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Fiber-based hybrid probe for non-invasive cerebral monitoring in neonatology

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ABSTRACT

Improved cerebral monitoring systems are needed to prevent preterm infants from long-term cognitive and motor restrictions. Combining advanced near-infrared diffuse spectroscopy measurement technologies, time-resolved spectroscopy (TRS) and diffuse correlation spectroscopy (DCS) will introduce novel indicators of cerebral oxygen metabolism and blood flow for neonatology. For non-invasive sensing a fiber-optical probe is used to send and receive light from the infant head. In this study we introduce a new fiber-based hybrid probe that is designed for volume production. The probe supports TRS and DCS measurements in a cross geometry, thus both technologies gain information on the same region inside the tissue. The probe is highly miniaturized to perform cerebral measurements on heads of extreme preterm infants down to head diameters of 6cm. Considerations concerning probe production focus on a reproducible accuracy in shape and precise optical alignment. In this way deviations in measurement data within a series of probes should be minimized. In addition to that, requirements for clinical use like robustness and hygiene are considered. An additional soft-touching sleeve made of FDA compatible silicone allows for a flexible attachment with respect to the individual anatomy of each patient. We present the technical concept of the hybrid probe and corresponding manufacturing methods. A prototype of the probe is shown and tested on tissue phantoms as well as in-vivo to verify its operational reliability.

Keywords: Hybrid probe, Preterm births, Time-resolved spectroscopy (TRS), Diffuse correlation spectroscopy (DCS), Optical fibers, in-vivo, $CMRO_2$

1. INTRODUCTION

Preterm infants often suffer from inadequate cerebral oxygen supply in the first weeks after birth. A resulting increased risk of brain injury may cause disabilities and learning difficulties at school. Thus innovative technologies are needed to monitor the cerebral oxygen supply in a way that accurate and precise information of the cerebral oxygen metabolism and blood flow can be extracted to prevent an insufficient supply. To ensure the cerebral oxygen supply in a first step oxygenated hemoglobin must be transported to the tissue. In a second step the oxygen must be extracted. Time-resolved near-infrared spectroscopy (TRS) can provide an estimation of oxygen saturation and gains information from the arterial and venous ends of the vasculature. The difference in oxygenation determines the oxygen extraction fraction (OEF). Diffuse correlation spectroscopy (DCS) can add information about blood flow which is necessary to determine the cerebral metabolic rate of oxygen extraction ($CMRO_2$) [1-3]. It reads as

$$CMRO_2 = OEF \times CBF \times C_a \quad (1)$$

with OEF is the normalized oxygen extraction fraction, CBF the cerebral blood flow and C_a the arterial oxygen concentration [4]. For the construction of a TRS/DCS hybrid probe both measurement technologies require own optical paths for illuminating the tissue and the detection of multi-scattered light. A cross-geometry allows for data acquisition of one region in the tissue to hold the requirement to determine $CMRO_2$. For accurate und precise measurements an efficient light coupling is essential. High optical and mechanical quality must be paired with a high degree of miniaturization since the probe must be applied to tiny preterm babies with heads down to a diameter of 6 cm. In

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addition to that, the neonates' skin is very sensitive to pressure and the probe must fulfill the clinical standards regarding disinfections.

In the context of BabyLux project the hybrid probe is developed to deliver reliable measurement data and to be prepared for mass production. Thus, the development bridges between available probes used for research purposes and commercial monitoring systems addressed in BabyLux project for clinical use.

2. METHODS

To perform cerebral monitoring on preterm infants a contact probe design (side-firing) is chosen which is typically used in brain and muscle studies on humans [5, 6]. The presented hybrid probe is innovative in three ways. First, precise alignment of all optical components allows for accurate measurements and high repeatability. Second, the probe is designed to match the requirements of clinical use with respect to robustness and hygiene. Third, the probe is designed to manufacture.

