Towards enhanced cancer therapy; Leveraging bioresorbable optical fibers for improved treatment outcomes

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Abstract. Bioresorbable photonic implants are emerging as potential material choice for interstitial theranostic and monitoring applications. They gradually dissolve within the physiological environment in a clinically relevant period, eliminating the need for extraction surgeries. In the present study, we tested the suitability of in-house fabricated bioresorbable optical fibres based on calcium phosphate (CaP) glass for diffuse correlation spectroscopic (DCS) and diffuse fluorescence tomographic (DFT) applications. The results represent the potential of bioresorbable fibers for the monitoring of interstitial microvascular blood flow and the spatial distribution of fluorescent photosensitizer drugs that are administered prior to therapies. Together or separate, the continuous monitoring of these parameters can have significant implications in planning, optimizing and in predicting or monitoring the outcomes in interstitial photodynamic therapy (PDT).

1 Introduction

Optical quality bioresorbable biomaterials have gained increasing interest for various interstitial biomedical applications in recent years. CaP glass based biomedical implants are significant among them which are emerging as potential implant material capable of performing several biomedical functionalities [1]. CaP glass based optical fibers have recently been studied for diffuse–near-infrared (NIR) optical methods capable of retrieving tissue absorption and scattering properties and oxygen saturation [2]. The possibility of tailoring the resorbability rate by adjusting the composition of the CaP glass makes them relevant as short-term implants that eventually dissolve within the physiological media, without any toxic effects.

Resorbable optical fibers have the potential in light based interstitial diagnosis, therapy, and in continuous monitoring of physiological signals. As has been previously reported [3], monitoring of PDT induced flow responses hold potential for predicting the treatment outcomes in humans. Similarly, the knowledge on spatial distribution of photosensitizer concentration can be beneficial for efficient treatment, by ensuring a sufficient light dose to the target tissue, while keeping the surrounding organs safe [4]. In this study, we tested the suitability of in-house fabricated CaP glass based optical fibers to assess their capability for microvascular blood flow measurements and to monitor the photosensitizer drug distribution in tumor respectively.

2 Materials and methods

2.1 Fabrication of CaP glass-based optical fiber

For these studies, we fabricated three types of fibers, both single mode (SM) (at 785nm) and multimode fibers (MM) (220µm core) for DCS and only MM fibers (400 µm core) for DFT using high purity biocompatible chemicals (P_2O_5–CaO–Na_2O–SiO_2–MgO). Details of fabrication has been previously explained in [5]. For DCS measurements, a 10 cm section of SM phosphate was FC-PC connectorized at one end to a 1-meter commercial SM silica patch cord. The MM fibers (1 meter for DCS and 25 cm for DFT) were connected to the DCS system via FC-PC connector and to DFT system via SMA connector.

2.2 DCS measurements

Ex vivo measurements were performed on a liquid phantom (Lipofundin 20%+ water) with reduced scattering coefficient of 5 cm^{-1} and water absorption at 785nm wavelength [6]. Fibers were positioned as in Fig.1.a). A MM fiber (alternately phosphate or silica) was used to launch 785 nm laser light into the phantom and the single mode fibers (both the silica and phosphate that are equidistantly placed (1.8 cm) from the source fiber) to simultaneously collect the diffused light and deliver it to single photon avalanche photodiodes (Excelitas, Canada).

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The single speckle intensity autocorrelation (g_2) function was calculated real time through a hardware correlator (HemoPhotonics, Spain), and then fitted with the solution of the electric field correlation diffusion equation for a semi-infinite homogeneous medium to obtain the Brownian diffusion coefficient Db of the particles [7]. The results were compared across the phosphate and silica fiber combinations as in Fig 1-b. Additionally, an *in vivo* vascular occlusion test [8] was also performed on human forearm muscle to test if the phosphate fibers can be used to track rapid dynamic changes in blood flow.

2.3 DFT measurements

For this test, a hybrid phantom [9] that contains a solid gelatin-based tumor-mimicking inclusion within an intralipid-based liquid phantom mimicking the optical properties of the prostate was prepared. The solid tumor inclusion contains the fluorescent photosensitizer (PS) verteporfin. The CaP MM fibers were inserted in the phantom as in figure 1 c. A 690 nm light was delivered through one of the fibers at a time to excite the PS, which emits the fluorescence signal that is collected by the remaining fibers. The measurement consists of the acquisition of the fluorescence signals from every source-detector fiber pair using SpectraCure's P18-4 system. These signals were then used for the tomographic reconstruction of the PS fluorophore absorption coefficient using MATLAB. The results were compared with those of the system equipped with standard commercial silica fibres.

3 Results and discussion

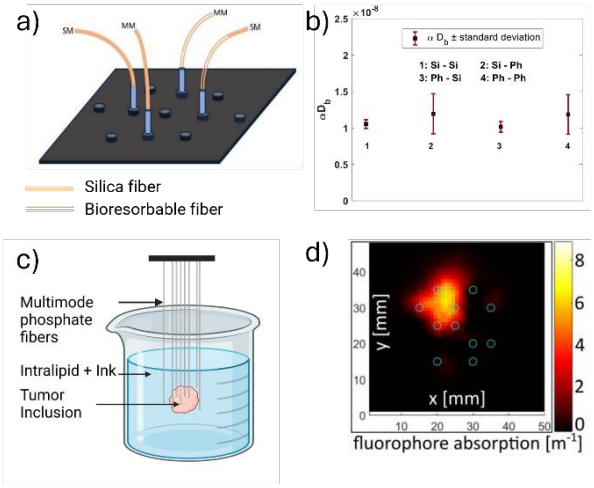

Fig. 1. a) schematic of the fiber positions during *ex vivo* DCS measurement. b) comparison of the retrieved scatterer Brownian diffusion coefficient (D_b) obtained from four different combinations of silica (Si) and phosphate (Ph) fibers as source and detectors. c) Experimental setup with the positioning of the phosphate fibers and the hybrid phantom; d) Reconstructed distribution of the photosensitizing drug at the plane of the tumor centre.

Results suggest that the bioresorbable phosphate fibers are suitable for both the microvascular blood flow measurements and drug distribution reconstruction applications. They performed similar to the DCS and DFT systems equipped with standard commercial silica fibers both during the *ex vivo* and *in vivo* tests (*in vivo* not reported here). The lower precision of DCS measurements (Fig 1.b) with phosphate detector fibers is mainly due to the photon losses at the manually connectorized FC-PC joints that can be easily resolved. The reconstructed absorption using phosphate fibers (Fig 1.d) is comparable but slightly different than that of using silica fibers (not reported here). Having the information about the actual fibre positions, instead of just recommended positions, would improve the accuracy of the reconstruction.

4 Conclusions

Bioresorbable fibers were validated successfully for retrieving microvascular blood flow and in monitoring photosensitizer distribution. This represents the potential towards a new class of biomedical devices that can be implanted in the patients to obtain continuous physiological information that can be used to plan the treatments and follow up the evolution after a surgical intervention, requiring no explant surgeries

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