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Diffuse Optics for Monitoring Brain Hemodynamics

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I will review recent diffuse optics experiments carried out at PENN which explore cerebral hemodynamics in a variety of patient populations. Generally speaking, the research demonstrates the feasibility of both diffuse correlation spectroscopy (DCS), for measurement of cerebral blood flow, and more 'traditional' near-infrared (NIR) measurements of cerebral blood volume and oxygen saturation. The optical methods are employed to assess cerebral responses to simple functional perturbations such as posture change. The optical methodologies are also directly compared to transcranial Doppler Ultrasound (TCD), Xenon-CT and MRI in some of these patient (and normal) populations.

I. Overview

NEAR-infrared light penetrates through scalp and skull into dura and human brain, and spectroscopic modeling based on the diffusion approximation extracts regional variations of oxy- and deoxy-hemoglobin concentrations in brain. Spectroscopic optical monitoring ("near-infrared spectroscopy" (NIRS) or "diffuse optical spectroscopy" (DOS)), for example, has been used for transcranial measurements of total hemoglobin concentration (THC), blood oxygen saturation [233, 238], and, indirectly, for cerebral blood flow (CBF) monitoring using an exogenous tracer [239]. During the last few years our group has demonstrated that diffuse correlation spectroscopy (DCS) (as opposed to DOS/NIRS) is a significant new diagnostic instrument for measuring cerebral blood flow in human brain [27]. Its clinical feasibility as a bed-side monitor was demonstrated for measurement of cerebral auto-regulation in acute stroke patients [251], in traumatic brain injury [252, 253], and for measuring the carbon dioxide reactivity of neonates with congenital heart defects [31]. The combination of DCS technology and traditional DOS, especially, has the potential to be very valuable for concurrent all-optical investigation of blood flow and blood oxygenation in human brain during functional activation and during the bedside manipulations of stroke patients. For example, we have obtained images of cerebral metabolic rate of oxygen ($CMRO_2$) variation in rat brain from the flow/oxygenation images [28, 29], and we similarly measured $CMRO_2$ variation in human brain during motor activation [27]. In this contribution I will present recent results from our lab along these lines.

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II. Recent Results

The talk will focus on three investigations. The first investigation [27] explored the clinical potential of concurrent bedside optical CBF and THC monitoring in acute ischemic stroke patients. In particular, we hypothesized that optical probes placed on the forehead of patients with acute ischemic stroke (AIS) affecting the anterior circulation, would detect differences in autoregulatory impairment between the affected and unaffected hemispheres during head-of-bed (HOB) manipulations. Here the term autoregulation (or lack thereof) is used to describe cerebral blood flow changes with HOB positioning.

Seventeen patients with AIS were recruited and studied on one or more occasions during their hospitalization. A comparison group of eight subjects with vascular risk factors was also studied on one occasion. At each time point, changes in CBF (rCBF) and THC (ΔTHC) from each hemisphere were measured sequentially at four HOB positions (30°, 15°, 0°, -5°, and 0°) and normalized to the value at HOB=30° (rCBF30°) for comparison between subjects and hemispheres.

The study demonstrated the feasibility of hybrid DCS-NIRS technology for monitoring differences in autoregulatory impairment between the affected and unaffected hemispheres in acute stroke patients. The presence of an ischemic infarct was significantly associated with changes in ipsilateral rCBF30° as HOB positions varied. In addition, repeat measurements at 0° HOB showed a high degree of intra-subject repeatability ($R>0.9$), suggesting that DCS provides reproducible measurements of CBF. A key observation was the variable impact of acute ischemic stroke on cerebrovascular autoregulation. While the results for the control group were similar between individuals and did not show any significant variations in rCBF30° response between hemispheres, the AIS group showed a large variability between subjects. Most importantly, for the AIS group, a statistically significant difference was observed between infarct and non-infarct hemispheres. For the AIS group, the majority of patients displayed maximal CBF at a HOB angle of 0° to -5°, while approximately 25% exhibited maximal CBF at an elevated HOB angle of 15° to 30°. All subjects of the control group, however, showed maximal CBF at -5°. The basis for a paradoxical response is uncertain, but could be due to elevated intracranial pressure (ICP), hemodynamic consequences of heart failure, or autonomic dysfunction. These findings provide the first demonstration of DCS as an effective modality for measuring changes of CBF in acute stroke patients, and suggest at the potential importance of the technique for individualizing therapy.

A second (ongoing) investigation monitored four very low birth-weight, very premature infants during a 12° postural elevation using diffuse correlation spectroscopy (DCS) to measure microvascular cerebral blood flow (CBF) and transcranial Doppler ultrasound (TCD) to measure macrovascular blood flow velocity in the middle cerebral artery.

Preliminary DCS data correlated significantly with peak systolic, end diastolic, and mean velocities measured by TCD (p=0.018, 0.013, 0.047). Moreover, population averaged TCD and DCS data recorded no significant hemodynamic response to this small postural change ($p>0.05$). We thus demonstrate feasibility of DCS in the very premature infant population, we show agreement between DCS and TCD for the first time, and we found that small postural changes do not affect CBF in this population.

The third (ongoing) investigation which I will discuss monitored adult patients in the neuro-ICU using diffuse correlation spectroscopy (DCS) concurrently with stable xenon-enhanced computed tomography (XeCT) during changes in blood pressure or $paCO_2$. Six patients with traumatic brain injury, subarachnoid hemorrhage, or ischemic stroke were included in a validation study. Relative CBFDCS (rCBFDCS) was measured continuously throughout two XeCT-scans: a baseline scan and a scan after blood pressure or paCO2 intervention. Regions-of-interest (ROIs) under the DCS probes (placed bilaterally on the forehead) were drawn on the CBFXeCT maps, and calculated relative CBFXeCT values were compared to values from DCS.

After exclusion of low confidence ROIs from both techniques, preliminary observations of changes in rCBFDCS and rCBFXeCT due to intervention showed good correlation (rs=0.65, p=0.037). Thus we validate DCS against stable xenon-enhanced CT as a measure of local, microvascular CBF. These results further demonstrate the potential for DCS to provide continuous, non-invasive bedside monitoring of CBF for the purpose of CBF management and individualized care.

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