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Novel Technologies for Time-Domain Diffuse Optics: Miniaturized Wearable Devices and Bioresorbable Optical Fibers

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Abstract: Time-Domain Diffuse Optics is undergoing fascinating technology advancements. After a brief review of recent innovations, here we present a miniaturized pulsed source enabling wearable systems and the ex-vivo validation of implantable bioresorbable optical fiber.

OCIS codes: (170.5280) Photon migration; (170.6920) Time-resolved imaging; (170.3660) Light propagation in tissues

1. Introduction

In the last decade Time-Domain Diffuse Optics (TDDO) is undergoing fascinating technology advancements, permitting to foresee the achievement of the same level of compactness, cost, speed and robustness as continuous wave (CW) instruments [1]. With respect to CW, TDDO systems guarantees higher information content, sensitivity, penetration in the tissue and insensibility to motion artifact. In order to maximize their performances, 4 conditions are needed, being nowadays the main technological challenges [2]: 1) dense distribution of miniaturized pulsed sources to maximize the injected power by distributing it over a large area to match the maximum permissible exposure of skin; 2) dense distribution of miniaturized probe-hosted TD detectors to maximize the harvesting of diffused light also thanks to their large numerical aperture (NA); 3) fast time-gating capability to implement the gated acquisition technique, thus achieving the largest dynamic range of acquisition [3]; 4) high throughput compact electronics for photon timing. Miniaturized probe-hosted detectors and sensors with on-chip timing circuits have been already presented in previous works [1], achieving almost the same level of compactness as CW instruments. However, TDDO sources are still far from the desired level of miniaturization. Compact probe-hosted pulsed VCSEL sources have been demonstrated [2], but each source still requires an external bulky ultrafast voltage pulse generator, resulting not suitable for the parallelization of multiple sources. To address this requirement, we present the validation of a small CMOS driver, used to pulse a double heterostructure laser diode operated in so-called "enhanced gain-switching mode" [4]. With the achievement of the 4 conditions, TDDO could reach a penetration depth of 6 cm in human tissue [2], with the possibility to probe new organs as for example the lung or the heart. However, higher penetration can be achieved with a different approach, combining it to endoscopy or surgical procedures, potentially reaching any part of the body. For instance, bioresorbable optical fibers [5] could be placed inside the body during surgical interventions to monitor the postoperative healing process or detect anomalous tissue response and they will spontaneously decay without dangers for the subject. Externally, a compact wearable TDDO device can be connected to such fibers, similarly to an Holter monitor. To move a first step, here we present an ex-vivo validation of Calcium Phosphate Glass (CPG) optical fibers for TDDO using state of the art laboratory systems.

2. Validation of miniaturized wearable laser source based on integrated CMOS driver

Fig.1(a) shows the miniaturized (12x6mm^2) laser board with a CMOS driver designed in 0.35μm high-voltage technology and a custom-designed quantum well laser diode operated in enhanced gain-switching mode, thus generating ~0.5W peak power optical pulses at ~800nm with ~100ps duration at a maximum pulsing rate of 1MHz. The detection chain is based on a probe-hosted silicon photomultiplier detector in contact with the sample under investigation to avoid the use of optical fibers, which is coupled to a time-correlated single-photon counting PC board. Additional details on the system are reported in [6]. After extensive phantom validation (not shown), the system has been used to monitor the contrast produced by venous cuff occlusions performed on the arm of healthy volunteers. The contrast produced by the change in optical properties has been computed as the relative change in the number of photon counts within a 500ps time-window along the histogram of times of flight [6]. Results are shown in Fig.1(b) where the timing of the 3 subsequent occlusions are highlighted by the gray regions of interest.

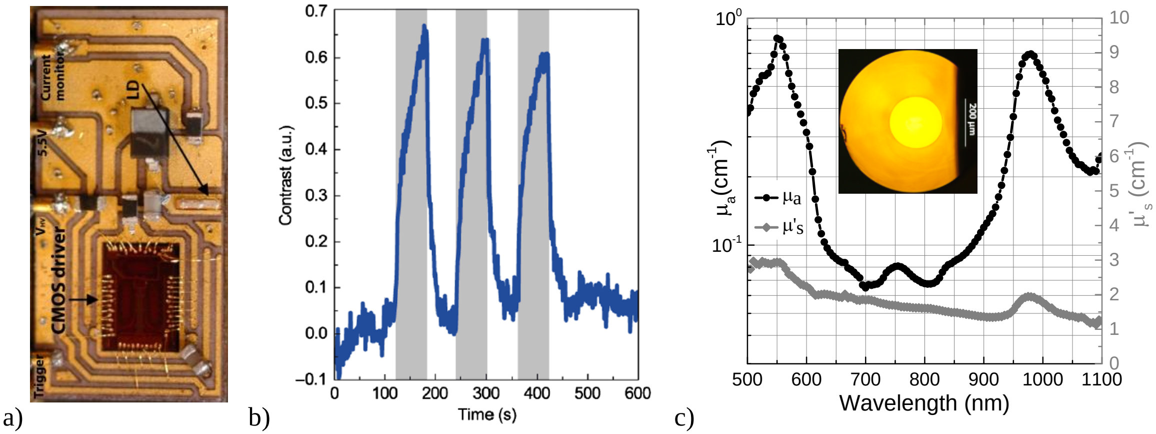

Fig. 1 a) Miniaturized (12x6 mm^2) laser board with CMOS laser driver, b) contrast produced by venous occlusion using the proposed laser driver, c) chicken breast optical properties measured with bioresorbable fibers, with microscopy image of a of a 200 μm core fiber section.

Since the laser wavelength is close to the isosbestic point of hemoglobins, it is sensitive to the total concentration of hemoglobin, which increases during the venous occlusion [6]. Overall, performances are in line with bulky and expensive TDDO systems, thus validating this laser technology and removing the last obstacle preventing the design of TDDO wearable systems.

3. Validation of implantable calcium phosphate glass bioresorbable optical fibers

Bioresorbable CPG optical fibers were fabricated as described in [7]. They feature different core diameters (i.e. 50, 100 and 200μm), a NA of 0.17 and a loss coefficient of ~4.1dB/m at 633nm. Two fibers (one for light injection and one for collection) were mounted on state-of-the-art TDDO laboratory systems (see [7] for details). Systems were characterized following shared protocols [1] for performance assessment on phantoms showing suitable instrument response functions and capability to retrieve absorption and scattering properties of phantoms similar to systems based on standard glass fibers (data not shown). One of the systems is equipped with supercontinuum laser (SuperK Extreme, NKT Photonics, Denmark) and a prism for selection of desired wavelength, thus allowing spectroscopic measurements. To demonstrate that CPG fibers can be used to recover optical properties inside living tissues, we inserted two 200μm optical fibers inside a cut of chicken breast, at 2cm source-detector separation and programmed the system to scan wavelengths at steps of 5nm between 500 and 1100nm. The recovered optical properties are shown in Fig.1(c). It is possible to distinguish three absorption peaks, at 550 and 750nm, due to the presence of deoxy-hemoglobin, and at 970nm, due to the presence of water. The low retrieved scattering can be due to the tissue structure, made of elongated fibers that can lower the scattering probability. Bioresorbable fibers can now open new clinical perspectives, as they could be inserted in the body during routine surgical interventions to monitor postoperative processes or for in-situ irradiation, without the need of secondary surgery to remove them.

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