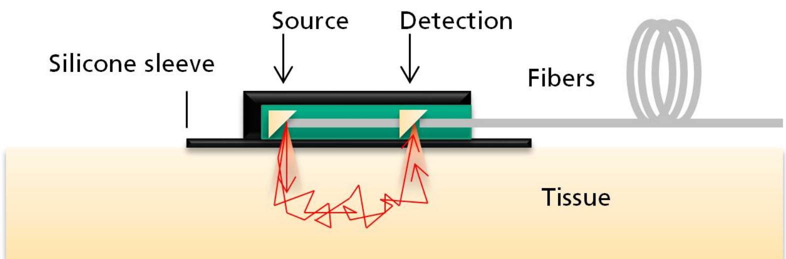

Figure 1. Scheme of the probe: The light path is illustrated for one measurement technology. The beam of a source fiber is deflected by 90° and penetrates the tissue. A fraction of scattered light is coupled into the detection fiber for analysis.

A non-flexible metal piece mounts all fibers, takes up mirror prisms for 90° beam deflection as shown in Figure 1 and is sealed with optical windows. The fibers are aligned such the probe supports TRS and DCS measurements in a cross geometry and both technologies gain information on the same region inside the tissue. A silicone sleeve is covering the probe for several reasons. It is soft touching, made of FDA compatible materials and therefore qualified for skin contact on neonates. Moreover it can be taken as disposable or reusable after autoclave treatment for hygienic reasons. Additionally, it improves shielding ambient light to increase the measurement signal quality due to its black color and flexible attachment. To keep the probe applicable to preterm infants, especially the non-flexible part of the probe is highly miniaturized. Size and weight are reduced to avoid negative mechanical impacts to the infants' skin.

For the creation of mechanical components for prototyping the hybrid probe, different manufacturing methods like micro milling, 3D printing or molding at room temperature are applied. On the one hand they are beneficial for low quantities due to low investment cost, but on the other hand they are time-consuming. Larger quantities of probes ask for production technologies for mechanical components that profit from short cycle times like injection molding. For this reason relevant mechanical components like the silicone sleeve are designed for injection molding.

Optical components like fibers or prisms used for this probe are available in large quantities. In addition to that, the assembly of probes is simplified by the design of its components. The non-flexible inner part of the probe picks up all optical components in pre-defined positions to minimize time-consuming alignments.

3. RESULTS

The developed fiber-optical hybrid probe is side-firing and its dimensions are 5mm thickness and 14mm width. It can be cleaned using common disinfectants and a disposable silicone sleeve made of FDA compatible materials is available. DCS measurements (in-vivo and on liquid phantoms) were performed without the silicone cover at ICFO in Barcelona (compare Figure 2). The characterization of the optical TRS path was performed at Politecnico di Milano on 32 calibrated tissue phantoms.

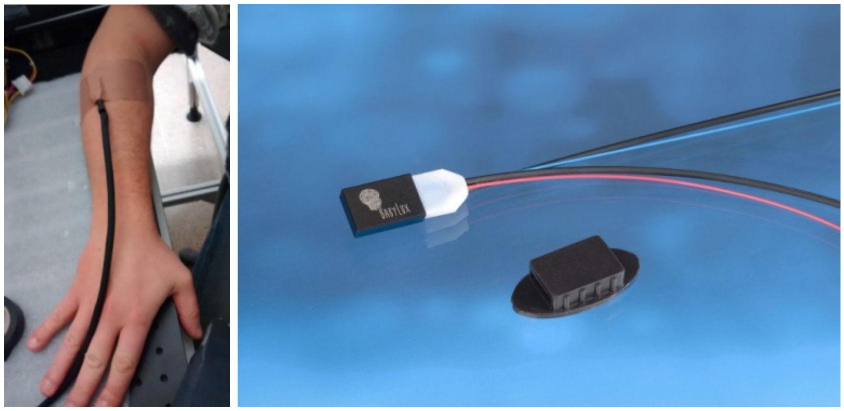

Figure 2. (Left) In-vivo DCS measurements on a human arm. (Right) Compact fiber-optical hybrid probe, a disposable silicone sleeve (ca. 40x20x7 millimeters) made of FDA compatible materials is shown on the bottom.

