Noninvasive measurements of tissue hemodynamics with hybrid diffuse optical methods

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Diffuse optical techniques were used to measure hemodynamics of tissues noninvasively. Spectroscopy and tomography of the brain, muscle, and implanted tumors were carried out in animal models and humans. Two qualitatively different methods, diffuse optical tomography and diffuse correlation tomography, were hybridized permitting simultaneous measurement of total hemoglobin concentration, blood oxygen saturation, and blood flow. This combination of information was processed further to derive estimates of oxygen metabolism (e.g., $CMRO_2$) in tissue. The diffuse correlation measurements of blood flow were demonstrated in human tissues, for the first time, demonstrating continous noninvasive imaging of oxygen metabolism in large tissue volumes several centimeters below the tissue surface. The bulk of these investigations focussed on cerebral hemodynamics. Extensive validation of this methodology was carried out in *in vivo* rat brain models. Three-dimensional images of deep tissue hemodynamics in middle cerebral artery occlusion and cortical spreading depression (CSD) were obtained. CSD hemodynamics were found to depend strongly on partial pressure of carbon dioxide. The technique was then adapted for measurement of human brain. All optical spectroscopic measurements of $CMRO_2$ during functional activation were obtained through *intact* human skull noninvasively. Finally, a high spatiotemporal resolution measurement of cerebral blood flow due to somatosensory cortex activation following electrical forepaw stimulation in rats was carried out with laser speckle flowmetry. New analysis methods were introduced for laser speckle flowmetry. In other organs, deep tissue hemodynamics were measured on human calf muscle during exercise and cuff-ischemia and were shown to have some clinical utility for peripheral vascular disease. In mice tumor models, the measured hemodynamics were shown to be predictive of photodynamic therapy efficacy, again suggesting the promise of clinical utility. In total, the research has pioneered the development of diffuse optical measurements of blood flow, oxygenation, and oxygen metabolism in a large range of research and clinical applications.