A 4D spatio-temporal model to estimate stroke lesion evolution on MR perfusion-diffusion imaging following acute ischemic stroke

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Introduction:

The spatio-temporal evolution of stroke lesions, from acute injury to final tissue damage, is complex. Currently there is no 4D dynamic model simulating the continuous evolution using MR observations. Acutely, the diffusion-weighted (DWI) and perfusion-weighted imaging (PWI) detection of early ischemic changes led to the concept of the "perfusion-diffusion mismatch" hypothetically reflecting salvageable tissue, also known as the "ischemic penumbra", assuming that the lesion core tends to grow into the observed mismatch without treatment. Several clinical trials and treatment strategies use the DWI-PWI mismatch concept for treatment decisions, although validation is incomplete [1, 2]. We aimed to estimate patient-specific 4D evolution scenarios for PWI (measured as Mean Transit Time, MTT) and DWI lesions from acute to subacute timepoints, to better determine the 4D dynamic DWI/PWI mismatch evolution process and expansion/contraction mean speed quantification. A current-based 4D dense diffeomorphic regression model was applied to manually-delineated MTT and DWI lesions acquired at three successive timepoints after acute ischemic stroke.

Material and Methods:

We selected 8 representative patients (5 males, 3 females; NIHSS = 11.63±7.8; age = 72±5.2) from a study of MR imaging in hyperacute stroke of 48 patients, to estimate the 4D perfusion/diffusion evolution scenarios, according to the following method-driven criteria: (a) the MTT and DWI lesions should be both visible at –at least- three timepoints, (b) the number of lesion connected components should not vary between timepoints (only one-connected component non-fragmented lesions were included at present),. The first acquisition timepoint was at around 5h, the second one at 5±1 days and the third at 10.5±2.5 days.

Acquisitions – all MR images were acquired using GE Signa LX 1.5-T MRI scanner (General Electric, Milwaukee, Wis) with a birdcage quadrature coil and a standardized protocol for acute stroke. The spin-echo echoplanar imaging diffusion-tensor axial sequences and dynamic susceptibility contrast echoplanar imaging PWI had 15 axial slices each of 6-mm thickness with an interslice gap of 0.97 mm and an imaging matrix 128x128 encompassing a 240x240 mm field of view. MTT perfusion maps were generated using PWI. Both DWI and MTT images were co-registered and their corresponding visible lesions were manually delineated.

Method – using the manually delineated DWI/MTT lesions (Fig. 1.a), we reconstructed their 3D surfaces, further considered as observations for the estimation of 4D evolution scenarios, modeled as currents as explained in [3]. The estimation of the DWI continuous diffeomorphic time-varying evolution function deforming the observed lesion shape at timepoint t1 into the two successive ones was based on the minimisation of an energy which combines the fidelity to data and a regularisation on the estimated deformation. The estimation depends on four main parameters, which are automatically fixed. Similarly, MTT 4D evolution scenario was estimated. An extra step is used in our further analysis: an additional spatial deformation function mapping DWI lesion at t1 into MTT lesion at t1 was estimated and the generated new estimated final shape was used as the baseline lesion shape for the MTT scenario at t1. After the estimation of both DWI/MTT evolution scenarios and the additional spatial deformation (Fig. 1.b), more relevant information was extracted to better investigate "the DWI/PWI mismatch" concept:

a) The norm of the speed was computed at each time step at each point of the continuously evolving lesion 3D surface (Fig. 1.b).

b) The contraction and expansion areas at t1 in DWI-estimated 4D evolution scenario were initially extracted according to the direction of the computed speed vector at every point of the lesion surface. A mean evolution speed of the initially depicted contraction (*vs.* expansion) areas is computed along the 4D DWI estimated evolution scenario. Using as an automatic contraction (*vs.* expansion) threshold the mean evolution speed minus (*vs.* plus) its standard deviation, the areas with high contractions (*vs.* expansions) are extracted (Fig. 2.b) (*vs.* (Fig. 2.c)) in DWI lesion surface at t1 then spatially mapped into the MTT lesion at t1.

c) After extracting both MTT and DWI areas with high expansions and contractions, a mean spatio-temporal evolution speed was computed for these areas over their spatio-temporal evolution for the 8 patients (Fig. 2.d).

