Identification of Intratumour Low Frequency Microvascular Components via BOLD Signal Fractal Dimension Mapping

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Introduction: Recent invivo MR imaging using T2* weighted Blood Oxygen Level Dependent (BOLD) signal has shown great potential in developing a method to noninvasively assess tissue microvasculature. Studies show that the BOLD signal fluctuations are not random in origin [1] and can be further broken down into metabolic linked and cardiac/ respiratory "noise" [2]. Given the erratic nature of these signal timecourses they may be best investigated by nonlinear (fractal dimension) frequency domain analysis. BOLD signal modulation is directly due to variation in the ratio of oxy to deoxyhaemoglobin and has shown to be sensitive to small changes in the microvessel environment [3]. Hence, this approach provides a strong basis to characterise tumour microvascular hemodynamics. Preliminary investigation of rectal cancer patients has shown that the fractal dimension of the tumour BOLD signal calculated using a frequency spectrum power law relationship [4] can help identify intratumour regions with timecourses of high temporal order or low fractal dimension (FD). The intratumour low FD signal timecourse and subsequent frequency spectrum are distinctive in nature and highlight regions in which multiple, large magnitude, low frequency components (<0.15Hz) are solely present. Literature results have suggested that low frequency components in this range are of particular relevance to the microvascular environment. [1, 5, 6]

Methods: In an institutional research ethics board approved study, subjects with clinically proven rectal carcinoma were scanned using a 3T GE Signa shortbore MRI system and 8 channel pelvic phased array RF coil. Standard T1 and T2 images were used to prescribe T2* (BOLD) weighted (α=70^o, TE/TR = 35/250ms, FOV24cm, 64x64 matrix) image acquisition through large volume, midtumour slices. 2400 temporally contiguous BOLD images were acquired over 10 minutes. at a sampling rate of 4Hz (1/250ms). BOLD data, spatially correlated with anatomical slices, was assessed for nonlinear microvascular characteristics using in-house programs written in Matlab (The Mathworks, Natick MA).

Results /Discussion: An example intratumour region of interest (ROI) is shown in Figure 1(b) along with the corresponding area of interest on the fractal dimension map 1(c). Signal time course and Frequency spectrum from this ROI are shown in Figure 2(a) and (b). The intratumour BOLD signal timecourse shows distinctly periodic behaviour. A fourier transform of this data yields a frequency spectrum with low frequency peaks ranging from 0.0078Hz to 0.1406Hz. Typical peristaltic motion occurs on average at 3 contractions per minute (0.05Hz) [7] and normal respiration frequencies are reported near 0.15Hz [5]. Hence, peaks reported at 0.0488 and 0.1406Hz may possibly be labeled as peristaltic and respiration cycles respectively. However, a 0.0957Hz line and cluster of low frequency peaks are significant features that seem to invoke correlations with key frequencies (<0.1Hz) relating to micro-vasomodulation in brain as measured by BOLD imaging [5]. Observed intratumour low fractal dimension (FD) frequencies also relate well with tumour studies investigating blood flow and oxygenation where spontaneous fluctuations in the BOLD signal has been associated with acute tumour hypoxia in murine tumours (<0.006Hz). Rat adenocarcinoma measurements of pO2 and blood flow also reveal significant low frequency components < 0.033Hz [6] .

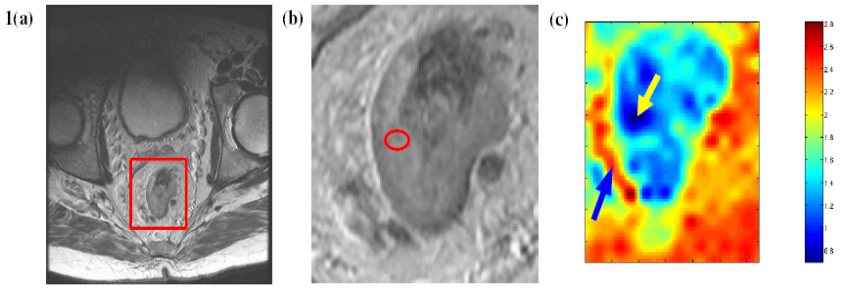
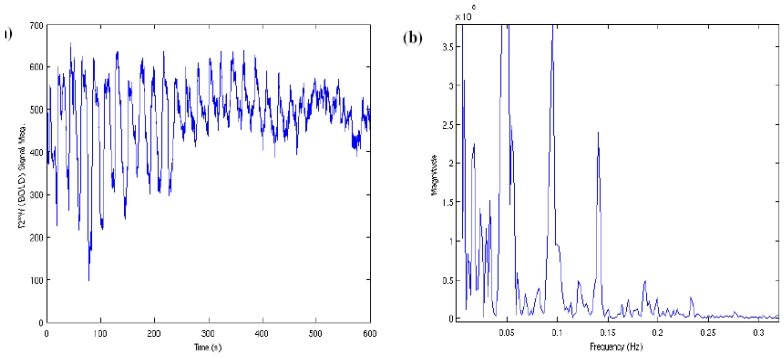


Figure 1: T2 weighted image (a) showing area of interest and close-up (b). Tumour region of interest circled in red. Corresponding Fractal Dimension (FD) map outlining regions of temporally well orderd (blue) and "chaotic" (red) BOLD signal (c). Intratumour low FD region of interest (yellow arrow). Mesorectal vessels seen as red-orange band (blue arrow).



ure 2: T2* signal timecourse (a) from intratumour low fractal dimension (FD) region of erest. Signal shows temporal periodicity and subsequent frequency spectrum(b) reveals a ster of peaks (<0.04Hz) as well as other large magnitude physiological peaks (0.0488Hz, 957Hz and 0.1406Hz). Low frequency peaks are implicated in tumour vascular function.

Conclusions Low frequency components in T2* signals have been reported as significant in the function of vasomodulation, as well as tumour growth and metabolism. We present here, a method which utilises a fractal dimension mapping approach to aid in selecting regions of regularised metabolism and microvascular behaviour. This shows significant potential in noninvasively assessing the tumour microenvironment which will have direct implications on treatment choices and efficacy.

[1] Baudelet C et. al. Physics in Medicine and Biology (2004) 49:33893411. **[2]** Kruger G and Glover GH. Mag. Res. Med. (2001) 46:631637. **[3]** Ogawa S et. al. Proc. Natl. Acad. Sci. USA (1990) 87:98699872,. **[4]** Schepers HE, Van Beek JHGM and Bassingthwaite JB. IEEE Engineering in Medicince and Biology (1992) 11(2):5764. **[5]** Biswal B et. al. J. Cerebral Blood Flow and Metabolism (1997) 17:301308. **[6]** Braun RD, Lanzen JL and DeWhirst MW. Am. J. Physiol., Heart Circ. Physiol. (1999) 46(2):H551H568. **[7]** Nishino M et. al. European Journal of Radiology (2005) 53:263267.