

**TARGET AUDIENCE:** Radiologists; Medical physicists developing quantitative DWI MRI techniques.

**PURPOSE:** The non-mono-exponential nature of the decay of diffusion-weighted imaging (DWI) signal in the prostate is well established. [1-3] Current advanced modeling methods use a two component model, *a priori*, and the data is fit for the fast (corresponding to the coherent motion in blood vessels) and slow (describing the inherent diffusion properties of the glandular tissue) components. [2,3] Using a new implementation of the inverse Laplace transform, we present evidence that multiple slow components can be present in the decaying DWI signal.

**METHODS:** Six healthy male adults (age 20-25 years) were scanned on a 1.5T Philips Achieva™ scanner using an 8-channel body surface coil, following an IRB-approved protocol, and with informed consent.

As part of the imaging protocol, a 27 b value (0, 5, 10, 15, 20, 25, 30, 35, 40, 50, 70, 100, 150, 200, 250, 300, 350, 400, 450, 500, 600, 700, 800, 900, 1000, 1100, 1200 s/mm<sup>2</sup>) SE-EPI DWI sequence was acquired in a single slice through the prostate, at mid-level (resolution 2 x 5 x 5 mm<sup>3</sup>, TR/TE = 2000/61 ms, duration 7.5 min). Signal at each b value was averaged over an ROI. An inverse Laplace transform  $L^{-1}()$  was implemented on the resulting  $S(b)$  curve by a least-squares fit to a series of 14 exponential terms:  $L^{-1}(S(b)) = A_i(D_i)$ , where  $S(b) = \sum(A_i \cdot dD_i \cdot \exp(-D_i b))$ .  $D_i$  were unevenly spaced between 0 and  $80 \cdot 10^{-3}$  mm<sup>2</sup>/s ( $D_i = 0.0, 0.1, 0.25, 0.5, 1, 2, 5, 10, 20, 30, 40, 50, 60, 80 \cdot 10^{-3}$  mm<sup>2</sup>/s).  $dD_i$  were introduced to account for term weighing, and were calculated as the interval surrounding each  $D_i$ :  $dD_i = (D_i + D_{i+1})/2 - (D_{i-1} + D_i)/2$ . The inverse Laplace transform thus resulted in power spectra  $A(D)$  which were *not* normalized here to an integral of 1.

**RESULTS:** Figure 1 depicts the  $S(b)$  data in bladder (left) and peripheral zone (right) ROIs, the fits to the data, and the corresponding power spectra  $A(D)$  (bottom). In bladder, a single asymmetric peak is present in the power spectrum, indicating a single component in the exponential decay of the DWI signal. In the peripheral zone example, three components can be identified in the power spectrum. The initial fast decay at  $b < 50 \cdot 10^{-3}$  mm<sup>2</sup>/s, generally attributed to perfusion and the most visible in this example ROI, is represented by the peak centered around  $30\text{-}40 \cdot 10^{-3}$  mm<sup>2</sup>/s. The central peak corresponds to the slow diffusion term, while the peak at lowest D values ( $< 0.5$  mm<sup>2</sup>/s) represents a component with very restricted diffusion. The  $S(b)$  data in prostate ROIs in other patients, including peripheral zone or whole gland, typically did not show the fast perfusion component, and the corresponding spectra did not show the presence of the fast peaks at  $D > 10 \cdot 10^{-3}$  mm<sup>2</sup>/s, though the slow ( $1\text{-}5 \cdot 10^{-3}$  mm<sup>2</sup>/s) and very slow ( $< 0.5 \cdot 10^{-3}$  mm<sup>2</sup>/s) components were present. The power spectra in the central gland typically showed one broad slow peak centered around  $0.4 \cdot 10^{-3}$  mm<sup>2</sup>/s. In all cases, the prostate DWI signal at the maximum b value of 1200 s/mm<sup>2</sup> did not reach the noise floor.

**DISCUSSION:** The single-component decay in the bladder is consistent with absence of vasculature and compartmentalization. The peak location is in general agreement with the literature value of the apparent diffusion constant for pure water at 37C, which is  $3.2 \cdot 10^{-3}$  mm<sup>2</sup>/s. In the prostate, multiple components were typically present, which is consistent with expected compartmentalization of tissue. In particular, the very slow component representing highly restricted diffusion may originate from intra-cellular water. Although with the maximum b value used in this work of 1200 s/mm<sup>2</sup>, it is not possible to resolve it from a constant baseline component ( $D = 0$  mm<sup>2</sup>/s), the fact that the signal is well above the noise floor at all b values points to restricted diffusion instead. Higher b values are needed for better peak resolution at low D. While it is not practical to image the whole prostate with a high number of b values, establishing expected values for intra- and extra-cellular compartments in different parts of the prostate can inform *a priori* fitting of data acquired with a lower number of b values. In addition, precise quantification of diffusion (number, position, width, kurtosis, etc. of peaks) in prostate lesions may be clinically feasible and may allow better correlation with Gleason score than what current quantitative DWI methods allow.

**CONCLUSION:** We were able to demonstrate the presence of multiple slow terms in the exponential decay of the DWI signal in the prostate. Imaging with a high number of b values could help characterize prostate lesions detected on MRI, or could inform modeling of DWI data acquired with a lower number of b values.

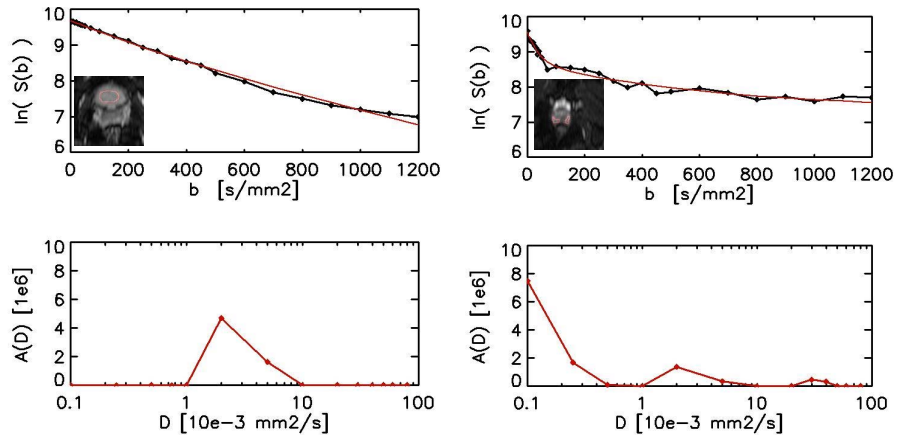


Figure 1: (TOP) The logarithm of the DWI signal  $S(b)$  is plotted (black) for a bladder ROI (left) and a peripheral zone ROI (right). The inserts depict the ROIs in each case. The red line represents the 14-term exponential fit to the data. (BOTTOM) Power spectra  $A(D)$  corresponding to the fits to the data are shown. The x axis is logarithmic for better resolution of peaks.

[1] Shinmoto et al., Am J Roentgenol. 2012 Oct;199(4):W496-500.

[3] Liu et al., Magn Reson Imaging. 2013 Oct;31(8):1318-24.

[2] Liu et al., Korean J Radiol. 2013 Mar-Apr;14(2):222-32.