simultaneous diffusion and perfusion imaging provides complementary functional data that can be used in the pre- and post therapeutic disease management in prostate cancer patients

G. Groenendaal[1], C. A. van den Berg[1], E. M. Roeloffzen[1], J. G. Korporaal[1], P. R. Luijten[2], M. van Vulpen[1], and U. A. van der Heide[1]

[1]Dept. of Radiotherapy, University Medical Center Utrecht, Utrecht, Utrecht, Netherlands, [2]Dept. of Radiology, University Medical Center Utrecht, Utrecht, Utrecht, Netherlands

Introduction

Dynamic contrast-enhanced (DCE) and diffusion-weighted imaging (DWI) have both shown to be able to discriminate benign from malignant regions in the prostate[1,2]. As contrast generated by these techniques stems from different physiology, we have studied the correlation between changes in perfusion and diffusion of suspicious regions found with both imaging techniques.

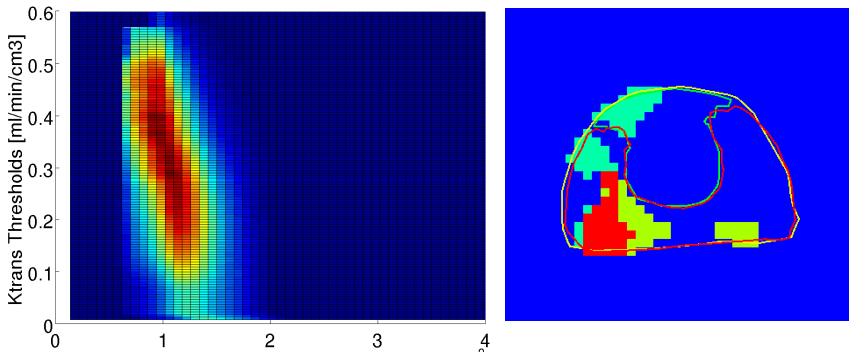
Methods

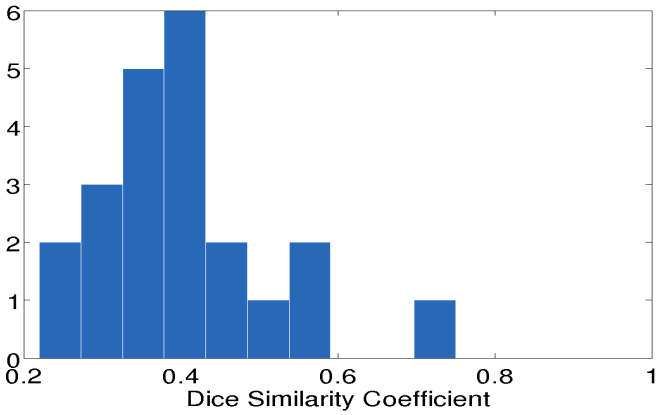
DCE-MRI and DWI scans were made with a 3 Tesla MRI system on 26 patients with biopsy proven prostate cancer. DWI scans were performed using a multi slice fat suppressed (SPAIR) single shot EPI sequence (TE=54 ms, TR=5000 ms), 1.95 mm in plane resolution and 5 mm in the z direction. Scans were made with b values of 0, 300, 500 and 1000 s/mm2. Apparent Diffusion Constants (ADC) were estimated from these data points using linear regression. To avoid perfusion effects influencing the value of ADC, the MR signal measured with a b value of 0 s/mm2 was not taken into account.

The DCE-MRI dynamic protocol consisted of a 3D spoiled gradient echo sequence (TR/TE=4/2.1 ms, flip angle 16°). 10 slices were scanned simultaneously for 120 times at 2.4s interval, with the same resolution as used for the DWI scans. 8 ml of gadolinium DTPA contrast was injected in 10 seconds followed by a saline flush. Concentration of the contrast agent was calculated from the MR signal using preceding small flip angle scans with 3 flip angles. For each voxel the concentration-time curves were analyzed using the Tofts model [3], yielding quantitative 3D maps of blood flow parameters, K^{trans}, k_{ep}, v_e. Of these three parameters the parameter K^{trans} was further investigated. K^{trans} is a parameter, which represents a combination of flow and the leakage of contrast agent [3].

