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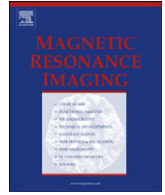
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## Prostate diffusion imaging with distortion correction☆



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### ABSTRACT

**Purpose:** Diffusion imaging in the prostate is susceptible to distortion from B0 inhomogeneity. Distortion correction in prostate imaging is not routinely performed, resulting in diffusion images without accurate localization of tumors. We performed and evaluated distortion correction for diffusion imaging in the prostate.

**Materials and methods:** 28 patients underwent pre-operative MRI (T2, Gadolinium perfusion, diffusion at  $b = 800$  s/mm<sup>2</sup>). The restriction spectrum protocol parameters included b-values of 0, 800, 1500, and 4000 s/mm<sup>2</sup> in 30 directions for each nonzero b-value. To correct for distortion, forward and reverse trajectories were collected at  $b = 0$  s/mm<sup>2</sup>. Distortion maps were generated to reflect the offset of the collected data versus the corrected data. Whole-mount histology was available for correlation.

**Results:** Across the 27 patients evaluated (excluding one patient due to data collection error), the average root mean square distortion distance of the prostate was 3.1 mm (standard deviation, 2.2 mm; and maximum distortion, 12 mm).

**Conclusion:** Improved localization of prostate cancer by MRI will allow better surgical planning, targeted biopsies and image-guided treatment therapies. Distortion distances of up to 12 mm due to standard diffusion imaging may grossly misdirect treatment decisions. Distortion correction for diffusion imaging in the prostate improves tumor localization.

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### 1. Introduction

In the United States, prostate cancer is the leading cause of cancer in men and the second leading cause of cancer deaths [1]. Multiparametric magnetic resonance imaging (MRI) plays a large role in staging and localizing prostate cancer, with diffusion imaging as a key component [2–16]. Diffusion imaging often increases the conspicuity of prostate cancers and detects them with greater accuracy than T2 or perfusion imaging [5,8,9]. However, standard diffusion sequences with echo planar imaging (EPI) for k-space

sampling suffer from distortion artifacts due to B0 inhomogeneity [17,18]. These distortion artifacts obscure the precise location of concerning findings with this technique. Improved tumor localization with diffusion imaging would enhance MRI's utility in evaluating prostate cancer. Surgical management of prostate cancer often depends on a priori knowledge of tumor extension beyond the prostatic capsule, determining nerve-sparing techniques versus aggressive surgery. In addition, novel techniques and treatments such as MRI-Ultrasound fusion guided biopsies [19] and high-intensity focused ultrasound treatment [20,21], depend on accurate localization of prostate cancer, where a subset may only be detected with diffusion MRI.

Routine standard of care diffusion with EPI does not incorporate correction for B0 inhomogeneity distortions. Techniques for distortion correction for diffusion imaging with EPI exist [22–24] and have been applied in the brain [23,24].

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**Table 1**  
MRI scan parameters.

Pulse sequence	Parameters
T2	Axial 3D TSE T2 (Siemens SPACE) TR/TE 3800–5040/101 ETL 13, 14 cm FOV, 256 × 256 matrix, 1.5 mm contiguous slices, 60 slices
Diffusion-weighted (Standard)	Echoplanar, TR/TE 3900/60, 21 × 26 cm FOV, 130 × 160 matrix, 3.6 mm slices, 4 NEX, b-values of 0, 100, 400, and 800 s/mm <sup>2</sup> , 20 slices, parallel imaging with a factor of 2
T1 Dynamic Perfusion Imaging	Siemens TWIST, TR./TE 3.9/1.4 ms, 12° flip angle, 26 × 26 cm FOV, 160 × 160 matrix, 3.6 mm slices, 4.75 s/acquisition over 6 min with 15 s injection delay, image analysis using iCAD Versavue,
Restriction Spectrum Imaging	Spin echo EPI, TR/TE 5500/137, 26 × 26 cm FOV, 128 × 96 matrix, 3.6 mm slices, 30 directions at each b-value, b-values of 0, 800, 1500, and 4000 s/mm <sup>2</sup> , 60 slices

In this paper, a diffusion MRI technique called Restriction Spectrum Imaging (RSI-MRI) [25–28] was used to evaluate 28 preoperative prostate cancer patients and assess the benefits of correcting for B0 distortion effects. This study is a further evaluation of data used in our initial proof of concept study of RSI-MRI of the prostate [28]. RSI-MRI incorporates distortion correction [23] as part of its image post-processing stream.

