Optimizing Repeatability of Independent Component Analysis applied to Dynamic Susceptibility Contrast MRI in 68 Brain Tumor Patients with Five Repeated Scans.

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Target Audience: Scientists and clinicians interested in brain perfusion modeling.

Purpose Independent component analysis (ICA) is an emerging technique in functional MRI (fMRI) data processing. ICA takes a data-driven, multivariate approach to voxel categorization based on temporal response patterns. Dynamic susceptibility contrast (DSC) data is acquired similar to fMRI acquisitions but during a rapid injection of contrast agent. As such, DSC data provides an additional platform to perform ICA. Previous studies have demonstrated the utility of ICA-DSC in studies of brain tumors[1,2]. In addition, ICA has shown the ability to separate brain vasculature into arterial and venous components[2], however, it remains unclear what number of components modeled results in the greatest repeatability of these components across multiple imaging sessions. This study explores the relationship between the number of components modeled and the repeatability of arterial and venous component mapping.

Methods *Patient Population* Sixty-eight patients with repeat imaging acquired as a part of brain cancer therapy follow-up were retrospectively analyzed for this study. Patients had 5 imaging sessions on one of three clinical scanners at our Institution. Twenty-nine patients had five imaging sessions on a 3T Siemens Verio scanner (Siemens, Malvern, PA), four patients had five imaging sessions on a 1.5T GE Optima MR450w scanner, and 35 patients had five sessions on a 1.5T GE Signa scanner (GE, Waukesha, WI). Immediately before dynamic imaging for DSC, a 0.05 to 0.1 mmol/kg (pre-load) dose of gadolinium (Gd) contrast agent was administered and clinical post-contrast T1-weighted images were obtained. Single shot gradient-echo echo-planar imaging (GE-EPI) images were acquired during a second 0.15-0.25-mmol/kg bolus injection of Gd injected at a rate of 3 mL/s. Typically, 13 slices of DSC data were acquired with the following parameters: 5mm, skip 1.5mm slice prescription, fat suppression, TE: 30ms, TR: 1s-1.65s, field of view: 220 x 220mm, matrix size: 128 x 128, and voxel size: 1.72x1.72x5mm. Fluid attenuated inversion recovery (FLAIR) and high-resolution spoiled gradient recalled echo (SPGR) images were acquired in all sessions using vendor provided sequences. All images within each session were co-registered to the SPGR, which was then co-registered and resampled to the earliest time point as a baseline. All images were then likewise transformed.

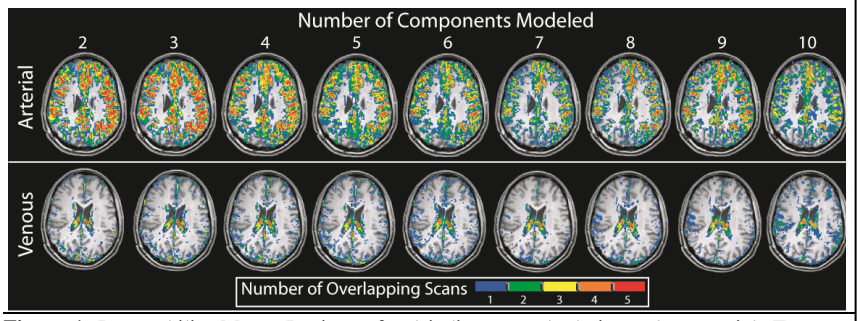

Figure 1. Repeatability Maps Regions of red indicate voxels designated as arterial (Top) or venous (Bottom) in 5/5 imaging sessions compared to the number of ICA components modeled.

ICA Pre-processing of the DSC data consisted of removing the first 4 time points and performing motion correction using MCFLIRT (FMRIB tool library). Data was then processed using probabilistic independent component analysis[3] as implemented in MELODIC (FMRIB tool library). For each patient and each session, 2-10 components were modeled. The resulting components were then visually sorted to determine which best represented the arterial and venous phase of Gd perfusion. Regions of brain tumor related FLAIR abnormality and/or resection cavities were masked from the analysis. The statistically thresholded[3] arterial and venous maps were then binarized and brought into the baseline SPGR space using a nearest neighbor interpolation. Repeatability maps were created to visualize the overlap of each session's arterial and venous components. Voxel values represent the number of sessions (of 5) with components present. An overall repeatability index (RI) was calculated for each number of components modeled for each patient using the equation shown, where N=5, and n_i is the number of voxels overlapping "i" times. The range of RI is between 0 and 1, where 1 indicates perfect repeatability. The RIs were compared across component numbers with a repeated-measures ANOVA corrected with Tukey's multiple comparison test.

$$RI = \frac{1}{(N-1)}\left(\frac{\sum_{i=1}^{N} i n_i}{\sum_{i=1}^{N} n_i} - 1\right)$$

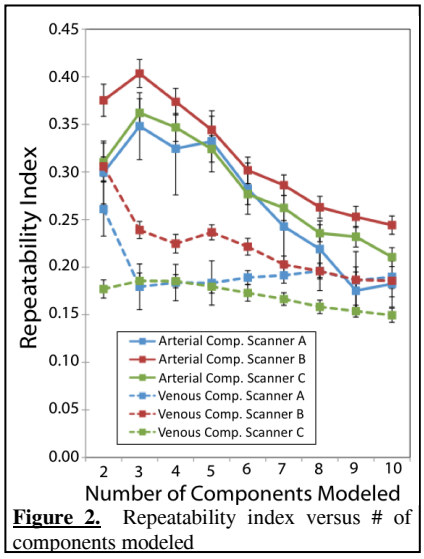

Figure 2. Repeatability index versus # of components modeled

Results Figure 1 shows the arterial and venous repeatability maps for a representative patient. The peak repeatability (i.e. the largest number of red voxels) empirically appears to occur at the lower numbers of components modeled for both the arterial and venous components. Plotting the mean RI for each scanner (Figure 2) revealed that the arterial RI peaked when 3 components were modeled (RI = 0.39), which proved to be significantly different than 4-10 modeled components ($p<0.001$). The mean venous RI peaked at two components modeled (RI = 0.27), which was significantly different than all other iterations ($p<0.001$), while the venous RI for three components modeled was significantly greater than 7-10 ($p<0.01$).

Discussion This study demonstrates that arterial and venous phases of DSC perfusion mapped with ICA are highly repeatable in patients across time. The maximal arterial RI occurred when three components were modeled, while the maximal venous RI occurred with two components modeled. There are disadvantages to only modeling two components, however. For example, large sources of variance, such as patient movement and scanner artifacts, require modeling. Selecting only two components forces voxels into either arterial or venous categories and doesn't allow for an additional noise component.

Conclusion Modeling three ICA-DSC components results in highly repeatable arterial and venous maps of the human brain.

References **1.** LaViolette, P.S., et al. *Proc ISMRM, Montreal Quebec* (2011). **2.** LaViolette, P.S., et al. *Proc ISMRM, Melbourne, Australia* (2012). **3.** Beckmann, C.F. & Smith, *IEEE Trans Med Imaging* **23**, 137-152 (2004).

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