Changes in Cerebral Blood Flow During Bolus Normal Saline Infusion after Ischemic Stroke

Online Supplement

Supplemental Methods:

Relative changes in cerebral blood flow were estimated for each subject, from measured DCS intensity autocorrelation functions at two source-detector separations. In particular, a 'two-layer' photon diffusion model was used in the analysis, to remove the effect of blood flow changes in superficial tissues (e.g., scalp/skull), and to increase sensitivity to cerebral tissues. The fiber optic probe used for the study facilitates measurements of DCS intensity autocorrelation functions at two source-detector separations that correspond to slightly different tissue sampling volumes. Here, the 1.0 cm source-detector separation primarily samples blood flow changes in the scalp and superficial blood vessels (extra-cerebral layer), while the 2.5 cm source-detector separation samples blood flow changes from both the extra-cerebral layer and cerebral tissues (cerebral layer).

An important pre-processing step concerns the removal of motion artifacts – typically caused by patient coughing (severe artifacts), moving head position (minor artifacts) and talking (minor artifacts). First, a preliminary measure of the blood flow index was estimated by fitting the DCS intensity autocorrelation function to a single layer semi-infinite light diffusion equation.[1-3] Next, the localized temporal variance in time series of cerebral blood flow was estimated as the standard deviation of CBF values within a 15-point moving window. Time points with local standard deviation over twice that of the average overall variance (i.e., over the entire measurement session) were identified to be due to motion artifacts, and raw data (intensity autocorrelation functions) corresponding to these time points were removed.[4] Finally, spline interpolation was performed to recover raw intensity autocorrelation functions removed due to motion artifacts, at both 1.0 and 2.5 cm source detector separations.

Post motion artifact correction, intensity autocorrelation functions at 1.0 and 2.5 cm source detector separations were processed together to estimate changes in cerebral blood flow. We used the modified

Beer Lambert law for flow, adapted for a two-layer tissue photon diffusion model, to account for and remove the influence of blood flow changes in the scalp (extra-cerebral layer).[5, 6] Briefly, the two-layer modified Beer-Lambert law approach expresses the *change* in DCS intensity autocorrelation function (i.e., from a baseline condition), as a linear combination of blood flow changes in the cerebral (rCBF) and extra-cerebral layers. The corresponding weighting/calibration factors were analytically computed with assumed values of tissue absorption and scattering coefficients (0.1 cm^{-1}, and 8 cm^{-1} respectively), and the thickness of the extra-cerebral layer (assumed to be 1.2 cm, based on literature).[6-8] We have previously employed such an approach to reduce extra-cerebral flow artifacts to measure flow changes during functional activation, and to characterize cerebral autoregulation.[6, 8] Relative CBF (rCBF) time courses were then averaged/'binned' to 15 second intervals to smooth the data. As a final post processing step, rCBF measurements that were less than -100% or greater than 250% were considered non-physiologic, and were removed to reduce potential bias from measurement error. This correction affected 1% of the measured CBF values.

Supplemental Table 1. Reasons for exclusion from the analysis

Subject	Reason for Exclusion
1-8	Old probe design, data not directly comparable to data collected on subsequent subjects
10	Head of bed changed during measurement, due to coughing.
13	Transient altered mental status during monitoring. Session halted for clinical evaluation.
27	Unacceptably low DCS signal
39	Poor data quality due to excessive motion artifacts
43	Unacceptably low DCS signal
51	Poor data quality due to excessive motion artifacts
52	Poor data quality due to excessive motion artifacts
55	Poor data quality due to excessive motion artifacts
59	Poor data quality due to excessive motion artifacts
61	Elevated blood pressure noticed. Session halted for clinical evaluation
63	Poor data quality due to excessive motion artifacts
64	Technical problem with DCS probe
65	Unacceptably low DCS signal
70	Unacceptably low DCS signal
74	Subject requested discontinuation of monitoring session after IV infiltration
78	Subject requested discontinuation of monitoring session, citing need to use the bathroom, refused restarting of monitoring session.

