Comparative Assessment of SAGE and GRE DSC Perfusion: Initial Assessment in a Stroke Cohort

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TARGET AUDIENCE: Physicists and clinicians interested in perfusion imaging and cerebrovascular disease.

PURPOSE: Dynamic susceptibility contrast (DSC) perfusion-weighted imaging (PWI) with a combined spin- and gradient-echo (SAGE) EPI sequence has demonstrated considerable benefits over conventional single-echo spin-echo or gradient-echo DSC [1-2]; because multiple (4) gradient echoes are obtained with SAGE, true T_2*-decay can be calculated, allowing correction for confounding T_1-effects; the spin-echo component provides information about capillary perfusion, which in combination with the large-vessel sensitivity of the gradient-echo component allows differentiation of small-*vs*-large vessel contributions in brain tumors and regions with potential capillary shunting. Despite the obvious benefits of using SAGE, studies, including stroke trials, have used only conventional single-echo gradient-echo (GRE) DSC PWI, and mismatch criteria are based on these data. Theoretically, the second gradient-echo of SAGE (with a TE of 35 ms) is comparable to conventional single-echo gradient-echo (GRE) DSC PWI, and offers direct backward compatibility to previous trial data (which is necessary for comparing the outcomes of a trial using SAGE with previous trials). *The purpose of this work* is to investigate the comparability between the 2nd gradient echo of SAGE and conventional GRE DSC PWI in patients with suspected stroke, in particular whether slight differences in scan parameters (e.g. matrix size, use of parallel imaging, *etc.*) between SAGE and GRE DSC PWI have a significant qualitative or quantitative diagnostic impact.

METHODS: All MRI scanning was performed on a clinical inpatient 3T unit (Discovery MR750w, GE Healthcare, Waukesha, WI) using either an 8-channel head-array or a neurovascular array. Scan parameters were as follows: (i) *GRE-DSC PWI:* Single-shot GRE EPI, TR/TE=1,800/35ms, 60 time points, 14 slices, FOV=24cm, 6mm/2mm gap, flip angle=80º, matrix=96x128, and ASSET x2. (ii) *SAGE-DSC PWI:* same scan parameters but matrix 84x84, GRAPPA x3, TE_1=17ms, TE_2=35ms, TE_3=65ms, TE_4=84ms, and spin-echo TE (TE_{SE})=103ms. The time series of the second GRE (TE_2) was used for further processing. *Postprocessing:* An FDA-approved software (RAPID 4.5, iSchemaView, Menlo Park, CA) was used to compute hemodynamic parameter maps, threshold ADC and Tmax images for subsequent diffusion-perfusion mismatch analysis, and calculate the DWI positive and Tmax(>6s) lesion volumes [3]. *Human Subjects:* A total of 53 consecutive patients presenting to our emergency department or stroke service with stroke-like symptoms underwent MRI for this IRB-approved study. In addition to the conventional stroke imaging protocol (which included DWI, GRE, TOF-MRA and GRE-DSC PWI), SAGE DSC PWI was acquired. To avoid increasing the total injected dose, a ½ standard dose of MultiHance (Bracco, Melville, NY) was administered (flow rate of 4-5ml/sec followed by a 25ml saline flush) for each PWI scan. In 5 patients, the order of GRE-DSC and SAGE PWI was reversed to investigate potential effects of contrast pre-dosing *Image analysis:* An experienced neuroradiologist, blinded to the image acquisition technique, reviewed SAGE 2nd echo images side-by-side with GRE DSC PWI images (CBV, CBF and Tmax maps and the raw data). Overall image quality, subjective SNR and subjective CNR were rated (equal; SAGE better; or GRE DSC PWI better). The Tmax (>6s) volumes (in mL) calculated by RAPID 4.5 were recorded, and regression analysis performed using Microsoft Excel 14.2.0 (Microsoft Corporation, 2010).