3.1 Characterization of the DCS signal

For DCS measurements, the light is collected by a single-mode fiber, single photon counting avalanche photo-diode and analyzed by a hardware auto-correlator. We present an analysis of the quality control parameter (β) which essentially checks the number of modes that are detected. Common DCS probes typically work at β≈0.45-0.5 which is comparable for t→0 to the in-vivo measurements shown in Figure 3. Extracted β-values are used to relate the measured intensity auto-correlation to the theoretical, normalized electric field auto-correlation function for the extraction of the blood-flow index Db. Figure 4 shows data from a 20 minutes data acquisition set and the statistical distribution as well as the time series of the blood flow index.

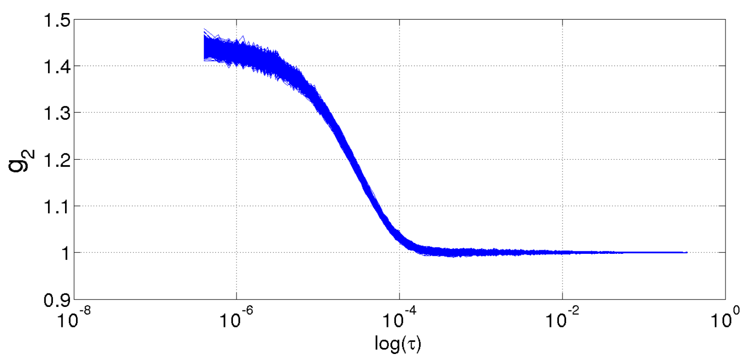

Figure 3. In-vivo DCS measurements on a human arm. 20 correlation curves are collected in total.

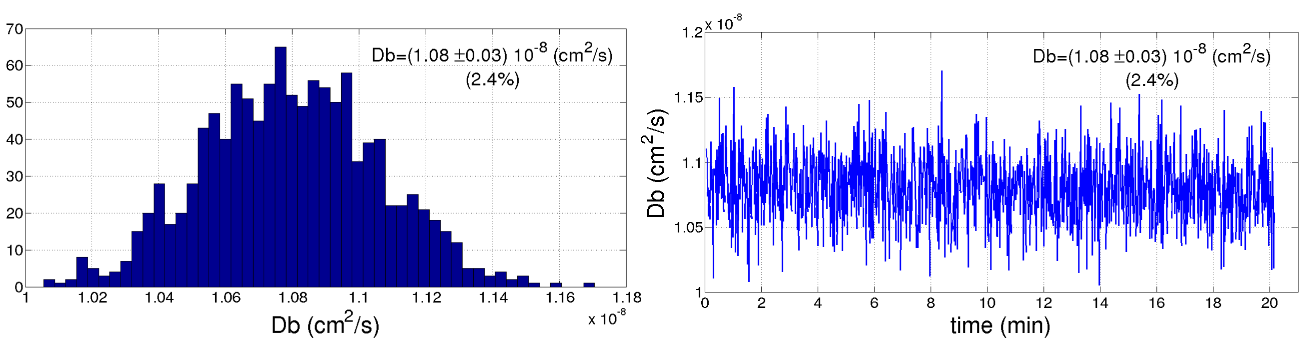

Figure 4. DCS measurements on liquid phantoms. Blood flow index values are collected for 20 minutes. (Left) Statistical distribution of blood flow index. (Right) Time series of blood flow index.

3.2 Characterization of the TRS signal

For TRS measurements picosecond pulses of up to 3 different wavelengths are coupled into phantoms via multimode gradient index fiber optics. Scattered light is collected and analyzed using reference light pulses on fast photomultiplier tubes. Absorption coefficients on 32 calibrated solid tissue phantoms (8 absorption values, labeled from 1 to 8, times 4 scattering values, labeled from A to D) could be characterized as shown in Figure 5. In addition, a multi wavelength characterization is performed on a single phantom to evaluate the repeatability. Figure 6 shows data for a manual repositioning. Ten repositioning measurements are performed, each consisting of ten repetitions.

