Optimisation of b-value Distribution for Intravoxel Incoherent Motion (IVIM) Imaging of Breast Cancer with Clinical Results

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TARGET AUDIENCE: MR breast researchers – scientists and clinicians

PURPOSE: Intravoxel incoherent motion imaging (IVIM) is a technique that enables the measurement of cellularity and vascularity using diffusion-weighted (DW) imaging.[1] The IVIM technique has been applied to various cancer types including breast cancer, but not extensively. Further validation of the technique and its effectiveness in breast cancer diagnosis and treatment is needed. The aim of this investigation was to find an optimised clinical b-value protocol for IVIM imaging in breast lesions and to apply this protocol in breast cancer patients.

METHODS: Firstly, sets of b-values were generated using exponential and power-law spacing from 0 s/mm^2 to 1000 s/mm^2 with a spacing coefficient, r, sampled from 0 to 10 in increments of 0.01 for 10 b-values (shown to be the minimum 'optimal' number of b-values needed[2]). The IVIM model, described by Le Bihan[1], is based on the biexponential $S = S_0[(1-f)e^{-bD} + fe^{-bD^*}]$ where S is the diffusion-weighted signal, f is the perfusion fraction, D is the diffusion coefficient and D* is the pseudodiffusion coefficient. The model yields four parameters to optimise. In order to determine the optimal set of b-values for IVIM in the breast, the Cramer-Rao Lower Bound (CRLB) of the standard deviation (SD) of the IVIM equation parameters were calculated. Three sets of initial values of the model's parameters were taken from the literature for malignant breast tissue [4, 5, 6] and each of the three sets were evaluated separately as follows. The CRLB of the SD of the *k*th of these parameters, $s(\theta_k)$, was calculated using $s(\theta_k) = \sqrt{(\mathbf{F}^{-1})_{kk}}$ for the *kk*th element where **F** is the Fisher information matrix given by $\mathbf{F}_{jk} = \sum_{b's}(\frac{\partial s}{\partial \phi_j}\frac{\partial s}{\partial \phi_k})$ where j and k correspond to pairs of parameters (S=1, f=2, D=3, D*=4). Each b-value in a set is evaluated for each pair of partial derivatives and are summed to give that Fisher matrix element. The main diagonal of the matrix represents the $s(\theta_k)$s for the four parameters. Calculations were coded and computed in MATLAB. Plotting $s(\theta_k)$ versus r and finding the minimum indicated the best sampling strategy for that parameter. An optimised b-value scheme was chosen based on a figure of merit[3], Γ ,to balance the relative errors of the parameters of interest by taking the square root of the sum of each CRLB over the corresponding initial parameter value used from the literature. DW-images of 9 breast cancer patients were acquired on a 3.0T MR750 scanner (GE Healthcare, Milwaukee, WI). DW-imaging was performed with an 8-channel breast coil using single-shot echo planar imaging (34x34cm field of view, 128x128 matrix, 4 NEX, 4m20s scan duration, b= 0, 10, 23, 46, 82, 140, 233, 382, 619, 1000 s/mm^2) with water only excitation. Normal clinical diffusion was also performed. Region of interests (ROIs) were drawn by an experienced Radiologist in the most malignant part of the lesion, with a mean area of 38mm^2. This signal data was fitted using a monoexponential model to calculate diffusion, D_m. Then the data was fitted to the biexponential IVIM equation using the Levenberg-Marquardt algorithm implemented in MATLAB. The curve was fitted with a cut-off value of b = 200 s/mm^2 for the single parameter D to neglect D* for b-values greater than 200 s/mm^2. Finally, the curve was fitted for f and D* over all b-values whilst keeping D constant. This increased robustness. The root mean square error (RMSE) for each fit was reported.

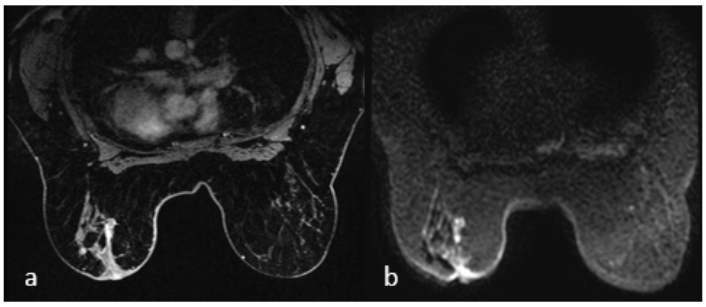

Figure 1: *An example (a) Post-contrast T1 image and (b) IVIM diffusion b=1000s/mm² image showing the lesion centrally in the left breast down to the nipple and invading the skin.*

Patient	D_m	*RMSE of mono- fit*	*D*	*f*	*D**	*RMSE of bi- fit*
1	0.0015	15	0.0014	0.067	0.0050	12
2	0.0011	23	0.00090	0.11	0.0062	15
3	0.00060	25	0.00065	0	0	27
4	0.00096	44	0.00091	0.022	0.0050	45
5	0.0011	40	0.00089	0.11	0.0058	31
6	0.00070	19	0.00055	0.11	0.0063	13
7	0.00080	24	0.00068	0.093	0.0058	15
8	0.00062	15	0.00058	0.031	0.014	11
9	0.0010	55	0.00086	0.095	0.0074	23

Table 1: *Results for D_m, D, F and D* with RMSEs for mono- and bi- exponential fits*

RESULTS: The minima for all r versus Γ for all exponentially spaced data were lower than all of the minima for all power-law spaced data, therefore exponential spacing of b-values was chosen. For 10 b-values, the average r from the minimas of the three sets of initial parameter values was 1.59 and the average Γ was 0.13. This corresponded to b-values$_{10}$ = 0, 9, 23, 46, 82, 140, 233, 382, 619, 1000 s/mm^2, with 4 NEX this gave a scan time of 4m20s. The MR system would not allow values less than 10 s/mm^2 that were not 0, so 10 s/mm^2 was used to replace 9 s/mm^2. Table 1 shows the values for D_m, D, f and D* in the most malignant part of the lesion with RMSEs for both fits.

DISCUSSION: The results for f, D and D* agree well with previously reported values.[4, 5, 6] The RMSEs indicate that the biexponential fit is better for the majority of cases. D_m is larger than D, showing that it is overestimated due to perfusion effects. Clinically this protocol has proved useful thus far, especially in visualising the lesion when contrast could not be given. The b-value scheme samples low b-values well (<200s/mm^2) and allows an acceptable amount of NEX for a short scan duration.

CONCLUSION: An optimised clinical b-value protocol for IVIM imaging in breast lesions was established and it was clinically applied to breast cancer patients. So far, results have yielded good fits and acceptable values for f, D and D*.

REFERENCES: (1) Le Bihan D *et al*. Radiology. 1988;168:497-505. (2) Lemke A *et al*. MRI. 2011;29:766-776. (3) Leporq B *et al*. JMRI. 2014. (4) Sigmund EE *et al*. MRM. 2011;65:1437-1447. (5) Bokacheva L *et al*. JMRI. 2013 (6) Liu C *et al*. Eur. Journal of Radiology. 2013;82:e782-e789.