## 2. Materials and methods

Preoperative MRI was performed on 28 prostate cancer patients in this IRB approved study. The patients underwent the standard multi-parametric prostate MRI protocol using 3 T MRI systems (TrioTim, Skyra, Siemens, Erlangen, Germany) with an endorectal coil (Medrad, Warrendale, PA) (Table 1): T2 weighted-MRI, dynamic contrast-enhanced (DCE) MRI with gadolinium-based contrast agent, and diffusion-weighted MRI ( $b = 800 \text{ s/mm}^2$ ). In addition, the diffusion protocol included b values of 0, 800, 1500, and 4000 s/mm<sup>2</sup> in 30 unique diffusion directions for each nonzero b-value. The distortion-correction algorithm [23] utilizes the symmetry of the distortion from B0 inhomogeneity (Fig. 1). By collecting images at  $b = 0 \text{ s/mm}^2$  in both the forward and reverse phase encode trajectories, a deformation field map can be calculated and used to correct the entire diffusion data set. For one patient out of the 28 patients, there was an error in the scan parameters for the forward and reverse images, and thus distortion correction could not be performed. This patient was excluded from the evaluation, leaving 27 patients for analysis.

RSI-MRI cellularity maps were reconstructed based on all b-values [25], distortion corrected and then standardized across the sample with z-score maps. The z-score maps were calculated by

**Table 2**  
Distortion distance of the whole prostate and tumor regions of interest due to B0 inhomogeneity.

	Mean (standard deviation) (mm)	Maximum distortion (mm)
Whole prostate distortion	3.2 (2.2)	12
Tumor ROI distortion	3.2 (2.4)	13

(1) measuring the mean and standard deviation of normal prostate signal from the raw cellularity maps across the patient pool, (2) subtracting this measured mean value from each subject's cellularity map, and (3) dividing by the measured normal prostate standard deviation. Distortion maps were also generated to reflect the offset of the collected data in the phase encode direction versus the distortion corrected data. In addition to multi b-value cellularity maps, a low b-value ADC ( $b = 800 \text{ s/mm}^2$ ) map was also generated and distortion-corrected. Whole-mount histopathology was available for correlation. With whole-mount histopathology, the tumor area was identified by an experienced uropathologist.

With the T2 weighted-image, a radiologist delineated a region of interest determined by the prostatic capsule. The region of interest was overlaid on the distortion correction map to measure the mean and standard deviation of the distortion correction in the phase encode direction. This information was used to calculate the root mean square (RMS) distortion distance for the entire prostate in a single slice according to the following relationship:

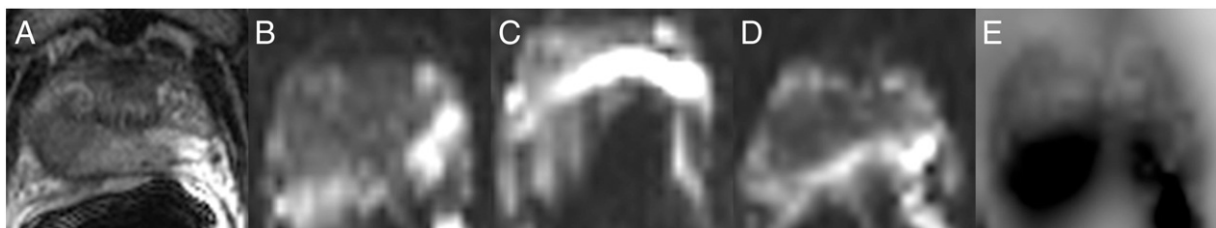
$$RMS_{\text{distortion}} = 2 \times \sqrt{(\mu_{\text{distortion distance}})^2 + \sigma_{\text{distortion distance}}^2}$$

where  $\mu_{\text{distortion distance}}$  is the mean distortion distance and  $\sigma_{\text{distortion distance}}$  is the standard deviation of the distortion distance measured on the distortion maps.

