Methodology for the Histopathologic Correlation with Functional MR Images of the Prostate by Successive Morphing

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Introduction

Improvements in the delivery of external beam radiotherapy and brachytherapy for the treatment of prostate cancer has made the identification of highly sensitive and specific non-invasive MR tumour markers a clinical priority. Comparison of non-invasive MR parameters with histopathologic evaluation of tissue samples has been associated with significant practical difficulties. Problems with this process include uncertainties arising from distortions in images, specimen deformation in the process of slicing and the ability to register MR images to histopathalogic slices. The presented methodology reduces these uncertainties to a minimum.

Methods/Materials

Imaging: Patients are scanned on a 1.5T Philips Gyroscan Intera using the phased-array body coil. The following 2D high-resolution sagittal T2 weighted images provide visualisation of the posterior base of the prostate. Once identified the following 2 and 3D scans are performed orthogonal to the prostate base and using a slice width of 4mm and a slice gap of 0mm: high-resolution axial T2-weighted slices (TR/TE = 2011/100 msec, field of view (FOV)=170mm), diffusion weighted echo planar imaging (TR/TE=2500/69, b values=0, 300, 500, 800 s/mm^2, sensitisation in three orthogonal directions, FOV= 200mm, slice width of 6mm interpolated to 4mm), a multi-echo GRASE sequence (TR/TE = 1800/40,80,120,160,200ms, FOV=435mm), a series of 3D fast gradient-echo scans (8 slices, flip angles = 1, 3, 7, 5, 10, 15, 20, 25, FOV=300) and a dynamic contrast enhanced scan using a 3D fast gradient echo (8 slices, flip angle 10, TR/TE=3.7/1.19ms, FOV=300). The scanning protocol takes 30 minutes. The patients undergo radical prostatectomy within 1 day of the MR exam.

Histopathology: The fresh whole-mount prostate is placed on its posterior base and sliced with a patented multi-blade cutter that produces parallel 4mm slices, thus ensuring similar imaging slice/specimen slice orientation. The fresh slices are photographed using a digital camera (Nikon D100 SLR, Nikkor MicroLens), formalin fixated, embedded in paraffin, sectioned and stained. After staining, tumour tissue within the gland is outlined by an experienced histopathologist and these outlines are again photographed.

Registration: Using gtkMorph (GNU General Public License) one control mesh is created between the high-resolution MR image and the photograph of the fresh slice and another between the fresh slice and the stained section. The morphing is first applied to the photograph of the stained section with tumour outlines so as to shape it like the fresh-tissue slice. In a second step, the morphing transformation that links the fresh tissue slice to the high-resolution T2-weighted MR image is obtained and applied to the previously morphed stained tissue section. The prostate is rich in landmarks that can be used to attach the control mesh, namely the gland capsule, outline of the peripheral zone, urethra and ejaculatory ducts. The successively morphed microsection with appropriately altered outlines identified as containing tumour cells can then be used for a pixel-by-pixel correlation of one or several of the functional MR parameters (T2 contrast, ADC, T2 map, dynamic contrast uptake and wash-out parameters) measured in this protocol.

Results

Fig. 1a shows the photograph of a fresh slice as well as the section after staining (Fig. 1b). The inevitable distortion and shrinking during fixation and sectioning can be removed from the picture by assigning a control mesh to both images for morphing (Fig. 1c). Note that the morphing process effectively resolves the tissue tear observed in Fig 2b - such tears commonly arise during sectioning. The morphed section and appropriately altered tumour outlines can now be compared with the morphological and functional MR images demonstrated in Fig. 2. Fig. 2 shows a coincident high-resolution axial T2-weighted scan (Fig 2a) and parametric map (Fig 2b). Fig 2b represents the area under the curve associated with the signal change over the period of the dynamic contrast enhanced T1 weighted scan.. Maps of T2 and apparent diffusion coefficients (not shown) are similarly inherently registered to the high-resolution axial T2-weighted scan and can be used to perform pixel-by-pixel correlations with results determined form histology.

Discussion

This procedure should enable us to determine which MR parameters, used either singly or in combination, will reliably detect the presence of tumour in the prostate gland. MR examinations that have shown early promise include conventional high-resolution T2 weighted images, apparent diffusion coefficient maps, dynamic contrast uptake parameters (demonstrating tumour microvascularity and angiogenesis) as well as direct metabolic information from MRSI [1]. Of the 20 patients in this study 2 have been scanned while the remainder will be examined over the coming months.

Acknowledgement

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References

[1] J.Kurhanewicz *et al.* Combined MRI & SI Approach to Molecular Imaging of Prostate Cancer, J Magn Reson Imaging **16**: 451-463 (2002)

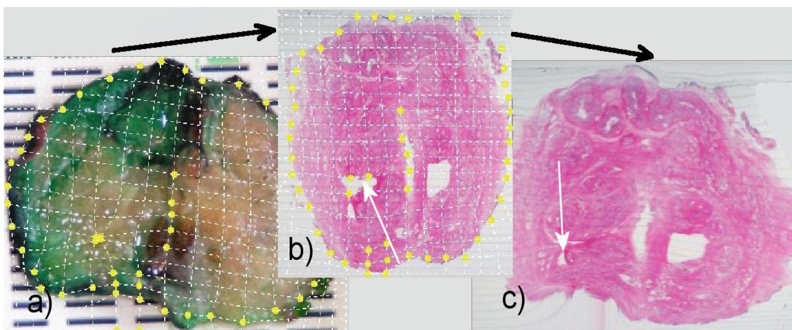

Figure 1: Fresh slice of whole-mount prostate specimen and morphed tissue section.(b) shows the control mesh as assigned with the help of landmarks

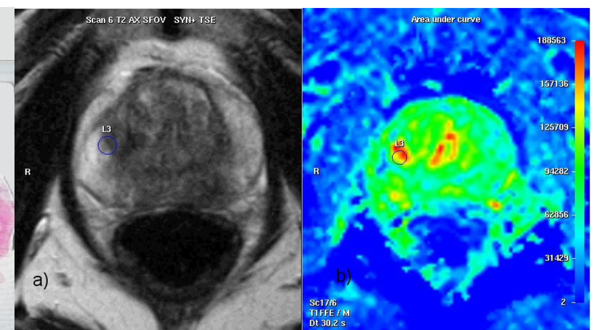

Figure 2: T2 weighted axial image (a) and map of area under the curve for T1 contrast enhancement during first pass dynamic contrast uptake (b)