Abstract:

Purpose
Prostate cancer (PCA) is the second most frequent cause of cancer-related death in men in the United States and Europe. Transrectal ultrasound (TRUS) guided systematic prostate biopsy is the standard of care for detection and diagnosis of PCA. However, due to inadequate visualization of PCA in ultrasound, the false negative rate of systematic TRUS-guided biopsy is 15-30%. Magnetic resonance imaging (MRI) has demonstrated tremendous potential for PCA diagnosis and staging, but MRI in-gantry procedure guidance is challenging [1]. In this work, a novel prostate guidance system using image fusion of live TRUS with pre-acquired MRI is presented and validated in pre-clinical and clinical studies.

Methods
(A) Fusion guidance system: Endorectal ultrasound probe (Philips C9-5, Andover, MA, USA) biopsy guides were equipped with electromagnetic (EM) tracking sensors. The pose of the sensors was calibrated relative to the ultrasound image, enabling realtime spatial tracking of the TRUS images. A software application was created supporting registration of the live ultrasound with pre-acquired MRI using the following steps. (1) The prostate in the 3-dimensional (3D) MRI image was segmented using a semi-automatic segmentation tool. (2) A spatial sweep (base to apex in transverse view) across the prostate with the tracked TRUS probe was reconstructed into a 3D TRUS volume and was segmented automatically using adaptive local shape statistics [2]. (3) Registration between the TRUS volume and the MRI volume was initialized based on the known sweep geometry and the TRUS and MRI segmentations. (4) The TRUS-MRI registration was optimized iteratively by combining manual manipulation of individual rotational and translational degrees of freedom (DOFs) with subsequent automatic optimization using the iterative closest point (ICP) algorithm. (5) After registration, the live 2D TRUS image was shown side-by-side with the corresponding multi-planar reconstruction (MPR) of the MRI image. The MRI-based segmentation and any MRI-identified points of interest (POIs) were also superimposed on the live images.

(B) Validation: The system and workflow were validated in phantom studies (as reported earlier [3]), dog models, and clinical studies. In 5 dog models, MRI-visible but ultrasound-occult targets were created by injecting 1/32” synthetic ruby balls, diluted Gadolinium, or diluted Feridex® into the dog prostate. The fusion system was used to inject a secondary ruby or Feridex® marker in the MRI-identified target location. The spatial distance between the primary and secondary injections in subsequent MRI were used to define the overall spatial accuracy. Figure 1 shows T1-weighted MRI slices of one of the injected targets in a dog prostate (white arrow) before and after the secondary injection, and the targeted injection of the secondary fiducial (black arrow).

(C) Clinical study: In 203 patients with elevated prostate-specific antigen (PSA) or abnormal digital rectal exam (DRE), multi-parametric MRI (T2-weighted, diffusion-weighted, dynamic contrast-enhanced, and magnetic resonance spectroscopy) of the prostate was obtained on a 3 Tesla Philips Achieva (Andover, MA, USA) using an endorectal coil (BPX-30; Medrad, Pittsburgh, Pa, USA). The MRI was read by 2 radiologists and lesions suspicious for PCA were identified. The MRI lesions were categorized into low, moderate and high suspicion based on the number of MRI sequences positive for that lesion (1-2 sequences positive: low; 3: moderate; 4:
Subsequently, all patients underwent systematic 12-core TRUS-guided biopsy and TRUS-MRI fusion-targeted biopsy of MRI-identified suspicious lesions. All patients provided written informed consent. 10 patients were inevaluable because non-standard equipment was used or because of other reasons. The positive biopsy rates for systematic biopsy, targeted biopsy and for the combined approach (systematic + targeted) were compared, and were correlated with the MRI suspicion labels.

Results

In 5 dog prostates, a total of 10 target markers (2 Feridex, 4 Gadolinium and 4 synthetic ruby balls) and 10 secondary fiducials (2 ruby balls, 8 Feridex injections) were injected. All 10 of the targets and 9 of the fiducials could be identified in follow-up MRI. The mean ± standard deviation of the distance between targets and secondary injections was 5.0 ± 2.5 mm.

The clinical patient population had a mean age of 61.5 years (median 61, range 40 – 82) and a mean PSA of 8.5 ng/ml (mean 5.8, range 0.0 – 103.0). 133 patients had prior prostate biopsy, of which 75 were positive. Figure 2 shows the fusion display provided for biopsy of an MRI-identified “high suspicion” target in a 67 year old male. In the study population there was a significant increase in the per-patient and per-core positive biopsy rates with increasing MRI suspicion level, for systematic as well as for targeted and combined biopsies. Also, targeted positive core rates were significantly (p<0.01) higher than systematic core rates in patients with moderate or high MRI-suspicion but were equivalent in patients with low suspicion (Figure 3). For high suspicion patients, the targeted positive core rate (46.5%) was more than double the systematic positive core rate (22.4%). Furthermore, in the patient group with moderate or high suspicion, the combined approach had significantly (p<0.05) higher per-patient positive biopsy rates than systematic biopsy alone.

Conclusions

A system enabling MRI-targeted prostate biopsy by fusing pre-acquired MRI with live TRUS outside the MRI gantry was developed, validated, and clinically tested. The spatial accuracy of the fusion system was sufficient to target clinically significant prostate cancer (1cm lesion diameter). MRI-based cancer suspicion categories correlated well with biopsy-proven cancer detection rates, suggesting an important role of MRI in prostate cancer management. MRI fusion targeting significantly increased cancer detection rates in select patient groups, and may allow improved out-of-gantry management of patients with moderate or high MRI suspicion.

References

Figure 1: T1-weighted MRI of artificial target (white arrow) and injected fiducial (black arrow) in an in vivo dog model before (left) and after (right) the fusion-targeted injection of the fiducial.

Figure 2: Fusion biopsy with live ultrasound (left) and corresponding MRI (right). The MRI target is identified in blue (with red center). The MRI-based prostate segmentation is shown in green.
Figure 3: Positive biopsy core rates for systematic and fusion-targeted biopsy