European Journal of Radiology 80 (2011) e34–e41

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

High-resolution diffusion tensor imaging of prostate cancer using a reduced FOV technique

Carolin Reischauer[a,*], Bertram J. Wilm[a], Johannes M. Froehlich[b], Andreas Gutzeit[c], Ladislav Prikler[d], Roger Gablinger[d], Peter Boesiger[a], Klaus-Ulrich Wentz[a,e]

[a] Institute for Biomedical Engineering, ETH and University of Zurich, Gloriastrasse 35, CH-8092 Zurich, Switzerland
[b] Guerbet AG, Scientific Affairs, Winterthurerstrasse 92, CH-8006 Zurich, Switzerland
[c] Department of Radiology, Cantonal Hospital Winterthur, Brauerstrasse 15, CH-8401 Winterthur, Switzerland
[d] Uroviva, Specialist Hospital for Urology, Zuerichstrasse 5, CH-8180 Buelach, Switzerland
[e] Department of Radiology, Cantonal Hospital Muensterlingen, CH-8596 Muensterlingen, Switzerland

ARTICLE INFO

Article history:
Received 5 March 2010
Received in revised form 17 June 2010
Accepted 18 June 2010

Keywords:
Diffusion magnetic resonance imaging
Apparent diffusion coefficient
Reduced field-of-view
Cancer
Prostatic neoplasm

ABSTRACT

Objective: Diffusion tensor imaging (DTI) offers the promise of improved tumor localization in prostate cancer but the technique suffers from susceptibility-induced artifacts that limit the achievable resolution. The present work employs a reduced field-of-view technique that enables high-resolution DTI of the prostate at 3 T. Feasibility of the approach is demonstrated in a clinical study including 26 patients and 14 controls.

Materials and methods: Reduced field-of-view acquisition was established by non-coplanar application of the excitation and the refocusing pulse in conjunction with outer volume suppression. Accuracy for cancer detection of apparent diffusion coefficient (ADC) mapping and T_2-weighted imaging was calculated and compared with reference to the findings of trans-rectal ultrasound-guided octant biopsy. Mean ADCs and fractional anisotropy (FA) values in the patients with positive and negative biopsies were compared to each other and to the controls.

Results: Fine anatomical details were successfully depicted on the ADC maps with sub-millimeter resolution. Accuracy for prostate cancer detection was 73.5% for ADC maps and 71% for T_2-weighted images, respectively. Cohen's kappa ($\kappa = 0.48$) indicated moderate agreement of the two methods. The mean ADCs were significantly lower, the FA values higher, in the patients with positive biopsy than in the patients with negative biopsy and the controls. Monte Carlo simulations showed that the FA values, but not the ADCs, were slightly overestimated. Bootstrap analysis revealed that the ADC, but not the FA value, is a highly repeatable marker.

Conclusion: In conclusion, the present work introduces a new approach for high-resolution DTI of the prostate enabling a more accurate detection of focal tumors especially useful in screening populations or as a potential navigator for image-guided biopsy.

1. Introduction

Prostate cancer is the most frequently diagnosed malignant carcinoma (25%) and the second leading cause of cancer death (10%) in men in the United States [1].

Early diagnosis is important to identify cancer at a treatable stage, thus increasing the chance for successful therapy and reducing mortality rates. Modern diagnostics and treatment of prostate carcinomas are in an increasing state of flux as imaging the exact localization of tumors must be continually improved to, on the one hand, perform more specific therapies and, on the other hand, make an attempt to locate tumors earlier and more accurately. For this reason, magnetic resonance (MR) diagnostics are becoming more and more important in this field. In addition to MR-guided biopsies, new techniques such as spectroscopy are gaining importance in being able to detect and classify the tumor earlier and more specifically. It is well known that screening has been significantly improved by the introduction of prostate-specific antigen (PSA) testing. Although the method exhibits relatively high specificity it is impeded by rather low sensitivity and the best suited threshold value of the PSA level for prostate cancer screening is an ongoing topic of discussion. The diagnosis of prostate cancer finally relies on histopathological examination of trans-rectal ultrasound (TRUS)-guided needle biopsy samples but the technique offers relatively low sensitivity. However, this form of diagnosis is the most widespread technique used worldwide as it is widely available and relatively inexpensive.

* Corresponding author. Tel.: +41 44 632 88 54; fax: +41 44 632 11 93.
E-mail address: reischauer@biomed.ee.ethz.ch (C. Reischauer).

0720-048X/$ – see front matter © 2010 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.ejrad.2010.06.038

As already mentioned, magnetic resonance imaging (MRI) can provide significant incremental value to clinical variables such as the localization and staging of prostate cancer. Although the reported accuracy of prostate cancer staging varies widely, high-spatial resolution T_2-weighted MRI has been acknowledged as one of the best performing pulse sequences to depict prostate cancer. Cancer usually demonstrates low signal intensity relative to the high signal intensity of the non-cancerous peripheral zone (PZ). But it has become apparent that morphological information alone does not provide enough information for accurate diagnosis.

Recently, several studies have employed diffusion-weighted imaging (DWI) [2–8] and diffusion tensor imaging (DTI) [2,9] to extract additional functional information. In contrast to DWI which represents diffusion restriction of water molecules in the tissue under investigation, DTI additionally derives estimates of diffusion anisotropy and thereby information of the underlying tissue structure by means of the fractional anisotropy (FA) value. It could be demonstrated that the apparent diffusion coefficient (ADC) can potentially differentiate between tumor and non-cancerous PZ [2,5,6] whereby the decreased ADCs in tumor tissue have been shown to be correlated with increased cell density [8]. Furthermore, it was suggested that the FA value might be correlated with the degree of tumor malignancy [9].

