Combined Diffusion Weighted and Dynamic Contrast Enhanced MRI for prostate cancer diagnosis - correlation with histopathology

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Introduction

The non-invasive diagnosis of prostate cancer remains challenging. Several MRI techniques have been used to distinguish between benign prostate and prostate cancer (PCa). However, their sensitivity remains problematic. Two such techniques, Diffusion Weighted (DW) MRI and Dynamic Contrast Enhanced (DCE) MRI have recently shown particularly promising results in diagnosing prostate cancer [1, 2]. In this pilot study we correlated the results of both DW and DCE MRI techniques with histology to test the hypothesis that the combination of these techniques will provide higher diagnostic sensitivity than each technique alone.

Methods

Thirteen patients with a high clinical suspicion for prostate cancer (elevated PSA and/or prostate nodule) with no prior treatment were recruited to the study. Subjects underwent MRI examination prior to TRUS guided biopsies.

All MRI exams were carried out on a 1.5T GE clinical scanner. Ten axial slices (5 mm, no gap) across the prostate gland were acquired for both DW and DCE MRI data with FOV of 40 cm. DW MRI data was acquired using a single shot FSE sequence developed at UCSF (128x128, BW=62.5kHz, b-value=600). DCE MRI was performed using a multi-slice FSPGR sequence: 256x128, TE=3ms, TR=11ms (T1) or 120 ms (PD), flip angle = 25^0 (T1) or 8^0 (PD), and the time resolution of 22 sec per 10 slices. 45 time points were acquired following a bolus injection of Gd-DTPA (0.1 mmol/kg within 10 s followed by a 20 ml flush of saline).

Average Apparent Diffusion Coefficient (ADC) values were calculated from the ROIs defined as the hypointense areas in ADC maps. Mean diffusivity was calculated as an average of ADCx, ADCy, and ADCz. Average values of DCE parameters were calculated from the ROIs defined as the fast enhancing areas in Gd-DTPA concentration maps. Pharmacokinetic modelling parameters (K^{trans}, extra-vascular extra-cellular space - v_e, and maximum concentration of Gd-DTPA) were calculated by fitting the average ROI's concentration vs. time curve to a standard compartmental model [3]. Time-signal intensity parameters (maximum enhancement, onset time, and mean gradient) [1] were calculated within the same ROIs from the T1 weighted images. Control ADC and DCE parameter values were calculated from ROIs defined in the areas that were deemed normal based on both MRI and histology results. Correlation with histology was based on the results of biopsy and prostatectomy (where available), and MRI and histology data were mapped into a standard octant biopsy maps. Statistical analysis of differences between cancer, benign peripheral zone, and benighn transition zone was carried out using a Tukey-Kramer test.

Results

Nine of the 13 biopsies were positive for carcinoma; 7 of these 9 patients underwent radical prostatectomy. Average values of all MRI parameters (with the exception of extra-vascular extra-cellular space - v_e) showed significant differences between cancer and benign prostate (see Table I). PCa in Table I correspond to the areas identified as prostate cancer with both MRI and histological data. Sensitivity and specificity of the ADC data were equal to 59% and 97% respectively. DCE data showed similar sensitivity of 60% but lower specificity of 83%. When both ADC and DCE results were combined the sensitivity increased to 85% while specificity lowered to 80%.

Table I. Average values (mean ± SD) of mean diffusivity and CDE MRI parameters

	ADC [10^{-3}mm²/sec]	K^{trans} [min⁻¹]	v_e	Max. Conc. [mM]	.Max. Enh.	OT [min]	Mean. Grad.
PZ	1.6417 ± 0.0628	0.2410 ± 0.1695	0.1833 ± 0.0783	0.1296 ± 0.0498	0.9154 ± 0.2163	0.8966 ± 0.1039	0.6657 ± 0.2708
TZ	1.2437 ± 0.1717[c]	0.6157 ± 0.3172[e]	0.2700 ± 0.0436	0.2091 ± 0.0378	1.2819 ± 0.1916[h]	0.8042 ± 0.1204	1.2588 ± 0.3565[h]
PCa	1.1415 ± 0.1739[a,b]	1.2444 ± 0.6214[d]	0.2825 ± 0.1093	0.2290 ± 0.0846[f]	1.3086 ± 0.1397[a,g]	0.6063 ± 0.0356[a,i]	2.3978 ± 0.9156[a,g]

ADC – mean diffusivity, Max. Conc. – maximum concentration of Gd-DTPA, Max. Enh. – maximum enhancement, OT – onset time, Mean Grad. – mean gradient
PZ – benign peripheral zone (n=6), TZ – benign transitional zone (n=6), PCa – cancer (ADC: n=16, K^{trans}, v_e, Max. Conc.: n=14; Max. Enh., OT, Mean Grad.: n=21)
a – PCa significantly different from PZ (p<0.001), b – PCa significantly different from TZ (p<0.05), c – TZ significantly different from PZ (p<0.001), d - PCa significantly different from PZ (p<0.01), e – TZ significantly different from PZ (p<0.05), f - PCa significantly different from PZ (p<0.05), g - PCa significantly different from TZ (p<0.01), h - TZ significantly different from PZ (p<0.01), i - PCa significantly different from TZ (p<0.001)

Discussion

The results of our pilot study confirmed that either DW or DCE MRI can be used for non-invasive prostate cancer diagnosis, albeit with rather limited sensitivity. Specificity of the DCE technique is lower than DW, likely because glandular BPH will also show some degree of contrast enhancement [4]. When combined together the sensitivity improves significantly with a small decrease in specificity. This strongly suggests that both techniques provide complementary information regarding the structure and histology of the prostatic tissue. Indeed in many cases we noticed that the areas of low ADC did not completely coincide with the fast enhancing areas in Gd-DTPA concentration maps. This is likely because the areas of low ADC are associated with high cellular density with lower extra-cellular space [5], whereas the high contrast enhancement is attributed to greater extra-cellular extra-vascular space [4]. Since both types of tissue are present within the tumour, the combined ADC and DCE MRI techniques are more likely to provide accurate cancer detection, as found in our study.

Conclusion

All experimental parameters measured with DW and DCE MRI, with the exception of extra-vascular extra-cellular space, show significant differences between tumour and control prostatic tissue. Combining both techniques provides better sensitivity with a small decrease in specificity.

Acknowledgments

References: [1] Padhani AR, et al. *Clin Radiol* 2000: **55**, 99-109; [2] Vigneron D, et al. ISMRM Abstracts 2002: 457; [3] Galbraith SM, et al. *NMR Biomed* 2002: **15**, 132-142; [4] Noworolski SM, et al. ISMRM Abstracts 2000: 1464; [5] Lyng H, et al. *Magn Reson Med* 2000: **43**, 828-36.