Automated Stroke Disability Prediction and Mismatch Analysis by Employing Lesion Topography and Statistical Models

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INTRODUCTION — DWI and PWI have been demonstrated to be reliable surrogate imaging markers for infarct core and salvageable, but at-risk, tissue in acute stroke patients. Here, a substantial mismatch between infarct core and at-risk tissue predicts a favorable outcome if tissue is successfully reperfused, whereas either large DWI or PWI lesions represent a malignant profile and indicate that patients will most likely sustain harmful reperfusion injuries [1]. Thus far, imaging-based prediction of clinical outcome has been primarily on overall lesion size (e.g., malignant profile) or *volumetric mismatch* between stroke core and critically hypoperfused tissue. Volumetric mismatch neglects the impact of lesion topography on clinical disability. It is well known that stroke lesions at certain locations contribute more to disability than others. Here, we use a novel approach that employs *importance-weighting* to the mismatch analysis, where brain voxels contribute more or less to the scoring metric, based on their location and relative contribution to disability-based population statistics.

METHODS — Another way to look at mismatch between stroke core and at-risk tissue is the difference between lesion severity caused by at-risk tissue, S_{ART}, and stroke core, S_{CORE}, i.e., $\Delta S = S_{ART}\text{-}S_{CORE}$. We define severity, S, as the sum of all affected voxels (either core or at-risk tissue), each weighted by a local factor, $\omega(\mathbf{r})$, and reflecting the relative importance of a particular lesion voxel, L, at location, $\mathbf{r}=[x, y, z]^T$, to the overall disability, i.e., $S=\Sigma\{\omega(\mathbf{r}_i)\cdot L(\mathbf{r}_i)\}$. Note that summation is over all $i=1\ldots N_{voxels}$, where N_{voxels} is the number of brain voxel, and $L(\mathbf{r})$ is either "1" (lesion) or "0" (normal). Regular *volume mismatch* (VMM) can be computed with this approach in a similar fashion by assigning equal weights to each voxel, i.e. $\omega(\mathbf{r})$=const, while for the new *topography-weighted mismatch* (TWMM) the weights $\omega(\mathbf{r})$ vary depending on the relative importance of a specific brain region to the overall functional deficit. To derive $\omega(\mathbf{r})$, we built a statistical model [2], (i.e., stroke atlas) that combined existing non-linearly co-registered (to MINC atlas) and manually segmented day-5 FLAIR imaging data with day-5 NIHSS scores from a large acute stroke data repository comprising of data from 44 acute stroke patients from the NIH-funded DEFUSE trial (1). Here, we averaged over all existing $j=1\ldots M$ patients so that the weighting coefficients were: $\omega(\mathbf{r}_i)=M^{-1}\Sigma\{L_j(\mathbf{r}_i)\cdot NIHSS_j/LV_j\}$, where $NIHSS_j$ and LV_j are the disability score and lesion volume for the j-th patient, respectively, and the summation is over all j patients.

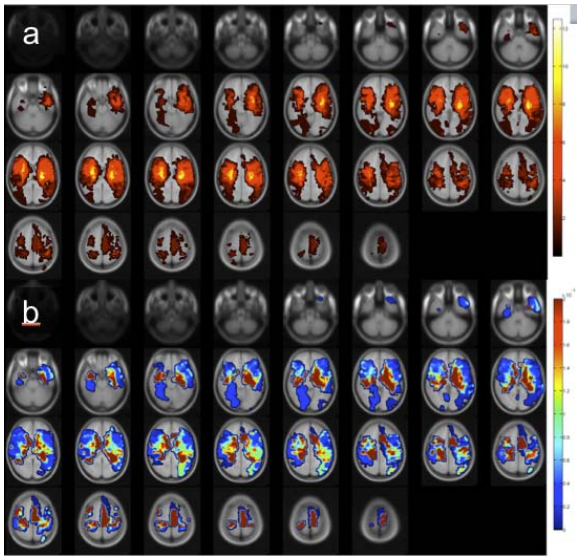

Fig. 1 *– (a) Regional strokes incidence. (b) Atlas reflecting how much an affected brain contributes to the total NIHSS.*

RESULTS — Figure 1a shows the stroke incidence on a per-voxel basis derived from 44 acute stroke patients in atlas space. Since DEFUSE enrolled mostly MCA strokes, the counts in the ACA territory and the posterior circulation were relatively sparse. Consequently, only contributions from the MCA to the final NIHSS could be reliably predicted. Both hemispheres had very similar stroke incidence rates for the MCA territory. Figure 1b shows the corresponding relative contributions of individual voxels to the final NIHSS in the normalized space. Of note in Fig.1b is the considerable hemispheric asymmetry of the spatial weight distributions. The latter is due mostly to the composition of the NIHSS, which accounts more points to the dominant hemisphere. Thus, lesions in the dominant hemisphere contribute more to disability than lesions in the non-dominant hemisphere. Using leave-one-out analysis, Fig. 2 shows the relationship between the topographically-weighted severity mismatch (i.e., predicted NIHSS) and the true NIHSS, which demonstrates high correlation.

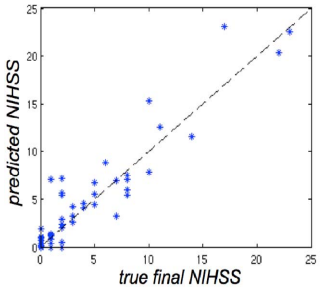

Fig. 2 *– Relationship between true final NIHSS in 44 patients and the predicted NIHSS using the FLAIR images and the atlas-based weights.*

DISCUSSION – The results from this pilot study demonstrate already very encouraging results that suggest the feasibility of automated processing of acute stroke disability scores. Currently, our atlas is limited to MCA territories. ACA and posterior territory strokes warrant more data to reliably determine NIHSS contributions from these vascular territories. Most striking was the hemispheric difference and the regionally localized contributions to NIHSS. Due to brain plasticity, NIHSS in patients with substantial pre-existing brain damage will most likely correlate less with lesion size or location. Thus, only "first-time" stroke patients without preexisting brain damage should be included in the construction of the atlas as well as for subsequent validation of this pilot study. Moreover, NIHSS is a composite score and tests several subcategories (e.g., visual, auditory, or sensoric capacity) on an ordinal scale. Thus, lesions in different brain regions can end up with the same overall NIHSS, which will be addressed in future work by regionally subcategorizing the atlas. Previous work on stroke atlases has been focusing ASPECT-derived scores [3] or on expert-based predetermined regions [4]. Our approach is a population-averaged variant of the data-driven method (#2) in [4] applied to a selected acute stroke population.

CONCLUSION — A new topographically weighted score for mismatch analysis has been introduced that considers not only volume but also the location of a stroke lesion. In a leave-one-out analysis it could be shown that an atlas built on this scoring metric can predict individual NIHSS very reliably. By reducing mismatch to a (NIHSS) disability score, automatic stroke triage based on well-known metrics by stroke neurologists can be used.

References [1] Albers GW *et al*., *Ann Neurol* 2006; 60: 508-517; [2] Friston KJ, *et al*., *HBM* 1995; 2:165-189; [3] Kosior RK *et al*., *Stroke* 2010; 41:455-460; Menezes NM *et al*., *Stroke* 2007; 38:194-197. – **Acknowledgements** 5R01EB002711, 5R01EB008706, 3R01EB008706, 5R01EB006526, 5R21EB006860, 2P41RR009784, 2R01NS39325.