A Novel Luminal Water Model for DCE MRI of Prostatic Tissues

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Introduction Dynamic contrast-enhanced MRI has been shown to be useful in identifying prostate cancer compared to healthy glandular tissues. It has been suggested that Gd-DTPA does not reach intact prostatic ducts [1,2]. Standard pharmacokinetic modeling of DCE MRI data of the prostate does not take this into account and therefore likely do not accurately represent the tissues. The purpose of this abstract is to present a novel pharmacokinetic model incorporating a Gd-inaccessible luminal water parameter and to demonstrate its differences versus an extended Tofts Kermode model [3] in simulations and in an in vivo example.

Methods A novel Luminal Water (LW) model of prostate tissue was designed based upon the assumption of Gd not reaching intact prostatic ductal lumen and the water in the lumen not having interacted with Gd through diffusion into the lumen. A luminal water volume parameter ($V_{Lw}$) was added to the extended Tofts Kermode (TK) model [3]. General assumptions of the Tofts Kermode model persist. The $T_1$ outside of the lumen was assumed to change with time due to the change in Gd concentration in those tissues: $T_1 = \frac{1}{\frac{1}{T_{1p}} + \frac{1}{1 - \exp(-TR/T_1)}}$. Input to this formula are $\alpha$ and $T_1$, obtained from the sequence parameters, and $T_{1p}$. $T_1$ was given above. Fitting the data to this equation, using standard models for $C_v$, leads to output parameters of $K_{trans}$, $V_{eef}$, and $V_1$. For this study, the population AIF presented by Tofts [3] was used, with variable, amplitude parameter. MR signal intensities versus time for healthy peripheral zone tissue were simulated using the LW model and the extended TK model.

This model was applied to data from a subject with biopsy proven, untreated prostate cancer. 3T DCE MRI was performed with a series of 3D FSPGR images (TR/TE/flip=5/2.1ms/6°, 2.7mm slices, matrix=192x128, 100 timepoints, bolus injection of 0.1mmol/Kg Gd-DTPA). Regions of interest were identified and manually drawn on the aligned, T2-weighted images, maintaining homogeneous tissues. The time of initial enhancement was manually identified and subsequent intensities versus time data were fit to 1) the novel LW model and 2) the extended TK model. Native $T_1$s were assumed to be 1.6sec.

Results Results of simulations with and without a luminal water component are shown in Table 1 and Figure 1. The extended Tofts Kermode tissue models are given, designed for matching the LW model with: 1) matching $K_{trans}$, 2) fitting the data, 3) matching late washout.

The in vivo example case had a region of high signal intensity (Figure 2) and was modeled as shown in Figure 3 and Table 2.

Discussion This Luminal Water model of prostate tissues reflects underlying histology, as theorized and as demonstrated in vivo. The major difference between the LW and TK models is the luminal water compartment in the LW model which allows for a slower washout, quite common in healthy and benign, glandular prostate tissues. Simulations demonstrated that the standard extended TK model would greatly underestimate $K_{trans}$ and $V_{eef}$ in glandular tissues (-27% in example given). $K_{trans}$ reductions less than this (12.5%) have been used to monitor therapy for prostate cancer [4]. Therefore, error in $K_{trans}$ accuracy may be relevant for treatment response, as cancerous tissues are frequently mixed with healthy tissue, particularly in the low and moderate grades, so changes in the relative percentages of healthy and cancerous tissues can result in changes in $K_{trans}$ without actual changes in the underlying vascular volume or permeability. Another implication of these simulations is that the $K_{trans}$ with TK fits will be affected by the DCE MRI acquisition time, relevant for comparing studies. A limitation of this model is that it introduces an additional fit parameter; some data may be overparameterized, leading to difficulty in finding optimal fits. As this model provides a metric of benign glands, it has promise to help in understanding prostate tissue histopathology and potentially aid in tissue discrimination.


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Dataset 1-2: simulated normal peripheral zone tissue (nPZ) with fits using an extended Tofts-Kermode model with $V_p=0.01$ and an AIF amplitude of 2.

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Table 1 - Simulated normal peripheral zone tissue (nPZ) with fits using an extended Tofts-Kermode model with $V_p=0.01$ and an AIF amplitude of 2.

![Figure 1](image1.png) Simulation of normal peripheral zone (solid line) using luminal water, Tofts-Kermode models without luminal water (dashed lines).

![Figure 2](image2.png) T2-weighted image with highly glandular/ductal (black arrow) and cancer (white dashed arrows).

![Figure 3](image3.png) Corresponding intensity vs. time curves and fits. The cancerous fits match (top) while the glandular (bottom) Tofts-Kermode fit (dotted) shows a slower enhancement than the data and than the Luminal Water model.

![Table 2](image4.png) Fits. The Luminal Water model yields a luminal water volume for the glandular tissue, but not the cancerous tissue, as expected biologically. The resultant Tofts-Kermode fit results in an underestimation of $K_{trans}$, $V_{eef}$, and $V_p$ for the glandular tissue.

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