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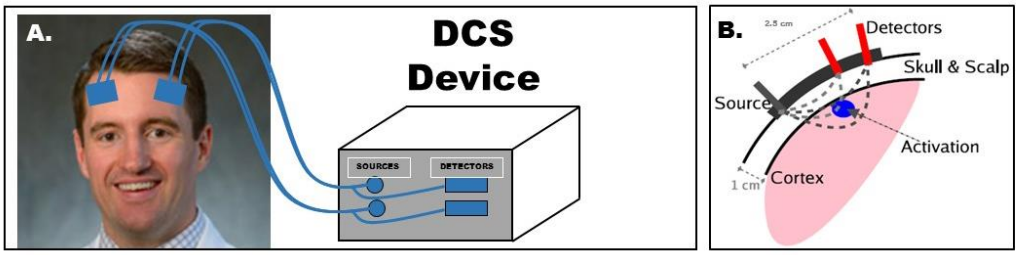
Supplemental Figure 1: Schematic representation of DCS probe.

Figure 1A shows a schematic of the DCS probes in position at the temporal margin of the forehead bilaterally. Figure 1B is a schematic representation of the sources and detectors on the probe, illustrating how the short (1cm) source-detector separations probe primarily extra-cerebral tissue, while the long (2.5cm) source-detector separations probe cerebral and extra-cerebral tissue.



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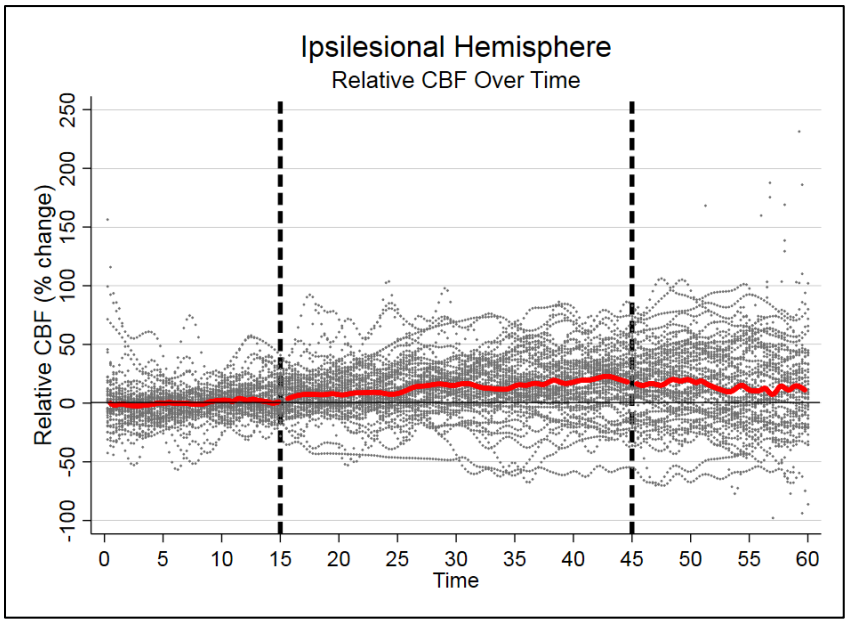
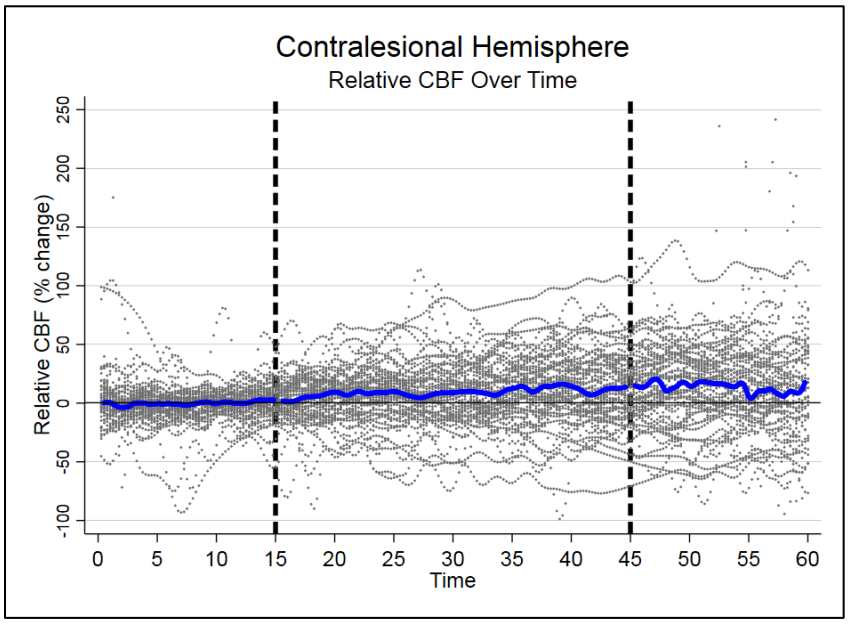
Supplementary Figure 2: Relative cerebral blood flow over time, during baseline, bolus, and post-bolus time periods is shown in the ipsilateral hemisphere (1A) and the contralateral hemisphere (1B). The bolus time period, during which 500cc of 0.9% normal saline was infused over 30 minutes, is the area between the dashed lines. Individual rCBF values are shown (small x) with a median spline estimate (solid line).

