Two compartment fitting for Luminal Water Imaging: multi-echo T2 in Prostate Cancer

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Synopsis

This work aims both to show that using a constrained fitting method for Luminal Water Imaging with fewer echoes produces accurate parameter estimates and that this fitting method is feasible for detecting and grading Prostate Cancer. Simulated signals were produced and the mean LWF across multiple iterations was calculated for two models. Then 19 patients were imaged and the images were contoured in both cancerous and benign regions. The simulation showed that the proposed constrained method is accurate and the in-vivo imaging reinforced the idea that multi-echo T2 modelling shows promise in detecting and grading PCa.

Introduction

Similar to methods developed for imaging myelin in the brain[1], Luminal Water Imaging (LWI), a fitting technique for multi-echo T2 data recently proposed by Sabouri et al.[2], calculates the percentage volume of lumen within a voxel. LWI has been shown to be closely related to the luminal space in prostatic tissue[2], with a recent study demonstrating the feasibility of luminal water imaging in the detection and grading of PCa[3]. However, the current method requires a 64-echo acquisition which is time consuming and may not be available without dedicated scanner research software. This work seeks to show that the combination of an appropriately refined fitting method and fewer acquired echoes provide values of the Luminal Water Fraction (LWF) that are in close agreement with those of the original LWI. Correlations to Gleason score were then performed along with the AUC, sensitivity and specificity of the detection of PCa.

Methods

Model The original fitting proposed by Sabouri et al[1] used a smoothed non-negative least squares (NNLS) fitting over many variables to produce a distribution p of T2 values[4]. The method proposed here constrains this distribution to consist of two Gaussians. This constraint was imposed because the vast majority of voxels in the Sabouri studies[2,3] showed two main signal components, which may provide a more robust fitting. The model relating the Signal S to the distribution p of T2 values is:

$$S = M_0 \int_0^\infty p(T2) exp(-\frac{TE}{T2}) dT2$$

where M_0 is the overall magnitude of the signal and TE is the echo time. For each voxel six parameters were estimated: overall scaling (M_0), relative fraction between the two compartments (α), mean and standard deviation of the short T2 peak (μ_1 and σ_1) and mean and standard deviation of the long T2 peak (μ_2 and σ_2). The LWF was calculated as the area under the long T2 component divided by the area under both components.

Simulation Simulated signal decays were produced for two separate underlying T2 distributions (two delta functions at $T2_{short}$ and $T2_{long}$ and two Gaussian distributions with means $T2_{short}$ and $T2_{long}$, fixed at $T2_{short}$ = 75ms and $T2_{long}$ = 600ms) with varying values of LWF, Signal-to-Noise Ratio (SNR) and Number of Echoes (NE). For each combination of parameters 50 iterations of the signal were created. For each iteration the original and new fitting methods were tested using 64-echo and 32-echo simulation signals respectively. The mean LWF across the 50 iterations was then calculated for both models in order to show how the two compare over a range of LWF and SNR values.

Data In order to investigate the relationship between this new fitting method and Gleason Score, 19 subjects were imaged for this study. The scan parameters are included in Figure 1. A board-certified radiologist contoured 15 lesions in 19 patients, which were confirmed to be cancers following targeted biopsy. Regions of interest (ROIs) were also placed in 16 areas of normal tissue in each of the subjects, all of which were histologically confirmed as benign.

Statistics A Spearman's rank correlation test was used to find the correlation between Gleason Score and LWF and the Area Under the Curve (AUC), sensitivity and specificity values were calculated using a Receiver Operating Characteristic (ROC) analysis with 5-fold cross validation to reduce problems arising from multiple ROIs coming from the same image.

Results

Figure 1 shows the scan parameters of the 32-echo acquisition. Figure 2 shows that for nearly all values of LWF and SNR, using either the delta function or Gaussian assumption, the LWF value produced by the new method is at least as accurate as the original. Using a Spearman's rank correlation test a correlation of -0.667 was found between Gleason Score and LWF in 31 ROIs. Figure 3 shows the AUC, sensitivity and specificity achieved by the new fitting method in 31 ROIs. Figure 4 is an example LWF map of the prostate. Note the higher LWF in the peripheral zone (PZ), consistent with histological findings of large regular acini and loosely woven stroma in the PZ[5].

