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Image-guided radiotherapy

Readout-segmented echo-planar diffusion-weighted imaging improves geometric performance for image-guided radiation therapy of pelvic tumors

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ABSTRACT

Background and purpose: Diffusion-weighted imaging using echo-planar imaging (EPI) is prone to geometric inaccuracy, which may limit application to image-guided radiation therapy planning, as well as for voxel-based quantitative multi-parametric or multi-modal approaches. This research investigates pelvic applications at 3 T of a standard single-shot (ssEPI) and a prototype readout-segmented (rsEPI) technique.

Materials and methods: Apparent diffusion coefficient (ADC) accuracy and geometric performance of rsEPI and ssEPI were compared using phantoms, and in vivo, involving 8 patients prior to MR-guided brachytherapy for locally advanced cervical cancer, and 19 patients with prostate cancer planned for tumor-targeted radiotherapy. Global and local deviations in geometric performance were tested using Dice Similarity Coefficients (DC) and Hausdorff Distances (HD).

Results: In cervix patients, DC increased from 0.76 ± 0.14 to 0.91 ± 0.05 for the high risk clinical target volume, and 0.62 ± 0.26 to 0.85 ± 0.08 for the gross tumor target volume. Tumors in the peripheral zone of the prostate gland were partly projected erroneously outside of the posterior anatomic boundary of the gland by 3.1 ± 1.6 mm in 11 of 19 patients using ADC-ssEPI but not with ADC-rsEPI.

Conclusions: Both cervix and prostate ssEPI are prone to clinically relevant geometric distortions at 3 T. rsEPI provides improved geometric performance without post-processing.

Diffusion-weighted imaging (DWI) is standard-of-care for radiologic assessment of many solid tumor sites, because cell-dense tumors restrict water diffusion, resulting in DWI signal hyperintensity [1]. Parameterization of the DWI signal as an apparent diffusion coefficient (ADC) can improve tumor visualization as hypointense regions, and provide a biomarker for histologic classification and treatment response monitoring [2]. Prostate tumor ADC varies with cellular and glandular densities [3]. Pre-treatment and post-treatment tumor ADC histogram features may have prognostic relevance for solid tumors including those local to the cervix [4]. Therefore, there is considerable interest to integrate ADC mapping into radiation therapy treatment planning, and into multi-parametric and multi-modal tumor response monitoring [5].

Implicit to successful translation of DWI into therapy planning is geometric performance which approaches that of T_2-weighted MR imaging. However, clinical DWI uses a single-shot echo-planar imaging (ssEPI) readout to achieve realistic imaging times. ssEPI samples the full field-of-view in the phase-encoding direction during each pulse sequence repetition, resulting in a very low bandwidth (BW_{phase}), approximated as the inverse of the product of the echo spacing and the number of pixels in the phase-encoding direction [6]. In comparison, the readout direction field-of-view is sampled relatively instantaneously. Consequently, poorly shimmed tissue regions present with a chemical shift artifact in the phase-encoding direction [7]. Schakel et al. measured a mean per voxel shift of 1 cm within the gross treatment volumes of 23 head-and-neck cancer patients at 3 T [8].

The most common strategy for ssEPI distortion correction is parallel imaging [7]. Radiation therapy applications have also applied voxel displacement maps from 'field' maps of the resonance frequency, but re-shifted voxels may present with blur and ADC bias [8,9]. Haack et al. applied field mapping and deformable registration to reduce DWI-ssEPI distortion in cervix brachytherapy patients at 3 T, and did not observe an ADC blurring artifact [9].

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More spatially robust DWI techniques increase BW_{phase} at the time of data acquisition. Zonal Oblique Multislice (ZOOM) reduces pixel number and field-of-view in the phase-encoding direction, while minimizing aliasing artifacts. Thereby ZOOM has improved detection of state 1a/1b1 cervical cancer [10]. 2D navigator-corrected readout-segmented echo-planar imaging (DW-rsEPI) reduces echo spacing by segmenting the readout direction in a contiguous motion-compensated multi-shot acquisition [11]. rsEPI has improved DWI image quality for brain, spinal cord, breast, pelvic, and head and neck cancers [11–15].

This research investigates DW-rsEPI to improve geometric performance in on-going clinical trials which are implementing functional imaging into image-guided radiotherapy of cervix and prostate tumors at 3 T. Namely, a prostate trial proposes to define the tumor volume from the ADC hypointense volume, and a cervix trial proposes to use multi-parametric MRI to improve tumor delineation for planning MR-guided brachytherapy. First, phantom experiments validate the geometric performance of rsEPI compared to ssEPI. Second, ssEPI and rsEPI ADC values are compared in phantoms and in vivo. Third, similarity metrics are applied to clinically-relevant regions-of-interest (ROIs) drawn on DW-ssEPI and DW-rsEPI images to demonstrate the improvement provided by DW-rsEPI for pelvic image-guided radiation therapy.

Materials and methods

All subjects were prospectively enrolled on a clinical trial approved by the Research Ethics Board of the host institution.