Supplemental Figure 2A



Supplemental Figure 2B



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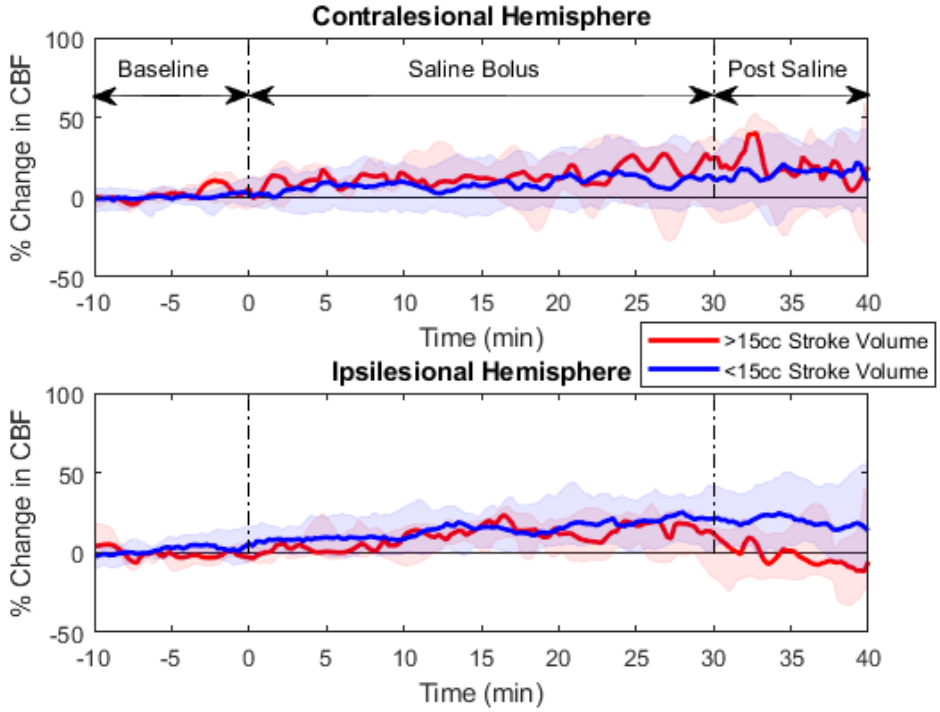
