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TITLE: Prostate Cancer Detection Using High-Spatial Resolution MRI at 7.0 Tesla: Correlation with Histopathologic Findings at Radical Prostatectomy

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14. ABSTRACT This study aims to develop high spatial-resolution prostate MRI at 7.0T. During the earlier phase of our study, we performed technical development and optimization of the necessary hardware and software to achieve standard T2-weighted imaging for 7.0T prostate MRI. Specifically, we implemented a novel surface coil array in conjunction with optimization of turbo-spin echo T2-weighted sequences to achieve high spatial-resolution high SNR images. This system employed two transmit-receive elements and six receive-only elements, avoiding parallel transmission and RF shimming, thereby achieving a much simpler design than has been explored by other groups for 7T prostate MRI. In the present study period, this system was applied in two men with prostate cancer prior to prostatectomy. In both of these patients, 7T T2WI readily demonstrated dominant peripheral zone tumors with excellent visual correspondence with pathologic findings from prostatectomy. This work is valuable given that while new 7T systems offer the possibility of imaging prostate cancer using contrast mechanisms that have not been reliably performed at 1.5T and 3T, such as arterial-spin labeling and multinuclear imaging, it is necessary to first be able to perform standard MR sequences at diagnostic quality at 7T. We have demonstrated such feasibility in our current study, thus creating opportunity to pursue integration of novel techniques into a potential 7T clinical MR examination.					
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Introduction

This study aims to develop high spatial-resolution MRI of the prostate at a field strength of 7.0T, with in-vivo validation in prostate cancer patients. Central to this project is development and optimization of the necessary hardware and software to be able to perform 7.0T prostate MRI in a clinical setting. Specifically, we aim to develop a novel surface coil array in conjunction with optimization of turbo-spin echo T2-weighted MRI sequences for such a coil, in order to achieve high spatial-resolution high signal-to-noise images of the prostate. This combination will then be used to image patients with proven prostate cancer prior to radical prostatectomy, with subsequent correlation of findings between the 7T MRI and pathologic assessment. It is hoped that our approach will allow for imaging patients with solely an external surface coil, yet attain images of similar if not better image quality than previously attained using an endorectal coil at lower field strengths. If successful, this project will facilitate the role of prostate MRI in influencing prognosis and treatment selection for men newly diagnosed with prostate cancer.

Body

During the initial phase of our study, as summarized in our previous annual report, we perform technical optimization of the external transmit/receive coil array and accompanying turbo spin-echo T2-weighted sequences for 7T prostate MRI. These designs were implemented to overcome extreme RF inhomogeneity encountered in imaging of deep torso structures, such as the prostate, at 7T. Given that prostate imaging entails coverage of just a small region of interest, we aimed to achieve excitation in the prostate through the use of only two transmitter elements, one anterior and one posterior, with fixed power split and phase relationship. We used the simulations to help optimize and build such a two-element transmit-receive plus eight-channel receive-only array for prostate imaging at 7.0T and tested initially in human volunteers. Such a system did not require parallel transmission. Simulation of the system demonstrated the ability to achieve reasonable magnitude and uniformity of excitation in the region of the prostate. SNR comparison to 3T showed a gain of 3.3. In addition, T2-weighted TSE images in volunteers showed good depiction of prostate anatomy and clinically relevant details. We thus demonstrated feasibility of a generally simple system that does not rely on parallel transmit or RF shimming, thereby making 7T prostate imaging possible on standard single transmitter 7T systems and overcoming challenges related to RF power availability at 7T.

In the current study period, we applied our previously designed system in prostate cancer patients, to assess depiction of focal lesions. The descriptions provided in this summary are based on a more formal presentation of our work: Specifically, two patients with biopsy-proven prostate cancer scheduled to undergo radical prostatectomy volunteered to undergo 7T MRI as part of a prospective IRB-approved. These patients had previously undergone a multi-parametric prostate MRI study at 3T as part of our standard institutional protocol. The 7T MRI in these men comprised use of our previously described external coil and TSE T2WI sequence. Axial TSE TWI was performed with the following parameters: TR/TE/BW=11,670ms/80ms/254Hz/pixel, flip angle=160°, FOV=192x192 mm, matrix= 256x256, slice thickness=3 mm, average=1, TA 3min19sec.

