Semi-Continuous Regularized Multi-Exponential Fitting Model for Diffusion Weighted Imaging of the Liver

Burkhard Mädler[1,2] and Jürgen Gieseke[2,3]

[1]*Neurosurgery, University of Freiburg, Freiburg, Germany,* [2]*Philips Healthcare, Hamburg, Germany,* [3]*Radiology, University of Bonn, Bonn, Germany*

Introduction: Diffusion-weighted MRI (DW-MRI) as a non-invasive imaging technique detects thermally driven, random motion of water molecules in living tissue and is able to characterize its interaction with cell membranes, macromolecules and potential diffusion barriers in terms of an apparent and/or restricted diffusion coefficient. A bi-exponential model to separate the intra- and extracellular diffusion from the incoherent motion of water molecules within randomly oriented capillaries was proposed by Le Bihan – IVIM [1-3]. Several studies have utilized this technique for various clinical applications in the abdomen (tumors, liver cirrhosis, kidneys), animal experiments, muscle, and brain [4-6]. The presence of noise and patient motion in DW-MRI images, which cannot be completely eliminated through postprocessing or special acquisition techniques, may substantially affect reliability of IVIM parameter estimation. Especially any low number of b-value acquisition suffers from the intrinsic inability to differentiate bulk or peripheral motion (whole body movement, bowel motion, breathing, pulsation due to cardiac cycle) from the incoherent molecular motion (diffusion and perfusion) that will be investigated. The deconvolution of multi-exponential processes is a strongly ill-posed problem and the necessity for a large number of signal points and SNR for a reliable separation of more than one exponential time constant is imminent from signal theory. This challenge cannot be simply overcome by more sophisticated fitting routines but must constitute a compromise between patient feasible scan times, highest possible number of b-values, adequate b-value range, and sufficient SNR [7-9].

Methods: Three healthy subjects were examined on a 3T whole body MR-system (Philips Ingenia, Best, The Netherlands) with a whole liver, free breathing single shot diffusion weighted sequence: voxel size 3x3x7mm^3, 12 slices, TR=2.1s, TE=55ms, matrix 116x112, 10 to 16 b-values from 0 to 800 s/mm^2 with a higher sampling density in the range of low b-values, three orthogonal gradient directions (x,y,z) – total scan time 2.5min.
The data were analyzed voxel as well as ROI-based with a regularized NNLS and the corresponding diffusion signal kernel for 121 log-spaced diffusion coefficients between 0.1 and 1000 µm^2/ms (Fig.1, top). Each analyzed signal decay curve results in a diffusion distribution (spectrum) displaying the diffusion fraction for each apparent diffusion coefficient ADC (in the following denoted as D) (Fig.1, bottom). Contrarily to brain tissue that exhibits highly anisotropic diffusion behaviour, liver is rather isotropic in its diffusion properties. Nevertheless, the signal decay was analyzed for each of three orthogonal diffusion gradient encoding and for an overall "isotropic" b-value weighting from all three gradient directions. All individual DW-images were eddy current corrected and registered to the b=0 image. The novelty of this hereby introduced approach lies in its semi-continuous nature and therefore its ability to derive quantitative diffusion fraction maps from any arbitrary D or range of D-values. For example, the vascular perfusion fraction vPF can be determined from the inverse solution of the signal decay function (fig.1, top right) by taking the ratio of the integral D between 10-100µm^2/ms and the total integral [8,9]. Figs. 1,2 illustrate the data acquisition and analysis process. Parameter maps (diffusion/perfusion fractions) can be derived from any arbitrary diffusion window, e.g. in fig.2 right, fractional maps from four significant diffusion regimes (depicted by numbers in fig.2 left) can be reconstructed.

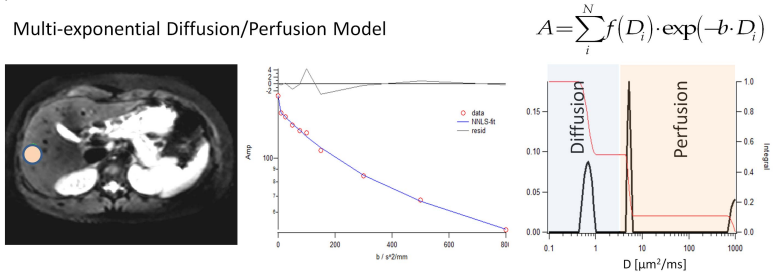

Fig.1: DWI(b0) image (left) with the signal decay (middle) and its multi-component decon-volution from a ROI depicted in yellow. Note the differentiation of various diffusion/per-fusion properties from the semi-continuous approach.

