systems, Erlangen, Germany) using the spine array coil and the body array coil. Sequences from our clinical protocol [12] used for MR imaging of cervical tumor patients were used: A T1-weighted (T1W) turbo spin-echo sequence (TR = 710 ms, TE = 14 ms, slice thickness = 3 mm, no gap, pixel size = 0.8 × 0.8 mm, read gradient in right-left direction) and a T2-weighted (T2W) turbo spin-echo (SE) sequence (TR = 4000 ms, TE = 112 ms, slice thickness = 4 mm, 1 mm gap, pixel size = 1.1 × 1.1 mm, read gradient in right-left direction). Both the T1W and the T2W sequences were acquired para-transversally placing the slices parallel to the ring of the applicator. The phantom was CT scanned (MX8000 IDT, Philips Medical Systems, Best, Netherlands) with 1 mm slice thickness.

The images were loaded into the Brachyvision treatment planning system (ver. 7.5, Varian Medical Systems, Charlottesville, VA, USA). MR and CT images were manually fused according to the acrylic marker rods and the stereotactic coordinate system. The signal void of the applicators in MR images was compared to the applicator geometry on CT. Furthermore, in the titanium tandem ring applicator and in the titanium needles, the geometric relation between artifacts and source channels was assessed. The placement of the source channel in the ring was localized on the MR images based on the signal from the CuSO4 catheter, and the deviation of the localization with respect to CT images was determined.

Applicator reconstruction procedure in clinical applications

Clinical MRI examinations were evaluated for 19 patients: 14 plastic and 5 titanium needle applications. In six cases, additional interstitial titanium needles were used. The para-transversal T1 and T2 MRI sequences described earlier were used. The T1W sequence was used for detailed anatomically information. In addition, T2W sagittal (TR = 4500 ms, TE = 130 ms, slice thickness = 4 mm, gap = 0.8 mm) and T2W para-coronal (TR = 3500 ms, TE = 154 ms, slice thickness = 5 mm, gap = 1 mm) images were obtained to aid the contouring of target and organs at risk.

T1W and T2W images were fused directly according to scanner coordinates unless patient motion required manual correction in relation to the applicator.

Contouring of target and organs at risk was done in T2W images. Tandem and needle were reconstructed individually by importing library applicators. Multiplanar reconstruction of the T1W images was used in this process due to better image resolution (pixel size and slice thickness) and thereby better visualization of applicator compared to the T2W images.

The position of the ring source channel was reconstructed based on the position of the source channel below the ring surface (as specified by the vendor and verified during applicator commissioning). In plastic applicators, this was verified by comparing the position of the CuSO4 signal in both T1W and T2W images (Fig. 2g and h). The rotation of the ring was determined from the angling between tandem and ring guide tubes in the vagina as visualized by CuSO4 signal. In the titanium applicator, the rotation of the ring was guided by the position of titanium artifacts in the ring region (Fig. 3f and g).

Tandem and needles were visualized in the sagittal and coronal reconstructions. Lateral and anterior–posterior positionings were determined from the signal void. For plastic tandem, the tip of the tandem was defined using the signal void as well. For titanium, the position of the tip of the tandem and needles was identified from the titanium artifacts (Fig. 3b and c).

To evaluate the reconstructions based on MR images, an interobserver study was performed. The applicator reconstructions were performed independently by the second skilled medical physicist, and the reconstruction differences in relation to the first reconstructions were measured. In total 69 applicators were reconstructed (plastic ring(15)/tandem(15), titanium ring(5)/tandem(5), titanium needles(29)). Rotational and translational shifts were measured, and mean and standard deviation were calculated.

Results

Plastic applicator

In phantom images (Fig. 2f), the CuSO4 catheter was clearly visible on all the T1W images. On the T2W images, the signal
from the catheter was weak, but it could be identified in all phantom scans. Using the stereotactic coordinate system in the phantom the position of the CuSO₄ catheters in the ring was measured. The center of the source channel is located 3 mm from the surface of the ring according to the applicator geometry specified by the vendor. On the CT images of the applicator in phantom this distance was measured to 3.4 mm. On MR images of the applicator in phantom, the same distance was measured to 4.0 and 5.8 mm for T1W and T2W images, respectively. The deviation between CT and MRI (0.6 and 2.4 mm, respectively) is within half of the MRI slice separation (3 and 5 mm, respectively), the slice separation being the slice thickness plus slice gap. Additionally, a source of uncertainty is that the catheter is 1.22 mm in diameter and the source channel is 2 mm in diame-
so that the catheter might not be in the center of the source channel. The signal void of the plastic material in the applicator on MR images was in correspondence with the applicator geometry as it appeared on CT in all cases. The tip of the tandem was identified on both T1W and T2W MR images with a deviation of less than 1.1 mm with respect to CT images.