Following the 7T MRI, the patients underwent radical prostatectomy by an experience urologic oncologist. The prostate specimen was processed by a uropathologist who fixed the intact prostate in formalin for 48 hours and then sectioned and processed the tissue using standard H&E stain. Slides were evaluated by the uropathologist, who outlined tumors in ink. Intact slices were digitally photographed prior to sectioning, and sections were digitally captured using a LEICA scanner. A fellowship-trained abdominal radiologist with dedicated experience in prostate MRI correlated the findings from the pathological assessment with the pre-operative MRI findings at 7T.

Patient 1 was a 56 year-old male with PSA of 8.1 who, on biopsy, had Gleason 4+3 tumor with maximal tumor involvement of 70% of the core; patient 2 was a 53 year-old male with PSA of 17.7 who, on biopsy, had Gleason 4+3 tumor with maximal tumor involvement of 20% of the core. Both patients successfully underwent 7T MRI using the described coil structure and high-resolution

TSE T2WI sequence. This examination demonstrated a focal region of decreased T2 signal in the peripheral zone suspicious for tumor in both patients. In patient 1, the suspicious area was located in the right posterolateral peripheral zone (Figure 1a); in patient 2, the suspicious area was located in the left posterolateral peripheral zone (Figure 1b). In each case, the suspicious area abutted the overlying prostate capsule, which appeared intact without evidence of extra-prostatic extension.

Following prostatectomy, pathologic analysis of the specimen demonstrated a dominant Gleason 3+4 tumor in the posterior right apical peripheral zone without extra-prostatic extension in patient 1 (Figure 2a), and a dominant Gleason 3+4 tumor in the posterior left midgland peripheral zone without extra-prostatic extension in patient 2 (Figure 2b). Thus, in both cases, there was good correspondence between findings on 7T T2WI and histopathologic assessment in terms of these aspects of the dominant peripheral zone tumor.

This work is valuable given that while new 7T systems offer the possibility of imaging prostate cancer using contrast mechanisms that have not been reliably performed at 1.5T and 3T, such as arterial-spin labeling and multinuclear imaging, it is necessary to first be able to perform standard MR sequences at diagnostic quality at 7T before being able to integrating novel techniques into a potential 7T clinical MR examination. Yet, performing standard sequences of prostate tumors at 7T is not straightforward and has not been previously published in the peer-reviewed literature as of this writing, to our knowledge. Greater RF transmitter inhomogeneity and power deposition preclude use of a whole-body transmit coil at 7T, as is the standard approach at lower field strengths. Thus, we implemented an alternative approach of using small local transmit coil elements with concomitant extensive hardware and software development and optimization.

Following the initial technical optimization, TSE T2WI was performed in two prostate cancer patients using the simple coil arrangement. The tumors were readily visible as a hypo-intense lesion on T2WI at 7T in both patients. In addition, while both lesions abutted the capsule, the 7T T2WI correctly indicated the absence of extra-prostatic extension in both patients, as confirmed by histopathologic assessment of the radical prostatectomy specimen. Overall, these two cases demonstrate the feasibility of our hardware and software design for performing high spatial-resolution non endorectal-coil T2WI at 7T for tumor evaluation.

Continued testing and optimization of our system in additional prostate cancer patients is clearly required. For instance, the potential impact of 7T MRI on assessment for tumors of varying size, grade, and location within the prostate must be systematically explored. In addition, for the 7T examination to replace clinical prostate studies at 1.5T or 3T, functional sequences must be developed to complement the T2WI performed in this report. The higher field strength has potential to improve the performance of currently used functional sequences such as MR spectroscopy via greater spectral separation of different metabolites, as well as of dynamic contrast-enhanced MRI via higher temporal resolution. Nonetheless, work until this point has established a framework for

performing standard anatomic imaging of prostate cancer at 7T, which can serve as a basis for future more detailed comparison with pathologic findings and findings at other field strengths, as well as incorporation of novel MR contrast mechanisms.

Key Research Accomplishments

- Various design options for construction of a 7T prostate coil compared via full wave simulations
- 7T coil that does not rely on parallel transmission or RF shimming constructed; uses simple two-coil transmit system
- Coil design allowed significant SNR gain compared with 3T imaging
- Additional 7T sequence modifications performed to further improve image quality
- Above hardware/software approach validated in-vivo in men with prostate cancer, in comparison with pathological findings

Reportable Outcomes

•Zhang B, Rosenkrantz A, Sodickson D, Taneja S, Stefanescu C, Wiggins G. 7T External Prostate Array with Single Channel

Transmit: Simulation and Experiment. Proceedings of the 20th annual meeting of the ISMRM, Melbourne, 2012 (2782).