To determine the overlap of the suspicious regions found with both techniques, a threshold needs to be set for both the ADC as the K^{trans} value. To be independent of threshold values, for both the 3D ADC maps as the K^{trans} maps, a range of thresholds was chosen, 0.0001-0.01 s/mm2 and 0.006-0.6 ml/min/cm3 respectively. For each given threshold the regions were identified, for which the values in the ADC map were lower than the given threshold. In the K^{trans} maps regions were identified which had values larger than the given thresholds. For each combination of ADC and K^{trans} thresholds, the overlap between the given regions in the prostate was calculated, as can be seen in figure 1. In this way the best possible overlap could be identified.

Overlap can be calculated using the Dice similarity coefficient: $2n(a+b)/(n(a)+n(b))$ and reflects the overlap between two volumes a and b, with n the number of voxels in the volume. We have performed a correction to cancel out the trivial solution, where the whole prostate fulfills the threshold criteria.





Results

In figure 1, the corrected dice coefficient of one single patient is shown. Threshold combinations, which result in a high dice score are shown in red, where blue represents threshold combinations which result in a low dice score. A local maximum is found for the overlap for the threshold values 0.00106 s/mm2 and 0.0366 ml/min/cm3 for ADC and K^{trans}, respectively. The dice similarity coefficient for these thresholds is 0.28. In figure 2, for one slice, the regions are shown for which the ADC (light blue) and K^{trans} (green) maps fulfill the threshold criteria for this patient. The overlap between the two regions is shown in red. As can be seen, the overlap is not complete. In figure 3 is shown that similar results are found for all investigated patients; even in the best case overlap is limited. Note that the threshold for which maximal overlap is reached lies in a relative small range for the ADC map (0.00074 – 0.00114 s/mm2), where the inter-patient K^{trans} threshold variability in the suspicious regions is much larger (0.018 – 0.6 ml/min/cm3).

Figure 1: Corrected dice similarity coefficient for one patient. Red means a relative large overlap, where blue means a limited overlap between the Ktrans and ADC regions. A local maximum is found at 0.00106 s/mm2 and 0.0366 ml/min/cm3. The dice coefficient is 0.28 **Figure 2:** Prostate with delineated central and peripheral zone. Overlap in low-ADC and high Ktrans regions is shown in red, high Ktrans only is shown in green and low ADC only in light blue. **Figure 3:** Histogram of best dice similarity coefficient for all patients.

Discussion

Low ADC values are thought to reflect high cell density, limiting the free water diffusion, whereas a high value for K^{trans} correlates with a high density of (leaky) vessels. Both features are indicative for tumor tissue inside the prostate. However, it is found that independent of the threshold taken, no complete overlap is found between regions with low ADC values and high K^{trans} values. BPH may affect the overlap in the central zone. Therefore it may be interesting to investigate the overlap of ADC and K^{trans} in the central and peripheral zone separately. The current results point at different underlying mechanisms causing the increased cell density and the increased density of leaky blood vessels in tumor tissue. Therefore, simultaneous diffusion and perfusion imaging provides complementary functional data that can be used in the pre- and post therapeutic disease management in prostate cancer patients.

References

1. Buckley DL *et al,* Prostate Cancer: Evaluation of vascular characteristics with Dynamic Contrast-Enhanced T1-weighted MR imaging – initial experience Radiology 233:709-715, 2004
2. Hosseinzadeh K *et al,* Endorectal diffusion-weighted imaging in prostate cancer to differentiate malignant and benign peripheral zone tissue, JMRI 20:654-661, 2004
3. Tofts PS *et* al, Estimating kinetic parameters from dynamic contrast-enhanced T1-weighted MRI of a diffusable tracer: standardized quantities and symbols, JMRI 10:223-232, 1999