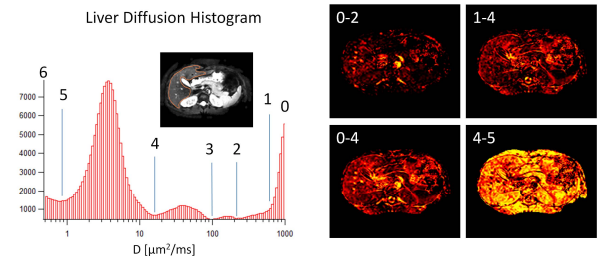

Fig.2: Liver diffusion histogram (left) showing various diffusion/perfusion regimes numbered 0 to 6 from which separate parameter maps, depicting the individual diffusion fraction, can be derived (right).

Results: The sequence allows for sufficient and patient friendly (free breathing) data acquisition with reliable NNLS diffusion times deconvolution (diffusion spectrum) from which fractional parameter maps of any arbitrary diffusion regime can be derived. Fig.3 depicts the fractional perfusion maps (vPF) from 2 consecutive slices of the fast diffusion regime (vascular perfusion) between 10-1000 µm^2/ms commonly declared as the IVIM-perfusion fraction. Subtle differences can be identified between the three orthogonal diffusion encoding settings (p-phase, m-measure, s-slice) but without significant differences in the mean values from the ROI for the NNLS approach (white solid line) (cf. table 1 right column). The two others numerical models (IVIM and bi-exponential fitting) estimate much lower mean vPF with individually significant differences between the diffusion encoding directions P,M, and S. The same trend was also observed for the other two subjects.

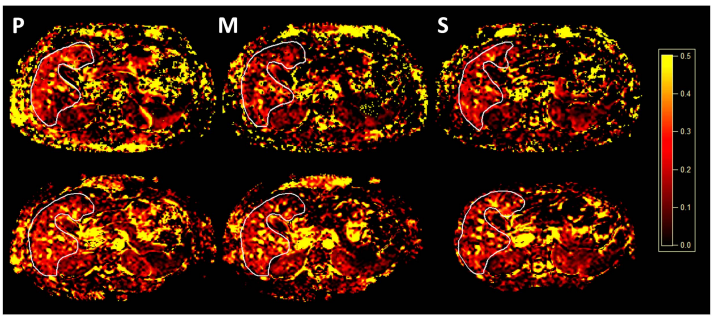

Fig.3: (left) vPF of two consecutive axial slices through the liver for three orthogonal diffusion encoding directions (P-M-S).

DW-direction	IVIM	Bi-exponential	reg.-NNLS
P	0.178 ± 0.145	0.201 ± 0.155	0.212 ± 0.153
M	0.160 ± 0.138	0.157 ± 0.155	0.208 ± 0168
S	0.136 ± 0.135	0.178 ± 0.139	0.193 ± 0.163

Table1: Mean vPF from ROI in fig.3 for three common numerical models.

Conclusion: The aim of this preliminary study was to test performance, reproducibility and feasibility of a new continuous approach and compare the derived perfusion fractions to the common models of IVIM and/or bi-exponential diffusion. From the known limitations and ill-posed nature of multi-exponential decaying systems [7-9] we conclude that it is essential to acquire more than four-to-six b-values for reliable vPF estimates. Furthermore, a continuous approach without prior assumptions about the number of underlying diffusion compartments and their diffusion times might be advantages for clinical validation, diagnosis and cross vendor studies.

References: [1]. Le Bihan D, Radiology 161 (1986):401. [2]. Le Bihan D, J Comput Assist Tomogr. 15 (1991),19; [3]. Le Bihan, D. et al. *Radiology,* 168 (1988) ,497; [4]Henkelman, R.M. et al., MRM 32 (1994), 464; [5] Henkelman, R.M., MRM 16 (1991), 470; [6] Kim, H.S. et al, AJNR (2013) epub.; [7] Whittall, K. et al. MRM 41 (1999) ; [8] Mädler, B. et al. Proc. ISMRM 2013 (3193); [9] Mädler, B. et al. Proc. ISMRM 2013 (1150)