MRI-TRUS fusion for electrode positioning during irreversible electroporation for treatment of prostate cancer

We aimed to introduce an approach for image-guided positioning of electrodes for irreversible electroporation (IRE) in patients with prostate cancer using a magnetic resonance imaging-transrectal ultrasonography (MRI-TRUS) fusion technique. In 10 consecutive patients with biopsy-proven Gleason score ≤3+4 prostate cancer, 19 G electrodes were inserted into the prostate using a transperineal access. Magnetic resonance images of the prostate acquired before IRE were fused with transrectal ultrasound images acquired during IRE. The position of the ultrasound probe was tracked via a sensor and corresponding magnetic resonance images were calculated in real-time. While MRI allowed delineation of the target volume, the position of the electrodes could be visualized on ultrasound images; the distance between individual electrode pairs was measured. Based on these measurements the software installed on the IRE unit was able to calculate the voltage necessary to generate the electric field for ablation. Using contrast-enhanced ultrasound, changes in perfusion within the ablation zone after IRE were documented. This technique allowed positioning of the electrodes around the target volume under image guidance in all patients treated with IRE. The target lesion and a safety margin were covered within the estimated ablation zone. MRI-TRUS guidance for IRE combines the advantages of good visualization of the target lesion on MRI with the ability of ultrasound to acquire imaging in real-time with a mobile device.
Patient preparation

All patients were treated under general anesthesia and full muscle relaxation since the electric field generated during IRE induces significant muscle contractions. Patients were placed on an operating table in lithotomy position. A transurethral urinary catheter was inserted before the procedure.

MRI-TRUS fusion

A high-end ultrasound unit (Aplio 500, Toshiba Medical Systems) was used in combination with a biplane transrectal ultrasound probe (11CL4, Toshiba Medical Systems). For image fusion proprietary Smart Fusion software installed on the ultrasound unit was used. The ultrasound probe was mounted on a frame developed for the implantation of brachytherapy seeds into the prostate (AccuSeed System 700-010, Ta¬man Medical). Thus, the ultrasound probe was fixated and the exact depth of rectal penetration as well as its rotation could be controlled (Fig. 1). Via a position sensor attached to the ultrasound probe, the position of the probe could be tracked in real-time in a magnetic field (0.1 T, miniBIRD Receiver).

DICOM data of multiparametric MRI of the prostate acquired within three months before IRE without using an endorectal coil were uploaded to the ultrasound unit. The target lesion was identified on multiparametric MRI and marked with a spherical volume-of-interest on T2-weighted imaging (Turbo spin-echo sequence, 3 mm slice thickness, no gap). The ultrasound probe was inserted into the rectum in a plane strictly orthogonal to the patient’s perineum. Ultrasound images of the prostate were acquired at 8–10 MHz in combination with techniques for image optimization (tissue harmonic imaging, spatial and frequency compounding). The height of the operating table was adjusted until an identical distance between the rectum and the prostate on axial T2-weighted imaging and axial ultrasound images resulted, without major deformation of the prostate.

For image registration selected anatomical landmarks that could be identified consistently in each patient (including the urinary bladder neck, the prostatic-semi¬nal vesicle angles, and the surface of the prostate) were initially marked on sagittal ultrasound images as well as on sagittal T2-weighted imaging. Afterwards, the previously selected landmarks were confirmed on axial ultrasound images as well as on axial T2-weighted imaging starting at the base of the prostate and finishing at the apex. Finally, the target lesion was visualized on axial ultrasound images and the surface of the prostate in proximity to the target lesion was marked on axial T2-weighted imaging as well as on axial ultrasound images. The ultrasound unit provided a digital overlay of the volume-of-interest used to mark the target lesion on T2-weighted imaging and on ultrasound images. As a result, the location of the target lesion could be tracked on ultrasound images.

Main points

- MRI-TRUS fusion can be used for image-guided positioning of electrodes for irreversible electroporation (IRE) in patients with prostate cancer.
- This approach combines the advantages of good visualization of the target lesion on MRI with the ability of ultrasonography to acquire imaging in real-time.
- This technique might help to take full advantage of the unique features of IRE allowing to control size, shape, and location of the ablation zone by positioning of the electrodes.

Figure 1. Photograph showing the setting used for treatment of prostate cancer with irreversible electroporation (IRE). A transrectal ultrasound probe (thin white arrow) with an attached position sensor (white arrow) is mounted on a frame (asterisk) that fixates the probe and allows for its exact positioning. A brachytherapy grid (open white arrow) is mounted on the frame just caudal of the patient’s perineum; the IRE electrodes are inserted through the grid using a transperineal approach. The patient is covered with surgical drapes.
the procedure.

tween the rectum and the prostate during imaging in a constant angle and distance be

plied. However, deformation of the prostate appreciated. The extension of the perfusion defect matches the estimated ablation zone.