Results and Discussion:

To evaluate the accuracy of this 4D estimation, we computed the mean and SD values of the dice index between the estimated and the original lesion at the three observation timepoints. Table 1 shows very promising estimation of the patient-specific 4D evolution scenarios for both MTT and DWI lesions as the 4D scenarios fit in the observed initial lesions at the second the third timepoints (Fig.1.b). Furthermore, the contraction/expansion dynamic spatio-temporal and kinetic behaviors revealed in the 8 patients did not show any common pattern confirming the "DWI/PWI mismatch" concept (Fig. 2.d). In fact, if the DWI/PWI hypothesis is correct then we would expect the areas of DWI expansion to correlate with the areas of MTT no change and the areas of MTT contraction to correlate with areas where DWI did not expand, but the contraction and expansion areas between MTT and DWI did not seem to coincide (arrows in Fig.1.b, Fig.2.b-c) and even completely overlap for the majority of the cases. To develop this novel 4D dynamic model further in ischemic stroke, topology change and focal lesion swelling will be incorporated in our further research work. A further validation of the 4D model in independent datasets will be important.

	DWI(t2)	DWI(t3)	DWI to MTT at t1	MTT(t2)	MTT(t3)
Mean(dice)	0.90	0.90	0.86	0.76	0.80
Std(dice)	0.02	0.02	0.06	0.09	0.08

Table 1: *The mean dice index value and its standard deviation are computed over the 8 patients between the estimated and the manually delineated DWI/MTT lesions at t2 and t3. They are also computed for the spatial deformation mapping DWI lesion at t1 into MTT lesion at t1.*

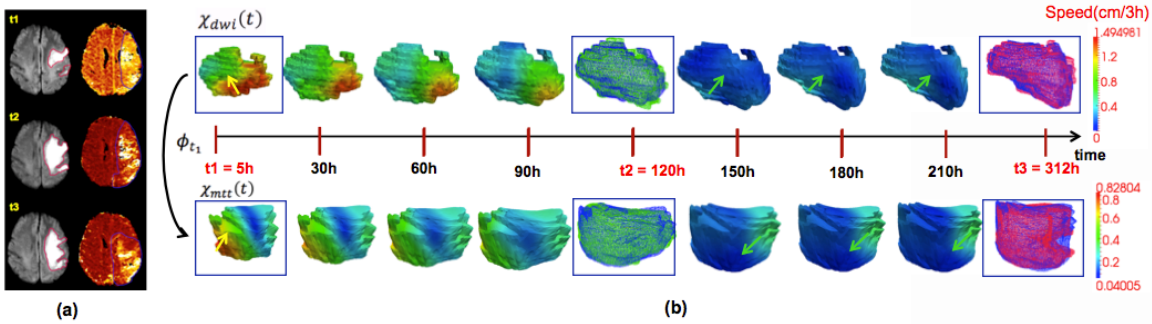

Fig1: *(a) DWI (vs. MTT) axial slice at 3 timepoints in the first (vs. second) column. (b) Estimated 4D DWI/MTT evolution scenarios with evolution speed quantification. At t2 (vs. t3), the green (vs. red) surface represents the observed lesion and the blue one represents the estimated lesion.*

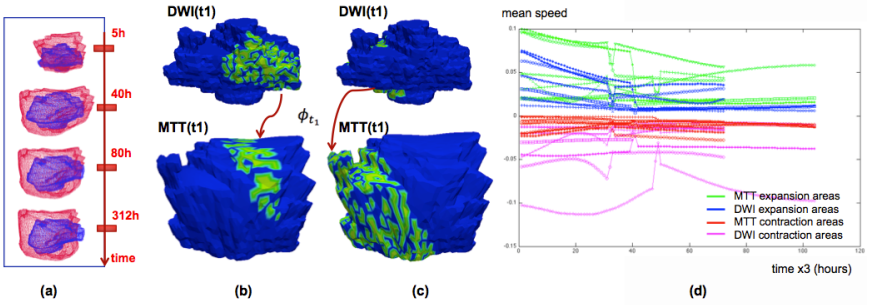

Fig2: *(a) The 4D evolution of the DWI/MTT mismatch. (b) Detection of high contraction (vs. expansion in (c)) areas in DWI lesion at t1 and spatially mapping them into the MTT lesion at t1.*

References: [1] P.Barber *et al.* Neurology, 51(2):418, 1998. [2] A. Arenillas *et al.* Stroke, vol. 33, pp. 2197-203, Sep 2002. [3] S. Durrleman *et al.* STIA 2010.