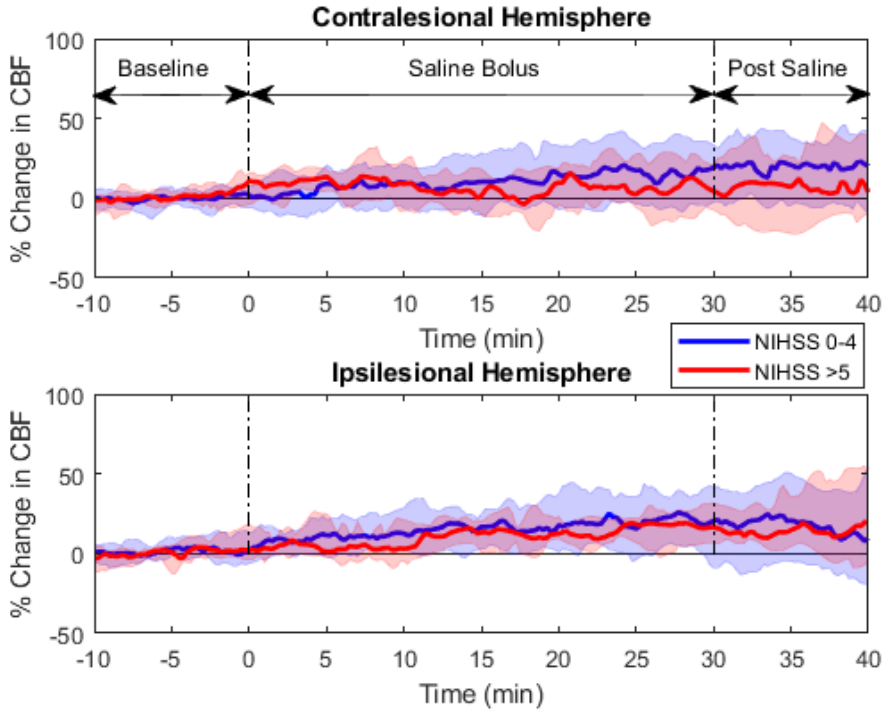
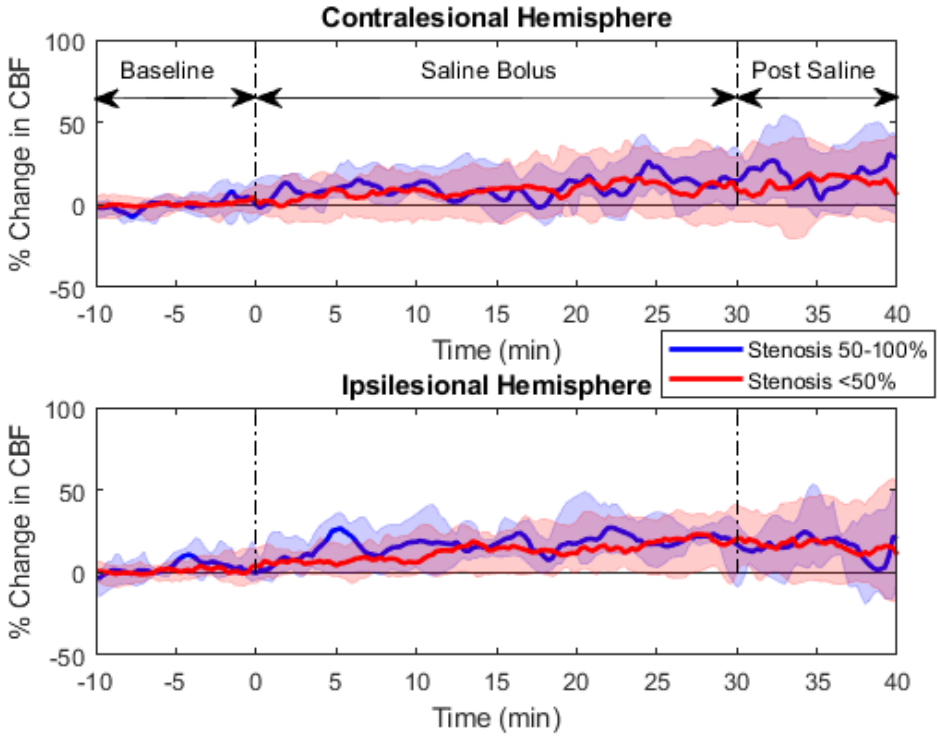
Supplemental Figure 3: Median rCBF and IQR by stroke volume



