
We thank Aries et al1 for their interest in our study.2 We agree that it is too soon to use diffusion correlation spectroscopy (DCS) to guide clinical management, but our experience with this technology suggests that it has strong potential for clinical monitoring of brain perfusion. The key findings of our study were that DCS detected significant head-of-bed (HOB)-induced changes in cerebral perfusion, whereas middle cerebral artery transcranial Doppler (TCD) velocity changes were not significant. Moreover, considerable heterogeneity in HOB response was found.

Aries et al1 questioned the lack of observed TCD changes in our data, noting that our study monitored patients for only 5 minutes in each position, which might not be sufficient to capture a TCD change. One prior study monitored for 15 minutes at each HOB angle,1 but a more recent study by Aries et al1 monitored with TCD for <5 minutes at various HOB positions.4 In that study, a 4% mean decrease in ipsilesional middle cerebral artery flow velocity was noted when raising a flat HOB to 70°, significant across 47 patients, but no change was noted when raising a flat HOB to 45°. In our study, HOB was only raised to 30°, and our sample size was considerably smaller (n=17). We did observe a subtle trend toward ipsilesional middle cerebral artery velocity reduction with HOB elevation, but the trend magnitude was less than changes observed by DCS.

The DCS signal originates largely from light scattered by red blood cells moving within the microvasculature and has been shown to correlate with perfusion measurements by other modalities.3 DCS signals are thought to arise predominantly from arterial, capillary, and venous components of the microvasculature, whereas contributions of large arteries and veins are attenuated because of absorption as in near infrared spectroscopy. We contend that DCS reflects local cerebral perfusion more precisely than TCD velocity measurements in proximal intracranial arteries (eg, by reflecting effects of collateral flow sources). DCS and TCD might, therefore, be expected to yield different and complementary information, especially in injured brain.

Aries et al1 also noted the need for testing healthy controls and measuring other physiological parameters such as end-tidal CO2, heart rate. In a prior investigation, we assessed the effects of posture changes on DCS signal in 60 healthy volunteers, where measurements of heart rate and end-tidal CO2 were performed: DCS showed reductions in frontal perfusion at HOB of 30° relative to supine, without changes in heart rate and end-tidal CO2. We agree that it would be valuable to monitor additional physiologic parameters in patients with stroke.

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Disclosures
US Patent no. 8082015, Optical Measurement of Tissue Blood Flow Hemodynamics and Oxygenation, granted for the present class of diffusion correlation spectroscopy applications (Drs Yodh and Detre). Part of the technology has been transferred to a spin-off company (Hemophotonics, S.L., Barcelona, Spain), but the authors do not have any financial relationship to the company, do not have shares, and do not receive royalties. A second spin-off company (Flox Medical, USA) was created recently and is negotiating with Penn for relevant intellectual property; authors have not been remunerated for their participation/interaction with Flox, but potential for eventual remuneration, primarily through intellectual property, is possible.

Rickson C. Mesquita, PhD
Institute of Physics
University of Campinas
São Paulo, Brazil

Christopher G. Favilla, MD
Department of Neurology
University of Pennsylvania
Philadelphia

Arjun G. Yodh, PhD
Department of Physics and Astronomy
University of Pennsylvania
Philadelphia

John A. Detre, MD
Department of Neurology
University of Pennsylvania
Philadelphia


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Response to Letter Regarding Article, "Optical Bedside Monitoring of Cerebral Blood Flow in Acute Ischemic Stroke Patients During Head-of-Bed Manipulation"
Rickson C. Mesquita, Christopher G. Favilla, Arjun G. Yodh and John A. Detre

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