Patient selection

Prostate cancer

Patients with localized prostate cancer were recruited from 1 of 3 prospective clinical trials integrating multiparametric MRI for the guidance of tumor-targeted radiotherapy. (ClinicalTrials.gov NCT01802242, NCT00775866, NCT00913939).

Cervix cancer

A single-arm, prospective pilot study to evaluate the utility of DWI, DCE-MRI and FDG-PET imaging for brachytherapy target delineation in locally advanced cervical cancer was initiated in October 2012. In addition to standard T_2W MRI simulation, the following images were acquired on the day of brachytherapy: DWI, dynamic contrast-enhanced MRI, and FDG-PET/CT.

MRI methods

All imaging used a 3 T Verio (Siemens Medical Systems, Erlangen, DE) mounted on rails (IMRIS, Winnipeg, Canada) with VQ gradients (40 mT/m peak amplitude; 200 T/m/s peak slew rate) and running syngo MR VB17 software. DW-rsEPI is a prototype method on the Verio and commercially available for recent platform releases. The imaging protocols are provided as Supplemental content. Of note are a 4-fold increase in BW_{phase} using rsEPI compared to ssEPI (from13 to 49 Hz/pixel), and the utilization of 4 *b*-values (0, 100, 600, 1000 s/mm^2) to check signal-to-noise (SNR) and allow for ADC comparisons with and without controversial $b = 0$ or 1000 s/mm^2 data [2]. Also, the rsEPI method used a monopolar diffusion scheme, which contributed to the shorter echo time, because the higher BW_{phase} imparts insensitivity to dynamic field perturbations associated with eddy currents [16]. The ssEPI method was implemented with a standard bipolar diffusion scheme to impart eddy current insensitivity [17].

Experimental design

Gel phantoms were used to investigate ssEPI versus rsEPI geometric performances relative to T_2-weighted imaging in vitro. Cylindrical gels of 10 cm diameter and 12 cm in length were constructed from 3% agarose, 0.2% $CuSO_4$, and 0.5% NaCl. Two 1 cm diameter channels were created during the gelling process, and in one channel, a 2.5 cm diameter balloon was inflated, and then deflated after gelling and removed. The regions of the channels and air pocket were imaged with an 8-channel head coil using prostate protocols (see Suppl. content), and an additional T_2-weighted image set with matched geometric features. Regions-of-interest (ROIs) corresponding to the air pockets were contoured in each slice using MIPAV software (National Institutes of Health, Bethesda, MD).

ADC-ssEPI and ADC-rsEPI accuracies were compared in vitro using the ice water standardization phantom [18]. A 50 cc conical tube was placed within a wide-mouth 500 ml container filled with crushed ice and wrapped within two insulating blue pads. Two hours were allotted for temperature equilibration between 0 and 0.2 degrees Celsius before centering in the bore within 5 mm of isocenter. Ice water ADC is 1100×10^{-6} mm^2/s [18]. Five repetitions of the prostate protocols (see Suppl. content) were interleaved, utilizing the spine array coil and anteriorly-placed 6 channel body matrix coil for RF signal reception. ADC maps were generated using in-line processing, and values were extracted from matched volumes-of-interest for each method and repetition using MIPAV.

In vivo testing consisted of sequential acquisitions of T_2-weighted, and DW-ssEPI and DW-rsEPI images sets, in the patient cohorts identified above, as follows:

Cervix cancer

Between October 2013 and November 2014, DW-ssEPI and DW-rsEPI were acquired sequentially in 8 patients on the day of pulsed- or high-dose rate brachytherapy. Prior to imaging, patients had an intrauterine brachytherapy applicator (Elekta interstitial ring applicator or custom applicator) ± interstitial needles inserted under general anesthesia. Upon recovery from anesthesia, they were imaged supine with a torso phased-array coil placed anterior, spine matrix array coil placed posterior, and with the brachytherapy applicator and foley catheter in situ.

Prostate cancer

Between November 2012 and November 2014, nineteen consecutive patients (17 with discernable PZ tumors; 2 with CG tumors only; 3 with both PZ and CG foci) were imaged prior to start of treatment, with T_2w, DW-ssEPI, and DW-rsEPI image sets acquired sequentially. As described previously [19], three small gold fiducial markers were implanted 3 days prior to imaging. Patients were sedated and underwent imaging immediately prior to a biopsy or brachytherapy procedure, using a four-channel phased-array surface coil placed anterior to the pelvis in combination with a 2-channel endorectal coil attached to a custom rigid encasement (Hologic, Inc. Bedford, MA).

Data analysis

Using MIPAV, matched ROIs were drawn on DW-ssEPI and DW-rsEPI images and copied across b-values, and the mean signals within each volume were extracted. ROIs included the gross tumor target volume at the time of brachytherapy (GTV_B) and high-risk clinical target volume (HRCTV) for cervical cases as per GEC-ESTRO guidelines [20]; and the central gland, peripheral zone, and tumor-dense regions for prostate cases. Image noise statistics were quantified from ROIs drawn on $b = 1000$ s/mm^2 images.