Discussion

The LWF values calculated in simulation using both fitting methods show that the new constrained method is just as accurate as the original. The correlation between Gleason Score and LWF then reinforces the idea that multi-echo T2 modelling shows promise as a method for detecting and grading PCa. The AUC, sensitivity and specificity of the detection of PCa are all lower in this study when compared to previous results6 but this may be down to a much lower number of ROIs.

Conclusion

This new method shows promise in being able to significantly reduce the number of measurements needed to carry out LWI, making it a more clinically viable method.

Acknowledgements

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References

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Figures

Parameter	32-echo
Number of echoes	32
TE (ms)	31.25
TR (ms)	8956
Acquisition voxel size (mm^3)	2x2x4
FOV (mm^3)	180x180x26
Scan Duration (mm:ss)	05:49

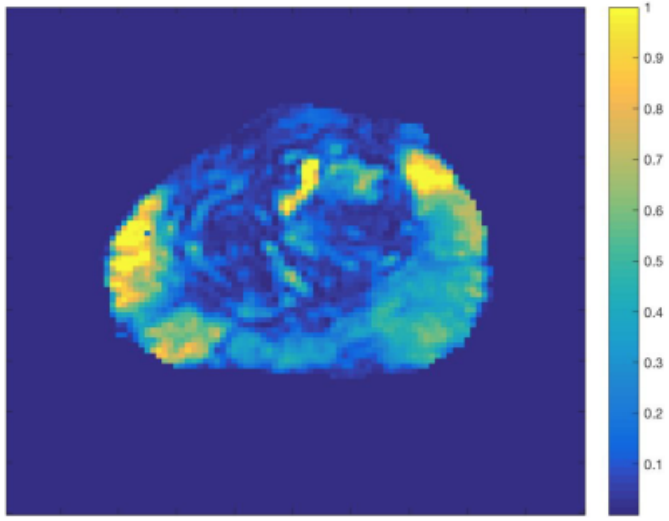
Scan parameters of the 32-echo acquisition.

		GAUSSIAN		DELTA-FUNCTION	
LWF	SNR(DB)	CONSTRAINED	NNLS	CONSTRAINED	NNLS
0.5	10	0.532	0.378	0.529	0.387
	30	0.499	0.497	0.497	0.495
	70	0.498	0.498	0.497	0.497
	100	0.498	0.498	0.497	0.497
0.35	10	0.379	0.216	0.368	0.224
	30	0.347	0.347	0.345	0.346
	70	0.347	0.348	0.345	0.347
	100	0.347	0.348	0.345	0.347
0.2	10	0.229	0.099	0.238	0.100
	30	0.198	0.197	0.197	0.197
	70	0.197	0.198	0.196	0.197
	100	0.197	0.198	0.196	0.197
0.05	10	0.106	0.035	0.106	0.035
	30	0.049	0.047	0.048	0.046
	70	0.049	0.048	0.048	0.047
	100	0.049	0.048	0.048	0.047

This table shows the predicted value of the LWF for both models for different actual LWF values and noise levels and using both delta function and Gaussian signal simulations. It shows that, for the majority of values of both LWF and SNR, the constrained model is at least as close to the actual value as the NNLS model.

Variable	No of ROIs	AUC	Sensitivity	Specificity
LWF (constrained)	31	0.80	69%	87%
LWF (NNLS)[6]	255	0.92	84%	88%

AUC, sensitivity and specificity achieved by the new fitting method against the original. The LWF calculated using NNLS is taken from a previous work for comparison[6].



LWF map of the prostate. Note the higher LWF in the peripheral zone (PZ), consistent with histological findings of large regular acini and loosely woven stroma in the PZ[5].