In patient images (Fig. 2g), the signal from the catheter was clearly visible on the T1W images in 14/14 clinical applications. On the T2W images (Fig. 2h), the signal from the catheter was weak but could be identified in 13/14 clinical MR studies. Applicator reconstruction was straightforward in all patients.

Titanium tandem ring applicator

CuSO4 catheters (Fig. 3f) were not visible in the titanium ring applicator due to susceptibility artifacts. However, there was a clear and reproducible susceptibility artifact pattern from the titanium material in the phantom scans. In coronally reconstructed images, there were bright regions to the left and right of tandem (Fig. 3b). In the region of the cap, there was a bright artifact just where the titanium source channel recedes into the ring cap (Fig. 3f). At the level of the titanium ring, there was a shift of signal due to susceptibility differences. The signal void of ring cap is shifted by 1 mm to the right (Fig. 5a) – in the direction of the read gradient. This phenomenon can only be seen in image sequences with a small slice thickness of 1 mm. In sequences with larger slice thickness, the signal is blurred and the shift can be considered as negligible during applicator reconstruction.

In all patients, the longitudinal position of the ring source channel could be defined in relation to the surface of the ring. The artifact pattern surrounding the tandem tip (Fig. 3c) was in accordance with the pattern found in phantom scans (Fig. 3b). The pattern was visible in all patients and allowed the localization of the tandem tip.

The inclination of the ring was determined from the artifact produced by the ring tube where it enters the ring. However, this artifact was not very bright (Fig. 3f and g), and in one patient it could not be distinguished due to patient motion during MR acquisition.

Titanium needles

As for the titanium tandem applicator, the titanium needles produced clear and reproducible susceptibility artifact pattern at the tip of the needles from the titanium material in the phantom scans. In the coronally reconstructed images, there were bright regions to the left and right of the needle tips (Fig. 4b). The center of the signal void of needles in para-transveral MR images was in agreement with the position of the center of the needles in CT images within 1 mm (Fig. 4e and f). The artifacts from needle tips were less bright than that from the tandem of the titanium applicator, and reconstruction was generally more difficult.

Inter-observer study

Rotational inter-observer uncertainties in sagittal and coronal planes were small with standard deviations below 2.4° for all applicators. Translational uncertainties and rotational uncertainty for the ring (in the ring plane) are shown in Table 1. Inter-observer uncertainties were generally small with standard deviations below 2 mm. Deviations larger than 4 mm were seen in 6/69 (9%) applicators: 1/30 (3%) plastic applicators, 5/39 (13%) titanium applicators. Deviations >4 mm were mostly seen in longitudinal direction (5/6 cases, all below 6 mm) and in 1/6 cases as a rotation in the ring plane in a titanium ring applicator (7 mm). The deviations were due to difficulties in interpretation of the images (3/6 cases) or manual errors in the reconstruction procedure (3/6).

Discussion

With the introduction of MRI-guided 3D brachytherapy in locally advanced cervix cancer, the need for better methods for visualization and reconstruction of MRI compatible brachytherapy applicators is greatly increased. This problem had previously been addressed for CT [2] but to our knowledge the current paper is the first published study including a clinically validated method for commercially available MRI compatible applicators.

