

Three-dimensional optical tomography of the newborn infant brain

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Abstract

A time-resolved imaging system has been used to perform optical tomography on premature infants. The technique is being developed as a means of generating three-dimensional images of cerebral oxygenation, haemodynamics and metabolism at the bedside.

Introduction

The pursuit of medical optical tomography over the past ten years has been motivated by the desire for a means of imaging tissue oxygenation and metabolism at the bedside and without using hazardous forms of radiation. Research at UCL has been focussed in particular on the potential of near-infrared imaging to detect incidence of hypoxic-ischaemic brain injury in newborn infants, and assessing the effectiveness of interventional and therapeutic procedures designed to reduce the incidence of permanent handicap. The diagnostic use of near-infrared radiation is primarily associated with the difference in the absorption spectra of the oxygenated and deoxygenated forms of hemoglobin. This has been exploited for nearly thirty years in the increasingly widespread clinical use of near-infrared spectroscopy (NIRS), including the study of the newborn infant brain [1,2]. Due to the overwhelming scatter of light in tissues, accurate quantitation and localization of tissue parameters using near-infrared light is difficult. Nevertheless, considerable effort is currently being devoted to the development of imaging methods, and two distinct approaches are being pursued. The most straightforward of these is optical topography, which involves acquiring multiple reflectance measurements at small source-detector separations over a large area of the head. By keeping the separation low, measured signals are relatively high and therefore may be acquired quickly, enabling hemodynamic changes with characteristic responses as fast as a few hundred milliseconds to be studied. However, small separations also imply an overwhelming sensitivity to surface (cortical) tissues, and little information is revealed about deeper regions of the brain. Topographic optical mapping of the neonatal cortex has been demonstrated by several groups, revealing the cortical response to sensory stimulation [3,4] and spontaneous oxygenation changes during sleep [5]. The second and more difficult approach is known as optical tomography, which involves generating a transverse slice or three-dimensional (3D) image. The sensitivity to deep tissues requires measurements at large source-detector separations, and consequently transmitted light must be integrated over periods of several seconds (or longer) per source in order to obtain adequate signal. Until recently, the only attempt to produce a tomographic image of the neonatal brain has been that of the group at Stanford [6], who employed time-domain measurements of light transmitted across the head. They employed a simple, direct reconstruction procedure to obtain two-dimensional cross-sectional images. However, the acknowledged simplicity of their approach ignores the inherent 3D nature of photon migration in tissues, and the highly heterogeneous structure of the human head.

A 32-channel time-resolved imaging system has been constructed at UCL specifically for the task of performing three-dimensional (3D) optical tomography on premature newborn infants in an intensive care environment [7]. The system measures the flight times of photons which are scattered diffusely between pairs of points on the surface of the head and images of internal absorbing and scattering properties are reconstructed using a complex non-linear algorithm based on finite-element models of photon transport [8]. The use of time-domain measurements avoids problems associated with variability in fibre/tissue coupling which can seriously inhibit imaging with straightforward intensity measurements. Our system utilises a custom-built light source which consists of two passively modelocked fiber lasers operating at 780 nm and 815 nm, pumped by a single oscillator. It provides interlaced trains of picosecond pulses at a 40 MHz repetition rate (per pair of pulses) and a mean power of up to 55 mW per wavelength. The pulses are coupled to the surface of the patient via a 32-way optical fiber switch. Transmitted light is collected simultaneously by 32 detector fiber bundles, which deliver the light to four 8-anode microchannel-plate photomultiplier tubes. The arrival time of each detected photon is measured with respect to a laser-generated reference signal, and histograms of photon flight times (temporal point spread functions, or TPSFs) are accumulated.

Clinical measurements

Attaching up to 32 source fibres and detector fibre bundles to a newborn infant head represents a significant challenge, particularly in the case of premature, and/or critically-ill infants. We currently employ a plastic, foam-lined helmet custom-built for each individual infant. The shape and dimensions of the helmet are based on a series of measurements acquired from digital photographs taken one or two days prior to the study. The outer shell of the helmet is constructed in two halves from low-temperature thermoplastic, and is lined with a soft NIR-absorbing foam, 10 mm thick. The source and detector fibres are attached via small sockets mounted on the thermoplastic shell. Figure 1 shows the helmet attached to the head of an infant during an imaging scan.

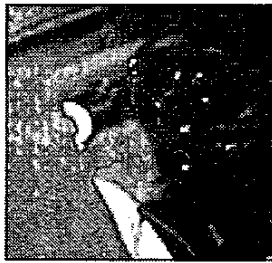


Figure 1. A fibre holder helmet on the head of an infant during an imaging scan

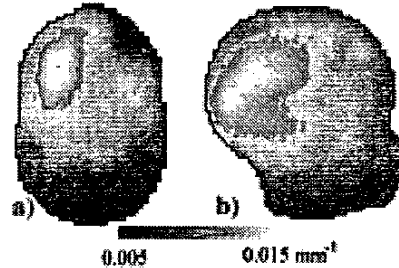


Figure 2. Absorption images of infant brain with left-side haemorrhage: a) Coronal and b) sagittal views.

A recent study was performed on a 35-week male infant who had suffered from a perinatal haemorrhage, predominantly located within the left ventricle. Imaging scans were performed at the cotside in the neonatal intensive care unit. Each source was illuminated for 15 seconds, and TPSFs were recorded by each detector simultaneously, resulting in a total scan time of about 9 minutes. Converting the time-resolved data into 3D images of the internal optical properties requires a finite-element mesh of the infant head with a realistic geometry. To obtain a crude forward model, we first acquired a 3D CT-scan of a realistic doll's head, from which we generated a surface mesh. The surface mesh was then mathematically "warped" in order to fit it to the measured locations of the sources and detectors. Finally, the resulting surface was used to construct a volume mesh. Images were reconstructed by calculating *differences* between the mean photon flight-times measured for the head and those measured on a homogenous reference phantom. The use of difference data partially alleviates problems associated with uncertainty in the true positions of the sources and detectors on the head (measured *after* the experiment using a 3D digitizer). The reference phantom consisted of a balloon filled with a solution of intralipid and dye, with precisely known scattering and absorbing properties, which was inserted into the helmet immediately following the infant scan. The images shown in figure 2 represent the reconstructed absorption coefficient at a wavelength of 780 nm displayed in coronal and sagittal views across the infant head. Despite some approximations involved in their reconstruction, the images are not unreasonable. Larger absorption is observed on the left side of the brain, consistent with the haemorrhage. An even stronger feature is observed at the back of the head, which is consistent with the sagittal sinus.

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