•Rosenkrantz AB, Zhang B, Ben-Eliezer N, Le Nobin J, Melamed J, Deng Fang-Ming, Taneja SS, Wiggins GC. T2-weighted Prostate

MRI at 7T Using a Simplified External Transmit-Receive Coil Array: Correlation with Radical Prostatectomy Findings in Two

Prostate Cancer Patients. Journal of Magnetic Resonance Imaging: In revision.

Conclusions

In conclusion, we executed extensive work toward optimization of a 7T coil arrangement for prostate MRI at 7T. Our system employs two transmit-receive elements and six receive-only elements, avoiding parallel transmission and RF shimming, thereby achieving a much simpler design than has been previously explored for 7T prostate MRI. This coil design was supplemented by investigation of sequence modifications to overcome challenges related to RF power availability at 7T. In combination, these hardware and software changes led to substantial improvements in SNR compared to 3T MRI, which is hoped to support high spatial-resolution non endorectal-coil clinical imaging at 7T. Initial testing of our design in two prostate cancer patients prior to prostatectomy provided T2WI that readily demonstrated peripheral zone tumors, with good correspondence with histopathologic results. While our early experience is promising, future studies will attempt to validate findings at 7T in a larger patient cohort prior to radical prostatectomy, as well as aim to develop complementary functional techniques taking advantage of the capabilities of the 7T system.

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2. Metzger GJ, van de Moortele PF, Akgun C, et al. Performance of external and internal coil configurations for prostate investigations at 7 T. *Magn Reson Med* 2010; 64:1625-1639
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Appendices

None.

Supporting Data

Figure 1-Evaluation of coil and sequence scheme in prostate cancer patient at 7T. (A) Axial T2-weighted MR image obtained at 7T shows focal area of decreased T2 signal within the right posterior apical peripheral zone, abutting an intact overlying prostate capsule (arrow). (B) Reconstructed whole-mount photomicrograph (H&E stain) shows dominant tumor in right posterior peripheral zone outlined in red, corresponding with focal lesion on MRI. No extra-prostatic extension was identified on histopathologic assessment.

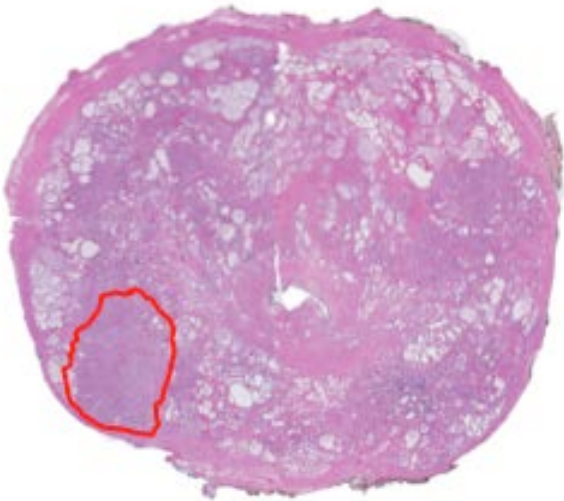
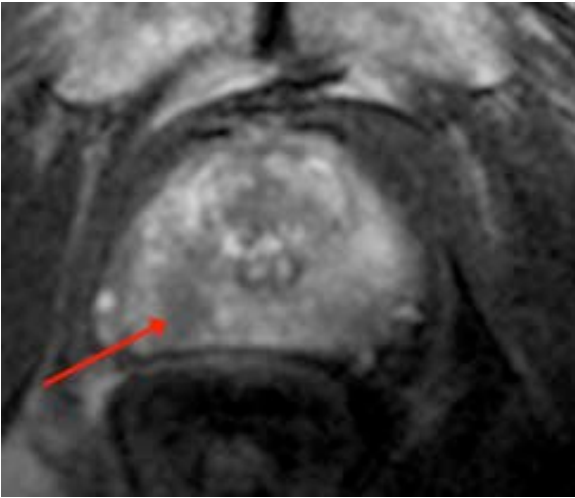


Figure 2-Evaluation of coil and sequence scheme in prostate cancer patient at 7T. (A) Axial T2-weighted MR image obtained at 7T shows focal area of decreased T2 signal within the left posterior midgland peripheral zone, abutting an intact overlying prostate capsule (arrow). (B) Reconstructed whole-mount photomicrograph (H&E stain) shows dominant tumor in left posterior peripheral zone outlined in red, corresponding with focal lesion on MRI. No extra-prostatic extension was identified on histopathologic assessment.

