Correlation of acute perfusion lesion volumes with neurological deficits depends on deconvolution algorithm

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Introduction: Mismatches between perfusion-weighted (PWI) and diffusion-weighted MRI (DWI) lesions in acute stroke patients have been assumed to be surrogates for salvageable tissue. Recent acute stroke trials have used DWI and PWI as a patient selection criteria [1, 2] under the assumption that this "mismatch" can identify patients with potentially salvageable tissue who may be most likely to benefit from therapy. However, degrees of these mismatches have been shown to be dependent on the choice of perfusion metric [3]. Previously, performances of different PWI algorithms were evaluated on the basis of how well they predicted the final infarct volume [4]. This may not be an optimal method since "salvaged" tissue may have been originally oligemic but not truly ischemic. Furthermore, most stroke patients receive some therapy that can alter the natural history of initially ischemic tissue. It has been proposed that the perfusion parameter that best correlates to acute clinical deficits most accurately reflects critically hypoperfused tissue [5]. We extend this approach for comparing deconvolution techniques. We evaluate different PWI algorithms and parametric maps and compare lesion volumes with respect to acute and follow-up clinical outcome scores.

Patients and Methods: A consecutive series of acute stroke patients who received DWI and PWI<12h of stroke onset (N=163) was retrospectively studied. Patients were excluded if they exhibited bilateral acute infarcts, unavailable admission NIH Stroke Scale scores (NIHSSS) or poor quality PWI raw data. PWI maps were calculated by deconvolution using standard truncated singular value decomposition (sSVD) [6] and tracer-arrival insensitive circular deconvolution with oscillation-index regularization (oSVD) [7]. PWI maps were calculated using sSVD and oSVD with automatically selected arterial input functions (AIF) [8]. MTT maps were calculated as the ratio of CBV/CBF. Tmax maps were measured as the peak time of the residue function. Lesion volumes on apparent diffusion coefficient (ADC) maps were automatically delineated as regions <80% of contralateral white matter. MTT and Tmax lesions were automatically demarcated as tissue > 2 SD from mean contralateral white matter values, and then manually adjusted to exclude artifacts by two independent readers. The average of the lesions were compared (ANOVA, with post-hoc SNK test) and then correlated with acute NIHSSS, follow-up (F/u) lesion volumes at >=5 days after stroke onset and 90 day clinical outcome scores (modified Rankin Score or NIHSSS) if available (Pearson's product-moment correlation). F/u analysis was performed only in patients not given thrombolytic or catheter-based therapy or enrolled in clinical trials.

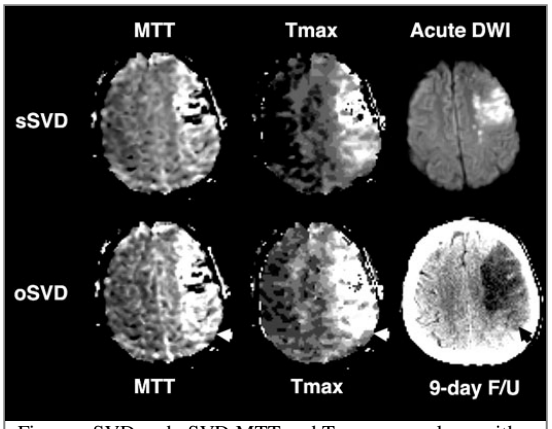

Figure: sSVD and oSVD MTT and Tmax maps along with acute DWI and 9 day F/u exam for 57 y.o male imaged <7h from stroke onset and NIH SSS=15. Lesions on F/u correspond best with those on oSVD MTT and Tmax maps.

Results: We analyzed 144 patients. Median acute NIHSSS was 6, interquartile range (IQR) 3–11. Onset-to-MRI time was 4.7±2.3 h, Median age was 72 (IQR: 55–80). 76 of the 144 patients were left-sided strokes and 83/144 were male patients. 26 received rt-PA prior to imaging. 29 had F/u lesion volumes, 92 patients had 3 month mRS scores (median 2) while 49 patients had follow-up NIHSS scores (median 1). ADC lesion volumes were 11±21 cm^3. sSVD calculated MTT (67±73 cm^3) and Tmax (71±78 cm^3) lesion volumes were significantly larger (P<0.001) than oSVD MTT (58±65 cm^3) and Tmax (62±68 cm^3) lesions. Lesion volumes were significantly correlated with acute NIHSSS (see Table), with oSVD Tmax having the greatest coefficient (P<0.01) and sSVD MTT having the lowest (P<0.05). oSVD lesions were significantly correlated with F/u lesion volumes, but not sSVD (see Figure). oSVD MTT maps had the greatest correlation coefficient (P≤0.01) with F/u. All lesions volumes were significantly correlated with clinical outcome scores at 90-day.

Table: Correlation of acute PWI lesion volumes as functions of deconvolution technique and parametric map

	sSVD		oSVD	
	MTT	Tmax	MTT	Tmax
Acute NIHSSS (N=144)	R=0.49 P<0.001	R=0.56 P<0.001	R=0.55 P<0.001	R=0.62 P<0.001
F/u Lesion (N=29)	R=0.29 P=0.13	R=0.36 P=0.06	R=0.57 P=0.001	R=0.45 P=0.01
90 day mRS (N=85)	R=0.30 P=0.006	R=0.35 P=0.001	R=0.35 P<0.001	R=0.39 P<0.001
90 day NIHSSS (N=49)	R=0.52 P<0.001	R=0.57 P<0.001	R=0.57 P<0.001	R=0.60 P<0.001

Discussion: Our results indicate that PWI maps correlate well with acute neurologic impairment scores, consistent with previous studies [9]. However, PWI maps generated using oSVD techniques correlate better with acute neurological deficits and clinical and imaging outcomes than results using sSVD techniques. Decoupling delay from perfusion estimates and using both maps for patient assessment will likely provide greater insight into stroke evolution and expected clinical and tissue outcome than either separately. Of the two PWI parametric maps that we examined in this study, our results suggest that acute stroke severity and clinical outcome correlate best with acute Tmax lesions. In patients not given interventional therapy, F/u infarct volumes correlated best with acute MTT lesions. We speculate that Tmax maps may be a reflection of collateralization that may encompass regions with delayed but not ischemic flow [10], while MTT maps represent tissue at greatest immediate risk of infarction.

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