On axial imaging (a), the position of four electrodes placed peripherally around the target volume can be detected as strong punctiform reflectors (white arrows). Goal is to enclose the target lesion as well as a safety margin between the electrodes. The distance between individual electrode pairs can be measured in this plane. On sagittal imaging (b), the depth of penetration of the electrodes can be detected. Goal is to position the parallel electrodes to cover the target lesion craniocaudally with the tip of the electrode being positioned above the lesion. On axial (c) and sagittal (d) contrast-enhanced ultrasound imaging acquired one day after IRE, a perfusion defect corresponding to the ablation zone can be appreciated. The extension of the perfusion defect matches the estimated ablation zone.

Figure 2. a–d. Example images of magnetic resonance imaging-transrectal ultrasonography (MRI-TRUS) fusion in a 71-year-old patient with Gleason 3+4 prostate cancer in the ventral transition zone. All images show pairs of fused MRI and ultrasound images and represent screenshots from the ultrasound unit. T2-weighted images acquired before IRE are shown on the left (a–d), while fused ultrasound images acquired during IRE are shown on the right (a, b). The target lesion is marked with a spherical volume-of-interest (circle). On axial imaging (a), the position of four electrodes can be detected as strong punctiform reflectors (white arrows). Goal is to enclose the target lesion as well as a safety margin between the electrodes. The distance between individual electrode pairs can be measured in this plane. On sagittal imaging (b), the depth of penetration of the electrodes can be detected. Goal is to position the parallel electrodes to cover the target lesion craniocaudally with the tip of the electrode being positioned above the lesion. On axial (c) and sagittal (d) contrast-enhanced ultrasound imaging acquired one day after IRE, a perfusion defect corresponding to the ablation zone can be appreciated. The extension of the perfusion defect matches the estimated ablation zone.

Figure 3. a, b. Example images of MRI-TRUS fusion in a 68-year-old patient with Gleason 3+3 prostate cancer on the right side in the dorsolateral peripheral zone. All images show pairs of fused MRI and ultrasound images and represent screenshots from the ultrasound unit. T2-weighted images acquired before IRE are shown on the left, while fused ultrasound images acquired during IRE are shown on the right. The target lesion is marked with a spherical volume-of-interest (circle). On axial imaging (a) the position of four electrodes placed peripherally around the target volume can be detected as strong punctiform reflectors (white arrows). On contrast-enhanced ultrasound imaging acquired one day after IRE (b) a perfusion defect corresponding to the ablation zone can be appreciated. The extension of the perfusion defect matches the estimated ablation zone.

A rigid image fusion algorithm was applied. However, deformation of the prostate was minimized due to the fixed position of the ultrasound probe and the fixed position of the patient on the operating table resulting in a constant angle and distance between the rectum and the prostate during the procedure.

Positioning of IRE electrodes

For generation of the electric field, monopolar needle-like 19 G electrodes (NanoKnife, AngioDynamics) were inserted into the prostate through a brachytherapy grid using transperineal access. Goal was to position the electrodes in parallel orientation around the target volume (consisting of the target lesion and a safety margin) covering it within the estimated ablation zone (Figs. 2, 3). The number of electrodes was determined by the shape and size of the target volume. An electric field sufficient for tumor ablation can be generated between each pair of individual electrodes and 5–10 mm around the electrodes. The distance between individual electrodes should be at least 10 mm, not exceeding 20 mm.

The version of the MRI-TRUS fusion system used for positioning of IRE electrodes in the patients described in this manuscript did not offer a digital overlay of the brachytherapy grid on ultrasound images. Therefore, the hole in the grid used for insertion of the first electrode had to be selected based on manual measurements of the distance of the desired position of the electrode and the transrectal ultrasound probe. The hole in the grid used for insertion of additional electrodes was selected based on the location of the first electrode.

Initially, every electrode was advanced deeper into the prostate than the visualized axial image plane showing the target lesion’s maximal extension. The position of each electrode was identified on axial ultrasound images after penetrating the visualized image plane as a strong punctiform reflector. The position of the electrodes around the target volume was documented. Now ultrasound images in a sagittal image plane were acquired and corresponding sagittal magnetic resonance images were displayed. The ultrasound probe was rotated to the side of the target lesion and advanced deeper into the rectum until the basal boundaries of the prostate and the seminal vesicles became visible. The tips of the electrodes were identified and the electrodes were pulled back until the tips of all electrodes were located at the same level just above of the target lesion (Fig. 2). The active tip length of the electrodes was adjusted by selective insulation (up to a length of 15 mm) determining the cranial-caudal extension of the ablation zone. After switching back to an axial image plane, the ultrasound probe was pulled back until the target lesion was visualized again, as well as the inserted electrodes. The distances between individual electrode pairs were measured.

