

# Probability maps for tumour localisation, using 3D <sup>1</sup>H-MRSI and LCModel fitting of model “Benign” and “Tumour” basis spectra.

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**Target audience.** Clinical oncologists, urologists, radiologists and spectroscopists interested in MR methods for prostate cancer localisation and staging.

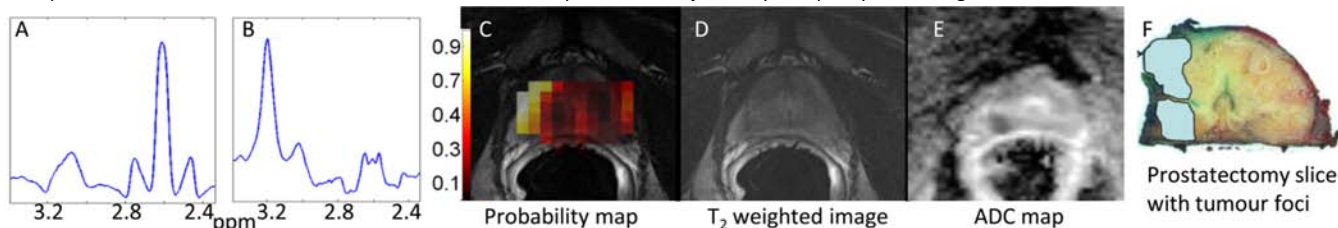
**Purpose.** Multi-parametric MRI (mpMRI) is a promising tool for prostate cancer localisation, staging and treatment planning. We have developed probability maps for prostate-cancer localisation based on 3D-<sup>1</sup>H MRSI that uses LCModel [1] to fit two basis-spectra, representing benign and tumour tissue, to each voxel's spectrum. Processing is fully automated to provide a simple to use, quantitative, image of probable-tumour location for radiological reading.

**Methods.** A database of training spectra was formed from <sup>1</sup>H-MRSI data sets, of patients with prostate cancer, acquired within an mpMRI [2] exam with a Siemens Magnetom Trio, 3T MRI (Siemens Medical Solutions, Erlangen, Germany). Voxels were selected by location within tumour or benign tissue with reference to T<sub>2</sub>-weighted images and histopathology of prostatectomy [2]. The spectra were quality controlled [3], leaving 2360 spectra (1239 benign, 1121 tumour) from 42 patients, which were then aligned and referenced with the citrate (CH<sub>2</sub>) group of resonances set at 2.62ppm. Two independent components were generated from these spectra using the Fast ICA algorithm [4]. The two components were defined as representing tumour and benign tissue and then used to generate an LCModel basis-set that found their linear combination that fit each of the 2360 training spectra. The coefficients of the two components (tumour and benign) were combined into a single score (see below), on which a linear classifier was trained. The posterior probabilities of the classifier were used to calculate an equation that related the score value to the probability of a spectrum corresponding to a region of tumour. LCModel analysis was also used to calculate a choline + spermine + creatine over citrate ratio (CSC/C) using simulated metabolite spectra. The independent components were used to find chemical shifts for the simulated metabolites and their spectral profiles were confirmed as accurate by comparison to phantom data; a spermine model spectrum was used to model all polyamine signals. Five new prostate cancer MR data sets were acquired and patients underwent prostatectomy and subsequent histopathology. The <sup>1</sup>H MRSI data from these scans were fitted with the independent components and their coefficients were used to calculate tumour probability scores as described above. These were then visualised as maps overlaid with T<sub>2</sub> weighted images using Matlab (The Mathworks, Natick, MA).

**Results.** The independent component analysis of the training spectra generated two components, the first (Figure A) contained features similar to benign tissue: citrate and polyamine resonances which are found at high concentrations in the luminal spaces of prostate. The second component (Figure B) had features similar to the singlets from choline containing compounds (3.2ppm) and creatines (3.0ppm) resembling the <sup>1</sup>H spectra of prostate cancer. Fitting of the training spectra with these components in LCModel allowed for a linear classifier to be generated from their relative linear contributions. The posterior probabilities of classified data were fit with the following equation to calculate the probability of a spectrum corresponding to a region of tumour tissue:

$$\text{tumour probability} = \frac{e^{6.1 \times (\text{score} - 0.426)}}{1 + e^{6.1 \times (\text{score} - 0.426)}} \quad \dots \text{where} \dots \quad \text{score} = \frac{\text{tumour}}{\text{tumour} + \text{benign}}$$

Tumour probability allowed a separation of tumour from benign spectra in the training set with an area under the receiver operating characteristic curve (AUC) of 0.782±0.018 (p<0.05 confidence interval) which was significantly higher than a (CSC/C) ratio calculated from an LCModel fitting with simulated metabolite spectra (AUC of 0.721±0.022). Comparison of MRI and <sup>1</sup>H MRSI data from five new patients (example in Figure C-F) to their histopathology data revealed multiple tumour foci (125µl) per patient and these co-localised to regions where more than two adjacent-voxels had a tumour probability >0.75. One tumour was outside the acquired <sup>1</sup>H MRSI PRESS excitation volume and one tumour's spectra were rejected by the quality control algorithm.



**Discussion.** LCModel was previously used to fit spectra representative of various tumours and benign tissue for the diagnosis of brain tumours [5], here we demonstrate that it can be similarly used to calculate tumour probability maps for prostate-cancer localisation. Regions of high tumour probability could not co-localise to the entire tumour if it extended beyond the fitted voxels but were often larger than the histological lesion, possibly due to the point spread function. Seminal glands have a high choline signal and gave a high tumour score but were easily identified with reference to the T<sub>2</sub> weighted MRI.

**Conclusion.** Tumour probability maps for localising prostate tumours may give a more accurate separation of tumour from benign spectra, compared to conventional metabolite-ratio methods, and are quicker to calculate. The <sup>1</sup>H-MRSI data is converted to maps in an automated process that can complement existing mpMRI techniques for radiological reading of prostate cancer where it could be used to improve the planning of MR guided biopsy or focal therapy.

**References.** [1] Provencher SW. Estimation of metabolite concentrations from localized in vivo proton NMR spectra. *Magn. Reson. Med.* 1993;30:672-679. [2] Kobus T, Hambrock T, Hulsbergen-van de Kaa CA, Wright AJ, Barentsz JO, Heerschap A, Scheenen TW. In vivo assessment of prostate cancer aggressiveness using magnetic resonance spectroscopic imaging at 3 T with an endorectal coil. *European urology* 2011; 60:1074-1080. [3] Wright AJ, Kobus T, Selnaes KM, Gribbestad IS, Weiland E, Scheenen TW, Heerschap A. Quality control of prostate <sup>1</sup>H MRSI data. *NMR in Biomed.* 2012; DOI: 10.1002/nbm.2835. [4] Hyvarinen A. Fast and robust fixed-point algorithms for independent component analysis. *Ieee TNN* 1999; 10:626-634. [5] Raschke F, Fuster-Garcia E, Opstad KS, Howe FA. Classification of single-voxel <sup>1</sup>H spectra of brain tumours using LCModel. *NMR in Biomed.* 2011; 25:322-331.