Software Solution For Automated Assessment of DWI/PWI Mismatch In Acute Stroke Patients: the RAPID MISMATCH

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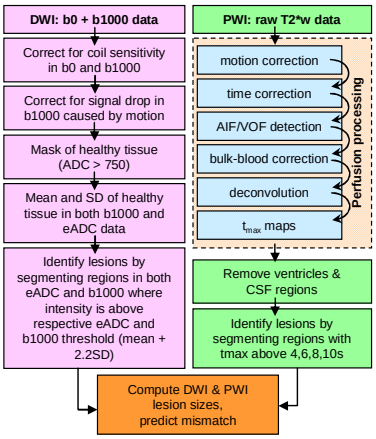

Fig.1. Processing of DWI and PWI data for mismatch analysis

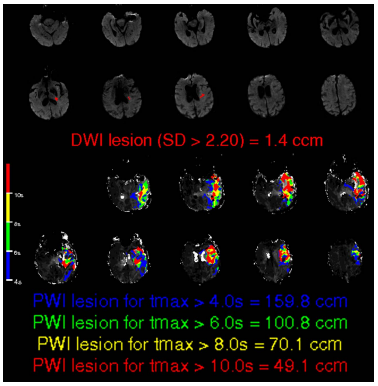

Fig.2. Typical result of mismatch evaluation in RAPID MISMATCH

PURPOSE: Diffusion/perfusion mismatch has long been viewed as a method for identification of acute stroke patients who are most likely to benefit from reperfusion therapies. However, application of this method in routine clinical care has been limited by the unacceptably long times needed to process perfusion maps manually and outline lesions on the PWI and DWI maps. To provide mismatch information within the limited time window available in acute stroke care, we aimed to develop a fully automated system (dubbed the RAPID MISMATCH) that: 1) will deliver estimates of DWI and PWI lesion volumes without human operator supervision; 2) will be linked to MR scanners and provide mismatch maps in 'real-time'; and 3) can be used as a reference implementation in multi-center trials for retrospective mismatch analyses.

METHODS: RAPID MISMATCH is an in-house developed research software application, consisting of perfusion and mismatch analysis modules. It is written in C++, runs under Linux and uses multi-threaded implementation to speed-up the data processing. The DWI/PWI mismatch analysis is based on comparing lesion sizes on diffusion data and PWI t_{max} maps. The t_{max} map which represents the time in which the perfusion residue function reaches its maximum is a good surrogate for the arterio-tissue delay and was shown to be a very sensitive parameter in diagnosing acute stroke [1]. To identify precisely and reliably the lesion volumes based on DWI and PWI data, we designed a processing pipeline shown in Fig. 1. For DWI, the lesions are identified in both eADC and b1000 data to reject regions with susceptibility pile-up and T2 shine-through artifacts. The threshold to segment the hyperintense lesions in the b1000 and eADC images is selected as $th_x = \mu_x + k_x\sigma_x$ (where $X \in$ {b1000, eADC}, μ_x is mean intensity value of the healthy tissue regions in X, σ_x is standard deviation of intensities therein) and we have chosen empirically $k_{b1000}=2.2$ and $k_{eADC} = 2.4$. Regions with $ADC > 750$ are used as a surrogate for the healthy tissue. For PWI lesion assessment, first the perfusion parameter maps are computed using the PWI pipeline shown in Fig. 1. The acquired PWI data are corrected for motion and varying slice acquisition time. Then, arterial input- (AIF) and venous output (VOF) functions are selected using a dedicated algorithm, followed by bulk-blood correction [2]. Quantitative perfusion maps (CBV, CBF, MTT, t_{max}) are obtained by deconvolving the tissue signals with the AIF. The delay-invariant frequency-domain deconvolution is regularized using optimal Wiener filter [3]. Next, the ventricles are removed by thresholding and considering the difference of signal intensities between the first non-steady-state and steady-state phases in the raw PWI data. The t_{max} lesions are segmented using thresholds $t_{max} > y$, where $y \in \{4s, 6s, 8s, 10s\}$. Finally, a PWI/DWI mismatch ratio is computed. A positive mismatch is predicted when 1) the difference between t_{max} and DWI lesions is at least 10 cm^3 and 2) simultaneously, the difference is at least 20% larger than the DWI lesion itself [1]. To analyze the robustness and performance of the above described approach, a large database of acute stroke cases from the DEFUSE study [1] was processed. The database consists of pre-treatment and post-treatment scans (74 patients, 32 male/42 female, age 32-92), acquired among multiple centers in the years 2001-05 with various acquisition parameters for DWI (EPI sequences, TR=3-6s, TE=71-133ms, resolution 128x128–256x256, slice thickness 5-7mm/gap 0-2mm, b=1000mm/s^2) and PWI (GRE-EPI sequences, TR=1.44-2s, TE=41-60ms, resolution 128x128–256x256, slice thickness 5-12mm/gap 0-2mm, flip angle 60°-90°) using stock Siemens, General Electric and Philips scanners. The DWI and PWI lesions in the data-base were previously segmented by a trained stroke neurologist [1] and were reprocessed using the computerized approach for this study. The sizes of identified lesions (for DWI and $t_{max} \in \{6s, 8s\}$) between manual and computerized readers were compared and the agreement in identification of mismatch cases between the two techniques was assessed. Within this data base, a subset of 'good' cases (N=20), that allowed automatic removal of ventricles by the program, were selected to mimic an optimized data acquisition (see conclusion section).