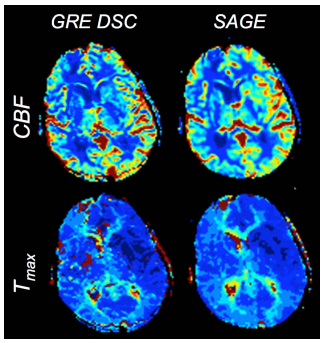

***Fig. 1** – Comparison of SAGE (right) and GRE DSC PWI CBF (top) and T_{max} (bottom) maps. SAGE shows better image quality and CNR of parameter maps.*

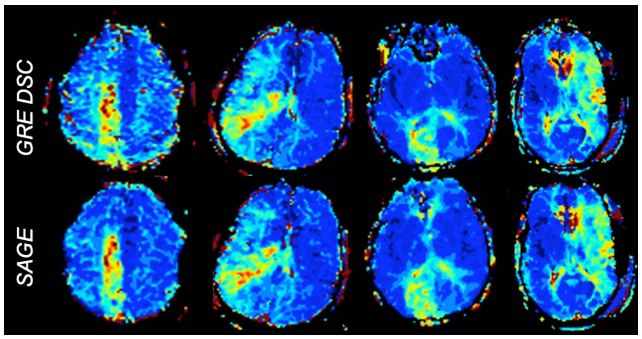

***Fig. 2** – Comparison of SAGE (bottom) and GRE DSC PWI (top) T_{max} maps in 4 stroke patients. GRE DSC Tmax maps appear slightly noisier but the T_{max} lesions are virtually identical and of similar conspicuity.*

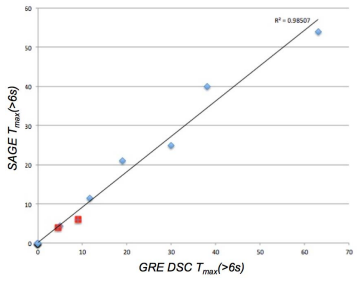

***Fig3** – Correlation between GRE DSC vs SAGE Tmax(>6s) volumes.*

RESULTS: Subjective overall image quality, subjective SNR and subjective CNR (CBV, CBF, Tmax, raw images) were superior or equivalent for SAGE than GRE DSC PWI (**Fig. 1**). 22 out of 53 had a positive finding of stroke (21 subacute, 1 chronic). Of these, Tmax(>6s) lesions were found in 10 patients (5 completed infarcts, 5 mismatch cases). Particularly, in the presence of blood products, surgical material or at the base of the brain, SAGE performed better than conventional GRE DSC. Major discordance between SAGE and GRE DSC Tmax(>6s) measurements can be mostly attributed to patient motion (1 SAGE, 2 SAGE & GRE DSC) or other technical errors such as failed bolus administration (1 SAGE, 1 SAGE & GRE DSC). **Fig 2** shows strong agreement between SAGE and GRE DSC PWI. After excluding discordant cases, **Fig 3** shows the correlation analysis for all stroke cases with a Tmax(>6s) (R^2=0.98507). There was no difference in image quality ratings or quantitative maps when the order of SAGE and GRE DSC PWI acquisition was reversed.

DISCUSSION AND CONCLUSION: After elimination of non-diagnostic 5 studies (due to either patient motion or technical errors), the parameter maps and raw images of SAGE were found to be of higher quality than GRE DSC PWI data from the same patient, regardless of the order in which they were acquired. Regarding accuracy, the computation of *tissue-at-risk*, represented by Tmax(>6s), yielded essentially the same results for both methods. In the 5 mismatch cases, both and GRE DSC PWI yielded the same mismatch classification: a target mismatch (mismatch ratio > 1.8, mismatch volume > 15 ml) in 3 patients and a non-target mismatch ratio in 2. The order in which SAGE or GRE DSC PWI was acquired had no impact on our results. This is likely attributable to the fact that extravasation in this population was a non-issue. Moreover, the baseline SNR for PWI scans at 3T was very high (>100), and both pre-dosing and the use of parallel imaging had very little effect on quality and parameter maps. The major source of error in PWI studies related to patient motion and technical factors (variability or failure of bolus injection), EPI ghost calibration, or parallel imaging calibration. Of note, even a ½ dose injection was sufficient at 3T to achieve high quality perfusion parameter maps; this warrants further investigation, given the applicability in elderly patients with impaired renal function. In conclusion, the 2nd gradient-echo of SAGE – when matching scan parameters are chosen – yields comparable results to conventional GRE DSC and therefore permits calibration of multi-echo SAGE data with conventional single-echo GRE DSC data, and the postprocessing algorithms optimized through clinical trials (e.g. DEFUSE [4]) to be used with SAGE data.

ACKNOWLEDGMENTS: The authors acknowledge the following sources of funding for this work: NIH R01EB2711. **REFERENCES:** [1] Schmiedeskamp et al. *MRM* 2012;68:30-40; [2] Schmiedeskamp et al. *JCBFM* 2013;33:732-43; [3] Straka et al. *JMRI* 2010;32:1024-37; [4] Albers et al. *Ann Neurol* 2006;60:508-17.