BIOMEDICAL OPTICS

Real-time Fluorescent Detection of Dynamic Organ Function

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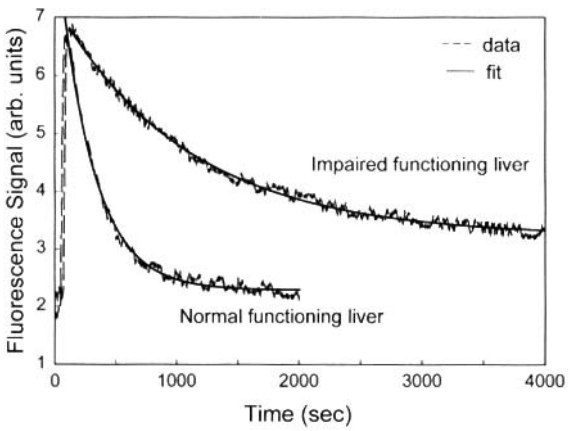
Medical diagnosis and care often require rapid assessment of excretory organ function, especially in an intensive or critical care setting. Current clinical methods for dynamic hepatic or renal function determinations involve laboratory analysis of blood or urine samples. These procedures require time, have associated labor costs, and expose medical and laboratory personnel to numerous health risks. Radiolabeled tracer tests are often the prescribed assay,[1] thus involving associated risks to the patient as well. Therefore, noninvasive methodologies for physiological function assessment are attracting interest as possible clinical alternatives to current practice. A noninvasive nuclear magnetic resonance method for monitoring renal status has been recently proposed using magnetic resonance contrast agents.[2] Light-based methodologies using absorbing optical contrast agents have also been previously investigated as organ function evaluation assays.[3,4]

Recently, the feasibility of employing noninvasive *in vivo* fluorescence detection to monitor hepatic function has been demonstrated in a rat model using a fluorescent optical contrast agent.[5] A laser of appropriate wavelength for excitation of the contrast agent is directed into one end of a fiber optic. The other end is positioned a few millimeters from the rat's ear. A second fiber optic is also positioned near the same ear to detect emitted fluorescent light, which is subsequently directed into the data collection system. In one demonstrated example, indocyanine green (a near-IR fluorescent dye known to be exclusively cleared from the bloodstream by the liver) was administered intravenously in rats, and the fluorescence at the ear was measured as a function of time. The results (see Fig. 1) show that quantitative differentiation in the fluorescence decay time is observed between a normal and an impaired functioning liver.

Several advantages of this fluorescent optical tracer methodology are immediately evident with respect to current radiolabeled tracer testing. The employment of non-ionizing radiation (light) rather than ionizing radiation (radioisotopes) is safer for both patient and healthcare provider. The signal generation and detection uses relatively inexpensive components (laser diodes and photodiodes) and obviates the need for an expensive hospital-based detector (gamma camera). In addition, the real-time aspect of this method should allow correlation of dynamic organ function to important physiologic events such as blood pressure, cardiac output, and state of hydration. The simplicity of the measurement, the rapid time scale of the measurement, and the inexpensive cost and compactness of the instrumentation should eventually evolve this methodology into clinical utility.



Dorshow Figure 1. The *in vivo* fluorescence time dependence after a bolus injection of indocyanine green in a rat with an impaired functioning liver, compared to a rat with a normal functioning liver. The decay times (obtained by fit to a single exponential) differ by an order of magnitude.

Application of this monitoring technique may be especially useful within the critical care unit, at the bedside, and/or in the physician's office. Monitoring kidney function to detect the onset of renal disease due to diabetes, the dosing of medication that is based on renal function, and monitoring organ function during chemotherapy are future clinical applications for this methodology. Development of optical contrast agent systems for measurement of specific aspects of hepatic or renal function (such as glomerular filtration rate or renal plasma flow) would have the greatest initial clinical utility.

References

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Photorefractive Polymers for Biomedical Imaging

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Imaging through highly scattering media using optical radiation has recently received particular attention due to potential applications in medical diagnostics.[1] By using optical radiation one can avoid the hazards of ionizing X-rays while obtaining high spatial resolution (potentially diffraction limited) images, offering a distinct advantage over current clinical techniques. However, optical radiation, unlike ionizing radiation, is heavily scattered in biological tissue by refractive index inhomogeneities. As a result, the transmitted light consists of photons that have experienced no scattering events (ballistic light), weakly scattered photons that emerge almost collinear with the incident radiation (so-called "snake-like" light), and highly scattered (or diffuse) photons. Holographic time gating (HTG) is a direct imaging technique that uses the coherence properties of the ballistic light to filter out the diffuse light.[2,3] In this method, a hologram is formed between the ballistic light of an object beam and a reference