	'Good' DWI	All DWI	'Good' t_{max}>6s	All t_{max}>6s	'Good' t_{max}>8s	All t_{max}>8s
Correlation	0.92	0.92	0.81	0.68	0.9	0.77
Regress. slope	0.7	0.71	1.42	1.05	1.24	0.97

Tab.1. Correlation between manual and automated estimation of lesion size in DWI/PWI mismatch

RESULTS: The RAPID software runs on a dedicated machine within the hospital network, is linked to the scanners with a standardized DICOM connection and thus is seamlessly integrated with equipment used in routine work. A typical processing time for generation of PWI and DWI maps and mismatch analysis was 3.5 min (2.5 min for perfusion maps, 1 min for mismatch analysis) on an Intel Pentium Xeon 1.6GHz CPU. Within the 2.5 min spent for PWI processing, a large portion (~90%) of the overall time was used for motion correction. Tab.1 summarizes correlation and regression line slopes in the processed data. This demonstrates overall good agreement between the human and computerized readings in all cases. In the 'good' subset, the correlation of lesion sizes is better than when all data were analyzed. This is because t_{max} lesion size identification can be confounded if ventricle regions can not be removed. The latter was the case for PWI scans from sites that discarded the initial transition phase into steady-state, which otherwise facilitated segmentation. This is also the reason segmentation consistently delivers better results for DWI, as can be seen in the Tab.1. The 'good' subset statistics indicate substantial agreement between the methods: $\kappa = 0.68$, the readers agreed in 17 cases (11 positive and 6 negative cases) and disagreed in 3.

CONCLUSION: We have developed and tested a fully automated software aimed at assessment of mismatch in acute stroke cases. The software runs on a dedicated machine within the hospital network, is linked to the scanners with a standardized DICOM connection, and thus is seamlessly integrated with equipment used in routine work. The DWI, PWI and mismatch results are presented to the clinicians as images on the MR scanner and on PACS for easy and rapid interpretation. The processing is sufficiently fast to deliver the important perfusion and mismatch information in less than 5 minutes after the scan protocol is finished. The quantitative evaluation showed substantial agreement between the human and computerized readers both in correlation of the outlined lesion sizes and mismatch prediction. The existing discrepancies need to be assigned to differences in interpretation of the data. In DWI, the algorithm identifies the lesions predominantly in eADC images, whereas the human reader relied mainly on the b1000 data. Due to presence of old strokes and T2 shine-through artifacts, the lesions on b1000 might appear larger - the automated approach tends to consistently deliver estimates of lesion sizes that are ~30% smaller than those from manual readings. In PWI, the major difference lies in capability of the software to remove ventricle regions. This identification is currently based on thresholding and analysis of the signal decay in the first few non-steady state time points of the PWI data. Depending on the scanner setup (number of disabled acquisitions) and used TR/TE combination, the data might not manifest sufficiently large difference between tissue and CSF - and the ventricle identification then fails. While this posed a problem in processing of the previously acquired DEFUSE data, it is easily adjusted in future scans. We conclude that the presented system (with necessary adjustments on the MR scanners linked to the RAPID processing system) has sufficient robustness and sensitivity to identify mismatch cases in clinical routine - and thus potential to significantly improve patient care in acute stroke cases.

ACKNOWLEDGEMENTS: This work was supported in part by the NIH (2R01EB002711, 1R01EB008706, 1R21EB006860), the Center of Advanced MR Technology at Stanford (P41RR09784), the Lucas foundation and the Oak foundation. **REFERENCES: [1]** Albers, GW et al.: Ann Neurol. 2006 Nov;60(5):508-1, 7; **[2]** Kjølby, BF et al.: Magn Reson Med. 2006 Jul;56(1):187-97 **[3]** Gobbel, GT et al.: Phys Med Biol. 1994 Nov;39(11):1833-54