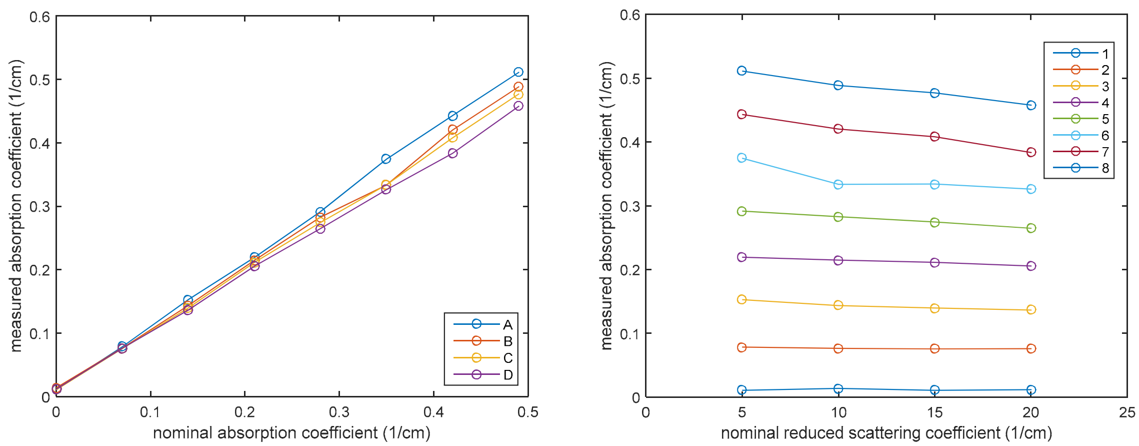

Figure 5. TRS measurements on 32 calibrated solid tissue phantoms at 690nm. (Left) Linearity on absorption coefficient (Right) Absorption for different samples.

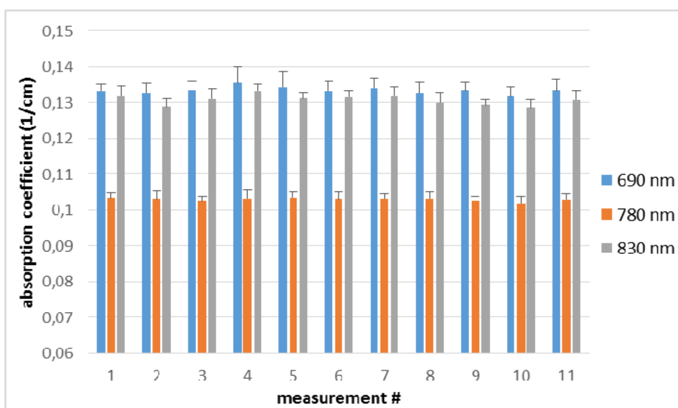

Figure 6. TRS measurements: The probe is repositioned ten times on the phantom. Measurement 11 gives the average value.

4. CONCLUSION

With the developed probe it is possible to perform DCS as well as TRS measurements. The fiber-based hybrid probe for non-invasive cerebral monitoring in neonatology is designed to manufacture, to match the clinical requirements and to provide accurate measurements and high repeatability. The overall approach of this probe is promising. Good quality auto-correlation measurements were obtained and all fitted values are within expected ranges. To further improve the signal quality represented by the control parameter (β) for DCS, additional probe-internal light shielding and a modified optical alignment must be evaluated.

5. ACKNOWLEDGEMENT

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Cerebral Oxygen Metabolism and Blood Flow for Neonatology - is a project that aims to provide an innovative and reliable tool to monitor and assess brain blood flow and oxygenation in extremely preterm neonates. The main goal is to diminish the risk of brain lesions in extremely preterm babies from 25% to 20%, eventually reducing the number of children with disabilities by more than 1,000 per year in Europe alone. BabyLux takes up complete R&D works and extends already tested prototypes to the level of demonstrator, bridging the gap between research products and commercialization.

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