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Phase-based metamorphosis of diffusion lesion in relation to perfusion values in acute ischemic stroke

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ABSTRACT

Examining the dynamics of stroke ischemia is limited by the standard use of 2D-volume or voxel-based analysis techniques. Recently developed spatiotemporal models such as the 4D metamorphosis model showed promise for capturing ischemia dynamics. We used a 4D metamorphosis model to evaluate acute ischemic stroke lesion morphology from the acute diffusion-weighted imaging (DWI) to final T2-weighted imaging (T2-w). In 20 representative patients, we metamorphosed the acute lesion to subacute lesion to final infarct. From the DWI lesion deformation maps we identified dynamic lesion areas and examined their association with perfusion values inside and around the lesion edges, blinded to reperfusion status. We then tested the model in ten independent patients from the STroke Imaging Repository (STIR). Perfusion values varied widely between and within patients, and were similar in contracting and expanding DWI areas in many patients in both datasets. In 25% of patients, the perfusion values were higher in DWI-contracting than DWI-expanding areas. A similar wide range of perfusion values and ongoing expansion and contraction of the DWI lesion were seen subacutely. There was more DWI contraction and less expansion in patients who received thrombolysis, although with widely ranging perfusion values that did not differ. 4D metamorphosis modeling shows promise as a method to improve use of multimodal imaging to understand the evolution of acute ischemic tissue towards its fate.

1. Introduction

The change in ischemic stroke lesions from acute presentation to final tissue damage is highly variable between individual patients as seen on magnetic resonance diffusion and perfusion imaging. Following the occlusion of a cerebral artery, ischemic tissue damage is seen as hyperintense on diffusion-weighted imaging (DWI) often within a larger area of hypoperfused at-risk, but potentially reversible tissue ischemia, detectable on perfusion-weighted imaging (PWI). Thereafter the ischemic tissue may grow or diminish depending on known and unknown factors. Subsequent growth of the lesion core, considered to be represented by DWI, is generally attributed to persistently reduced perfusion values around the core, whereas recovery of ischemic tissue is generally attributed to improvement in perfusion (Wardlaw, 2010).

Many imaging studies have investigated stroke lesion evolution mainly using 2D lesion volume or voxel-based analyses, but these may not capture the full spatiotemporal dynamics of perfusion and diffusion lesions as they may under-sample information about the location, direction or magnitude of the lesion dynamics in space and time (Rekik et al., 2012). Recently, we applied 4D shape deformation modeling methods to examine the highly contracting and expanding areas in DWI and PWI lesions (Rekik et al., 2013, 2014).

Of theses methods, the metamorphosis model (Trouvé and Younes, 2005; Younes, 2010; Rekik et al., 2014) handled both multi-component and solitary lesions and incorporated image intensity values from different sequences, and demonstrated elegance and accuracy of deforming the source image into a subsequent image, while tracking, point by point, a) the image intensity values inside and outside the lesion edges and b) the velocity of lesion deformation between timepoints. Notably, the proposed metamorphosis model in (Rekik et al., 2014) could follow ischemic stroke lesion change in perfusion weighted imaging from the acute to final infarct. It enabled to explore the perfusion dynamics in ischemic stroke and their relation to final T2-w lesion outcome (at ≥1 month). However, the role of diffusion weighted imaging, which is fundamental to understanding stroke

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dynamics, was overlooked. In this paper, we aim to investigate diffusion lesion local dynamic changes in relation to perfusion values in the affected hemisphere.

By applying this model to longitudinal images, the present study aims to: (1) model changes in the acute ischemic DWI lesion from the acute timepoint into the final infarct lesion, in both solitary and multi-component lesions; and (2) extract measurements of the most dynamic parts of the lesion to see the most rapid or largest areas of the DWI lesion expansion/contraction areas in relation to PWI values and clinical features such as stroke severity. We tested our model on stroke imaging data acquired in an observational study in one center (Rivers et al., 2006; Kane et al., 2007) and then validated the model in multicenter data obtained from STIR (Ali et al., 2007).

2. Material and methods

2.1. Patient selection

2.1.1. Development dataset

We first applied the metamorphosis model to 20 representative patients from a prospective observational study of MRI in hyperacute stroke (Rivers et al., 2006; Kane et al., 2007). Patients were first imaged <6 h of stroke and represented a typical range of stroke severities (NIHSS, median = 10, IQR: 6–14), ages (74.9 ± 9.2 years), acute DWI lesion volumes (34.6 ± 32.2 cm^3) and mean transit time (MTT) volumes (126.6 ± 102.2 cm^3). None of the 20 patients received rt-PA treatment, thus they represent the natural history of stroke lesion evolution, including any effects of spontaneous reperfusion. We included patients who had DWI images at acute (~5 h) and subacute (~5 ± 1 days) timepoints after stroke, a perfusion mean transit time (MTT) map at least at the acute timepoint, and T2-w lesion at ≥1 month after stroke. All patients had an MTT lesion at the first timepoint but only 12 had an MTT lesion visible at the second timepoint. Twelve patients had multi-component DWI/MTT lesions and eight had solitary lesions.