Generation of the electric field

The distances between electrode pairs were entered manually into the proprietary software installed on the IRE unit.
Documentation of the ablation zone

Every patient underwent transrectal contrast-enhanced ultrasonography (CEUS) the day before and the day after IRE to document changes in perfusion within the ablation zone. The same MRI-TRUS fusion technique that was used for positioning of IRE electrodes was used for CEUS. For CEUS, the novel ultrasound technique of superb microvascular imaging was used in combination with the intravenous application of 2.4 mL of ultrasound contrast agent SonoVue (Bracco). Loss of tissue perfusion in the ablation zone was documented on axial and sagittal ultrasound images (Figs. 2 and 3). The extension of the perfusion defect visualized by CEUS has been shown to correspond well with the extension of the ablation zone on histopathology (10).

Assessment of the agreement between the estimated ablation zone and the actual ablation zone

The area of the estimated ablation zone visualized by the proprietary software installed on the IRE unit was measured using ImageJ analysis software (ImageJ 1.50i, National Institutes of Health). The area of the ablation zone in terms of the largest extension of the perfusion defect visualized by CEUS on a single corresponding axial image was measured using a PACS workstation (Centricity Radiology RA1000, GE Healthcare). Agreement between the area of the estimated ablation zone and area of the actual ablation zone was assessed by Bland-Altman analysis (IBM SPSS Statistics, Version 21, IBM). In addition, agreement between shape and location of the estimated ablation zone and the actual ablation zone was evaluated visually by an experienced uroradiologist performing a side-by-side reading of multiparametric MRI acquired before IRE, visualization of the position of the electrodes, the estimated ablation zone provided by the proprietary software installed on the IRE unit, and ultrasound images acquired during and one day after IRE.

Results

Ten consecutive patients treated with IRE according to the protocol described above were included in this evaluation. Mean patient age was 62.4±7.3 years. Mean serum PSA before IRE was 9.1±3.6 ng/mL. Gleason score was 3+3 in three patients and 3+4 in seven patients. Mean lesion size was 15±5 mm. Seven lesions were localized in the peripheral zone of the prostate and 3 lesions were localized in the transition zone. Four electrodes were used in 8 patients and 3 electrodes were used in 2 patients.

In all patients, a satisfactory position of the electrodes was achieved resulting in coverage of the target lesion and a safety margin within the estimated ablation zone. Critical structures including the neurovascular bundle, the urethra, and the rectum could be excluded from the estimated ablation zone to the greatest possible extent. In all patients, a loss of tissue perfusion within the ablation zone was documented by CEUS, while larger capsular vessels stayed intact.

Bland-Altman analysis showed an acceptable agreement between the area of the estimated ablation zone and the actual ablation zone (Fig. 5). Shape and location of the estimated ablation zone and the actual ablation zone showed good agreement on visual evaluation in all patients, resulting in complete coverage of the target lesion within the ablation zone.

No major adverse events were observed during or immediately after IRE.

Discussion

The described MRI-TRUS fusion technique allows positioning of the electrodes...
under image guidance. Similar fusion techniques have already been established for targeted biopsies of the prostate (11). In a recent feasibility study, MRI-TRUS fusion was used for planning of focal ablative therapy for prostate cancer with high-intensity focused ultrasound (12).

This manuscript offers a description of MRI-TRUS fusion technique for real-time image-guided positioning of electrodes for IRE. Multiparametric MRI can detect clinically significant tumors in the prostate and allows an estimation of tumor volume necessary for planning of the target volume (13). TRUS offers real-time imaging with a mobile device that can be used in the operating room where IRE is performed under general anesthesia. However, prostate cancer often cannot be sufficiently visualized by TRUS alone. Thus, for planning of the target volume ultrasound imaging alone may be insufficient, even if the location of prostate cancer is known from previous multiparametric MRI (14). MRI-TRUS fusion combines the advantages of multiparametric MRI and TRUS. It has the potential to improve accuracy of IRE for prostate cancer under real-time image guidance.

An important limitation of this study is that no three-dimensional visualization of the estimated ablation zone could be obtained during IRE. In addition, no exact volumetric measurement of the true ablation zone could be performed. Therefore, further work correlating the estimated ablation zone planned based on MRI-TRUS fusion with histopathology is required.

In conclusion, in patients with prostate cancer the described MRI-TRUS fusion technique might help to take full advantage of the unique features of IRE allowing to control size, shape, and location of the ablation zone by positioning of the electrodes. Further studies are necessary to evaluate if this technical approach has a beneficial effect on the clinical outcome.

Conflict of interest disclosure
The authors declared no conflicts of interest.

References
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