Catheters containing CuSO4 could be used to visualize the source channels of plastic applicators. The catheters could be re-

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Fig. 3. Coronal (top row) and transversal (bottom row) images showing the titanium applicator in the phantom on CT images (a and e), in phantom on T1-weighted MR images (b and f), patient T1-weighted MR images (c and g) and patient T2-weighted MR images (d and h). The line on (b) shows the position of the applicator tip according to tip position found in the CT image (a). The arrows in (f and g) indicate the artifact used for determining the rotation of the ring.
used but the signal degraded after approximately 3 months. The small diameter of the applicator channel limits the volume of fluid in the catheters and thereby also the signal available on MRI. Furthermore, the T2W images have less signal intensity than the T1W images and it would increase the scan time considerably if more signals should be generated from the catheters. This would be at the expense of increased motion artifact from the bowels and patient motion. A larger volume of the catheter would increase the

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**Fig. 4.** Coronal (top row) and transversal (bottom row) images showing the applicator with titanium needles in phantom on CT images (a and e), in phantom on T1-weighted MR images (b and f), patient T1-weighted MR images (c and g) and patient T2-weighted MR images (d and h). The needles are positioned in the ring through holes. The position of the four needles on the transversal CT and MR phantom images (e and f) are marked with “x”. This shows the position of the needles related to the susceptibility artifacts on MR images caused by the titanium.

**Fig. 5.** The figure shows a coronal image of the ring from the titanium applicator and the resulting pixel shift in MR images caused by the titanium (a) and the corresponding CT image of the ring from the titanium applicator (b).
signal from the copper sulphate, thereby making it possible to clearly identify the channel in T2W images also. There may also be fluids that generate more signals in T2W images than CuSO₄.

Reconstruction of titanium applicators using MRI is more challenging than the plastic applicator. The source channels cannot be visualized by the CuSO₄ catheter, but susceptibility artifacts can be used to guide the reconstruction process. However, the size and pattern of the susceptibility artifacts depend on many MR parameters [15] such as field strength and read gradient direction [16]. The pattern also depends on the placement of the titanium applicator or needles as compared to the static magnetic field [17]. The artifact is minimal when the needle is placed in parallel to the main magnetic field. A gradient-echo (GRE) sequence will generate a larger artifact than a SE sequence and longer TE will also increase the artifact since the signal has more time to build up phase errors [18]. A change of frequency and phase encoding gradients will change the orientation of the pattern, and a change of spatial resolution in the frequency encoding direction will also change the size of the artifact: images required with a high resolution matrix and thin slices will show smaller artifacts [19]. Therefore, it is absolutely essential that the commissioning of applicators performed in the department includes phantom scans where MR images, produced using the clinical sequences, are fused with CT images in order to assess artifact pattern in MR images relative to the true applicator geometry as visualized in CT. Phantom scans should be performed in agarose gel or a similar material with relaxation times resembling human tissue. It is important that the MR sequence parameters and settings used are the same for all patients with titanium applicators, since the artifact pattern may change when changing the parameters. Furthermore, the signal intensity of the artifact patterns is variable in patients, and identification of the patterns can be difficult.

Further work should be done to find ways to visualize the applicators on T2W MR images. This could be the further development of “dummy wires”, catheters containing fluid, or it could be the development of markers to be inserted and fixed into the solid applicators to serve as anchor points during applicator reconstruction.

The inter-observer study shows that reconstruction based on MR images is feasible for both plastic and titanium applicators and for titanium needles. The largest deviations are found for the titanium applicator and titanium needles, where reconstruction is slightly more challenging – mostly due to difficulties in interpretation of the susceptibility artifacts. The largest deviation is found in the longitudinal direction. This uncertainty could most likely be reduced by using thinner slices or a 3D sequence instead. This would be at the expense of increased acquisition time and thereby also increasing the risk of motion artifacts. Another option is to acquire an additional CT scan – especially for oblique free needles this may increase the precision of defining the end of the applicator.

In this study, applicator reconstruction has been performed with tandem ring applicators and a specific treatment planning system on images from a 1.5 T MR scanner. At other field strengths, in other treatment planning systems, and with other applicators, reconstruction may well be performed in other ways. The strategy for applicator reconstruction presented in this paper may therefore not be directly applicable in other systems, but the general strategy should be the same. Phantom scans of “dummy wires” and applicator should always be performed before clinical implementation in order to verify the geometry.

In conclusion, we have developed procedures for the reconstruction of plastic and titanium tandem ring applicators in MR images. Catheters containing copper sulphate are clearly visible in plastic applicators on T1W MR images and on most T2W. Phantom MR and CT scans of the titanium applicator and the titanium needles make it possible to assess applicator geometry relative to the artifact pattern generated on MR images. However, applicator reconstruction of titanium applicators is more challenging than that of plastic applicators.

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