2.1.2. Exploratory dataset

We selected from STIR the first 10 of 290 potential cases with three MRI scans at acute (<6 h), subacute (5 days) and final (≥1 month). The first 10 patients that met the study criteria (age 59.6 ± 16.4 years, median admission NIHSS of 7 (IQR: 5–12)) had all received standard IV tPA thrombolysis. All had perfusion imaging <6 h but perfusion imaging was included per protocol at subacute (5 days).

2.2. MRI pre-processing

We used the MTT perfusion map as it is easily obtained and generally shows the PWI lesion as large (Rivers et al., 2006; Kane et al., 2007). The modeling was blind to all clinical data and imaging values. Arterial recanalization status and collaterals were not taken into account in the modeling as angiographic data were not available for all patients. STIR exploratory data were processed identically to the derivation data unless stated otherwise. Full details of image acquisition and processing were described previously (Rivers et al., 2006; Luby et al., 2006). We obtained MTT areas from the contralateral hemisphere by mirror reflection of the MTT lesion to the unaffected hemisphere. For each patient, we generated relative MTT (rMTT) lesion maps by dividing the value of each lesion voxel by the mean perfusion value of the contralateral MTT values. The resulting intensity 'rMTT' has no unit. An expert radiologist visually checked that tissue swelling did not distort the DWI lesion boundary.

2.3. Two-image based metamorphosis model

In our previous work (Rekik et al., 2014), we extended the image-to-image metamorphosis into a spatiotemporal metamorphosis that exactly fits the baseline image to subsequent observations in an ordered set $\Im = \{I_0, I_1, \ldots, I_T\}$ of images, which we applied to perfusion data in acute stroke. This model registers one source image to a target image while estimating two optimal evolution paths linking these images: (1) a geometric path encoding the smooth velocity of the deformation of one image into another, and (2) a photometric path representing the variation in image intensity. Both paths characterize the dynamics of the image metamorphosis from the source to the target image in small discrete time and space intervals.

Basically, a baseline image I_0 morphs under the action of a velocity vector field v_t that advects the scalar intensity field I_t (i.e. time-evolving image intensity) (Trouvé and Younes, 2005). Solving the advection equation with a residual allows to estimate both image intensity evolution and the velocity at which it moves.

We estimated the optimal metamorphosis path (I_t, I_v starting at I_0, while constraining it to smoothly and exactly go through any available intermediate observation, till reaching the final observation I_T. This was achieved through minimizing the following cost functional U using a standard alternating steepest gradient descent algorithm (Rekik et al., 2014):

$$U(I,v) = \int_0^T \left|vt\right|_V^2 d\,t + \frac{1}{\sigma^2}\int_0^T \left|\frac{dI(t)}{dt} + \nabla I_t.v_t\right|_{L^2}^2 dt$$

σ weighs the trade-off between the deformation smoothness (first term) and fidelity-to-data (second term). The term ∇I_t. v_t represents the spatial variation of the moving image I_t in the direction v_t. Furthermore, the moving intensity scalar field I_t is defined under the action of the diffeomorphism (invertible smooth mapping) ϕ_t on a baseline image $I_0 : I_t = \phi_t . I_0$. We associated to the action ϕ a velocity v that satisfies the flow equation rooted in the in-vogue large deformation diffeomorphic metric (LDDMM) framework (Trouvé, 1998):

$$\begin{cases} \frac{d_{\phi t}}{dt} = v(\phi_t(x)), \quad t \in [0;T] \\ \phi_0(x) = x \end{cases}.$$

In the present study, we used the estimated velocity vector field v_t to estimate the total DWI lesion deformation map in two phases.

1) In the first phase, we morphed acute (<6 h) DWI lesion to subacute (~5 days) DWI lesion in 20 patients; and
2) In the second phase, we morphed the subacute (~5 days) DWI lesion into the final T2-w (≥1 month) in the 12/20 patients with subacute perfusion imaging. Retaining these two distinct phases, 'acute to subacute' and 'subacute to final', facilitated testing of acute separately from subacute clinical information against the lesion parameters.

2.4. Extracting highly dynamic regions of DWI lesion

For both phases, in each patient, we generated a total 3D lesion deformation map, computed as the squared sum of the estimated speed along the metamorphosis path, and identified contracting and expanding DWI regions (as the 'negative' and 'positive' deformation values respectively) during each phase (Fig. 1). In the exploratory dataset (STIR), we were only able to estimate the acute to subacute phases since subacute perfusion imaging was not available for all 10 patients. We then automatically thresholded the two total metamorphosis deformation maps generated for the acute-subacute and subacute-late phases of DWI lesion evolution to compute the proportion by volume of the total DWI lesion boundary that was rapidly contracting or expanding for the acute-subacute and subacute-late phases.

2.5. rMTT values relation to DWI lesion dynamics

For each patient, for both phases, for every rMTT voxel value within the acute perfusion image we computed the mean amount of DWI