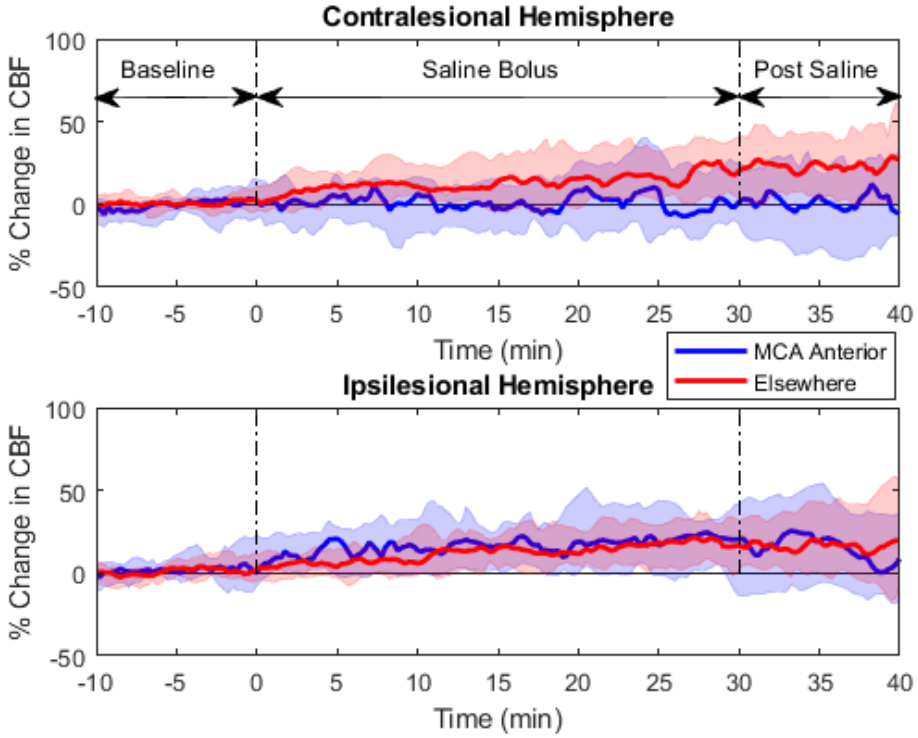
Supplemental Figure 4: Median rCBF and IQR by NIH stroke scale



Supplemental Figure 5: Median rCBF and IQR by presence of ipsilesional large vessel stenosis



Supplemental Figure 6: Median rCBF and IQR by stroke location



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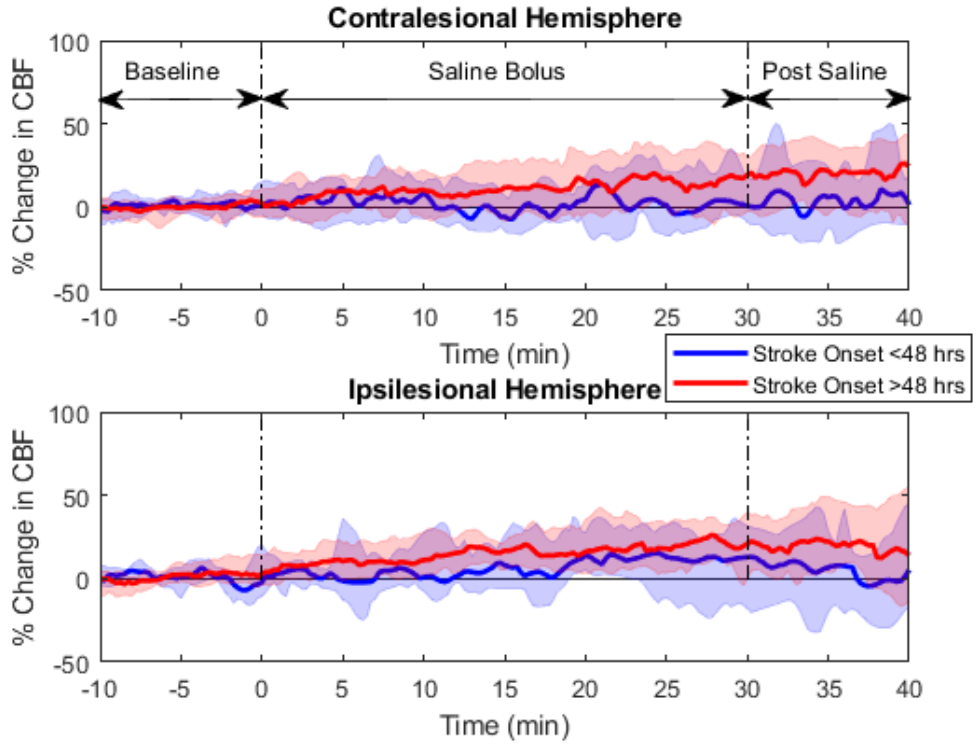
Supplemental Figure 7: Median rCBF and IQR by symptom duration



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Supplemental References

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