Most of these studies used single-shot spin-echo echo planar imaging (EPI) due to its high signal-to-noise ratio (*SNR*) efficiency and its insensitivity to motion-related artifacts. However, field inhomogeneities, primarily caused by local susceptibility variations in the sample, induce voxel shifts in the phase-encode direction. The ensuing image distortions are proportional to the EPI echo train length and rise linearly with the magnetic field strength. Moreover, each acquired *k*-space line carries a different T_2^* weighting which results in image blurring along the phase-encode direction. Both effects limit the achievable spatial resolution so that smaller focal tumors might not be detected.

DWI and DTI generally suffer from an intrinsically low *SNR*. The transition to higher field strengths promises an *SNR* gain but at the same time increasing susceptibility-related image distortions and T_2^* blurring limit the achievable image quality. Several prostate studies have addressed these problems using parallel imaging methods to shorten the echo train length [5,6]. However, the achievable reduction factor, and thereby the feasible image resolution, is limited by spatially inhomogeneous noise amplification due to the associated *g*-factor penalty. Reduced field-of-view (FOV) approaches [10,11] that likewise allow to shorten the readout train length suggest themselves when the object size allows ample truncation of the FOV in at least one dimension as, for instance, in the prostate.

The aim of the present work is to assess whether a spatially reduced FOV technique reliably achieves a sub-millimeter in-plane resolution for DTI of the prostate at 3 T. Detectability of tumors is tested in a prospective clinical study comparing T_2-weighted morphological images with ADC mapping in relation to the TRUS-guided biopsies. Mean ADCs and FA values in the patients with positive and negative biopsies are compared to each other and to the controls. Accuracy of the diffusion parameters is analyzed using Monte Carlo simulations and precision is investigated with bootstrap methods to examine reliability of the method in the clinical setting.

2. Materials and methods

2.1. High-resolution reduced FOV DTI

In the present study, a single-shot spin-echo EPI approach was employed with a reduced FOV (rFOV) in the phase-encode direction (see Fig. 1). Reduction of the spin-echo domain was achieved by non-coplanar application of the excitation and the refocusing pulse. By adjusting the tilt angle, this approach enables a trade-off between time-efficient multiple-slice imaging and FOV reduction (see Fig. 2) [10,11]. To achieve effective FOV reduction, while keeping multiple-slice capabilities, this method was combined with outer volume suppression (OVS) that abolishes signals arising from the transition bands (see hatched triangles in Fig. 2). Previous work has demonstrated that OVS can be effectively achieved by a series of quadratic phase pulses followed by crusher gradients prior to the slice excitation pulse [11].

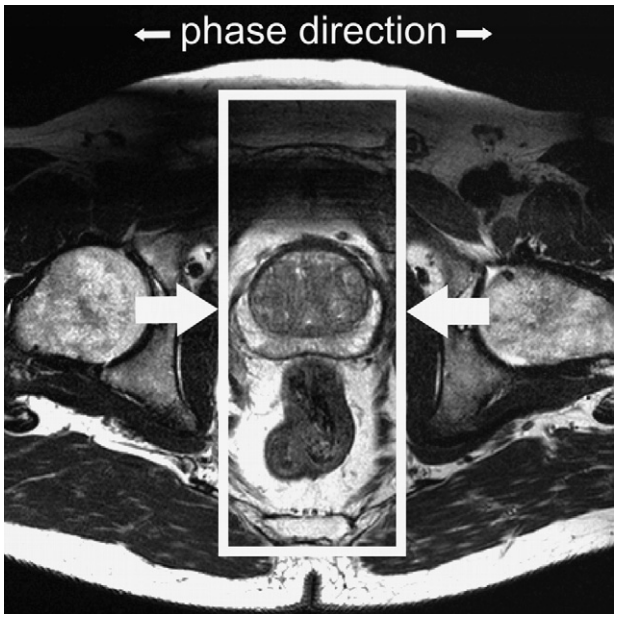

Fig. 1. On a T_2-weighted transverse MR image of the prostate outline of the typical aperture acquired using the reduced field-of-view (rFOV) technique in phase-encode direction. Thereby, the readout train length is shortened which leads to decreased susceptibility-related artifacts and T_2^*-blurring.

2.2. Subjects

26 patients (mean age = 65 years, age range = 54–79 years) who were suspected of suffering from prostate cancer due to an elevated PSA level (mean PSA level = 36.72 ± 8.71 ng/ml, median PSA level = 9 ng/ml) were investigated prospectively after written informed consent. This clinical trial protocol was approved by the local institutional review board. A planned TRUS-guided systematic octant biopsy was part of the inclusion criteria and was performed within seven days after MR imaging, the biopsy always being performed by the same urologist, who had over 10 years of practical experience. The biopsy sites were provided according to the guidelines of the European Association of Urology [12]. Additional cores would be obtained from suspect areas using this technique. Patients younger than 18 years, with contraindications to MR or participating in other studies were excluded. One patient had to be excluded secondarily due to implanted radioactive seeds in the prostate that rendered image analysis impossible.

In addition, 14 control subjects (mean age = 55 years, age range 40–75 years) underwent the identical scan session after informed consent. These volunteers had normal PSA values, did not have any symptoms of prostatic disease, and did not present suspicious lesions on the acquired MR images. One subject had to be excluded secondarily due to image artifacts caused by an air-filled rectum that lead to severe image distortions and signal drop out rendering image analysis impossible.