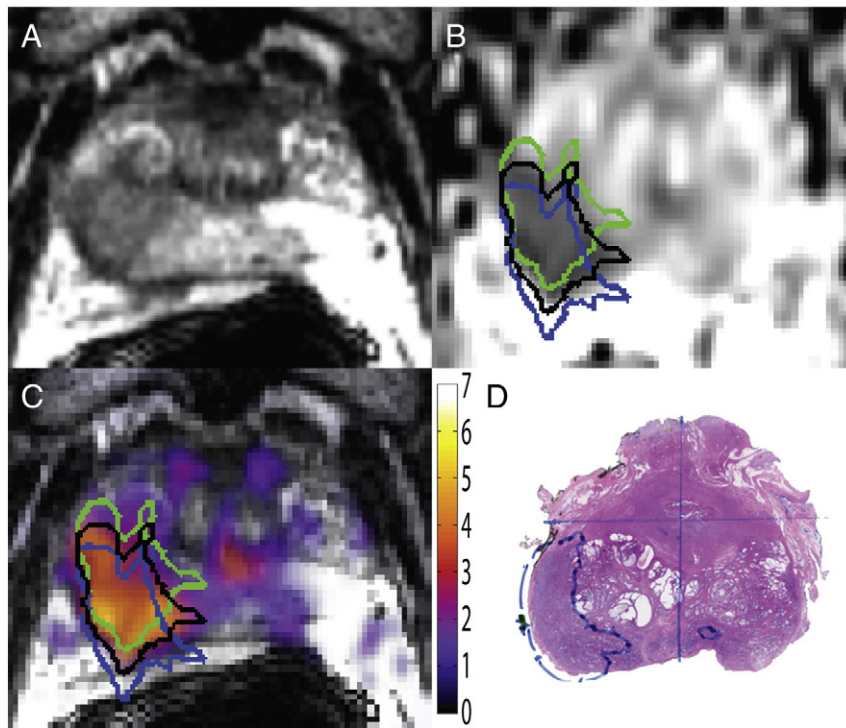
Low b-value ADC maps ( $b = 800 \text{ s/mm}^2$ ) were used to define malignant regions of interest, corresponding to tumors identified on whole mount pathology. In some patients, two regions of interest corresponded to tumor. If on the same slice, both of these tumor regions of interest were included in the analysis, for a total of 34 tumor regions of interest in 27 prostates.

## 3. Results

Across the 27 included patients, the average root mean square distortion distance of the prostate was 3.1 mm (standard deviation, 2.2 mm; maximum distortion, 12 mm). When specifically looking at the tumor regions, the average root mean square of the distortion distance of the tumors was similar at 3.1 mm (standard deviation, 2.3 mm; maximum distortion, 13 mm). Results are summarized in Table 2.



**Fig. 1.** Demonstration of distortion of diffusion MRI with EPI due to B0 inhomogeneity. (A) T2-weighted image of the prostate reflecting the prostate's MR anatomical appearance without distortion. (B) Demonstration of the distortion when the diffusion data are collected only in the forward phase encode direction with an EPI trajectory. (C) Demonstration of the distortion when the diffusion data are collected only in the reverse phase encode direction with an EPI trajectory. (D) Distortion corrected diffusion imaging at  $b = 0$ . (E) Deformation field map.



**Fig. 2.** Patient example of the effects of distortion on localizing tumor. (A) T2-weighted image, used as the imaging anatomic gold standard. Note that the tumor is in the right posterior quadrant. (B) Distortion-corrected low b-value ADC map, with the region of low ADC outlined in black. The blue and green ROIs represent the regions of low ADC without distortion correction (blue: in-phase encode direction, green: reverse phase encode direction). (C) RSI-MRI image that incorporates the distortion correction and converts the cellularity map based on multiple b-values to a standardized z-score map, overlaid on the T2-weighted anatomic image. The blue and green ROIs are the regions of RSI signal without distortion correction while the black ROI is distortion corrected. (D) Whole-mount histopathology confirming the location of extraprostatic extension in the right posterior quadrant.

Nine of the 27 patients demonstrated histologically proven extracapsular extension. Standard diffusion MR of the prostate only identified one tumor as definitively demonstrating extracapsular extension. The distortion correction maps demonstrated extracapsular extension in eight of the nine patients.

Fig. 2 shows an example of the calculated offset by 5.5 mm of root mean square distortion. This patient has histologically proven extraprostatic extension. Depending on the phase encode direction, the tumor area may incorrectly be localized anteriorly (thus not identifying extraprostatic extension), or appear to exceed the prostatic capsule in excess.

#### 4. Discussion

Diffusion imaging, because it uses an echo planar trajectory, is sensitive to  $B_0$  inhomogeneity. This manifests as distortion in the phase encode direction. By collecting data in both the forward and reverse phase encoding directions at  $b = 0$ , enough information is collected to correct for the distortion in the phase encode direction. This technique [23] is used to correct for the distortion in brain diffusion imaging. Although diffusion imaging in the prostate is becoming the standard of care in prostate MRI protocols, distortion correction has not yet been widely implemented for prostate diffusion imaging. Other distortion minimizing techniques are being evaluated in the prostate but focus on minimizing the distortion rather than correcting for distortion due to  $B_0$  inhomogeneity [29,30].

As demonstrated in this paper, distortion correction improves tumor localization for diffusion imaging. Diffusion imaging is often the best MR technique to detect prostate cancer. With the advent of MRI-ultrasound fusion guided biopsies [19] and high-intensity focused ultrasound treatment [20,21], accurate localization is

necessary. Surgical planning also depends on differentiating between extraprostatic extension of tumor and the tumor remaining within the capsule, a decision that could be made with accurate imaging. Distortion distances of up to 13 mm due to standard diffusion imaging may grossly misdirect treatment decisions and therapies. Distortion correction for diffusion imaging has the potential to improve the standard of care for prostate MRI.

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