The new thermometry with light: fiber optic sensors and spectral imaging for monitoring thermal-based therapies for localized tumors

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ABSTRACT

Thermal therapies are energy-based interventions that provide a minimally invasive treatment option for cancer patients who may not be surgical candidates. Being these therapies based on the increase of tissue temperature to achieve tumor necrosis, it is important to assure complete tumor destruction and simultaneous safety by minimizing collateral thermal damage. Thus, the availability of accurate tools for monitoring tissue temperature changes during the treatment and its control represents an important clinical need. This work presents an overview of two main optical tools (i.e., fiber optic sensors and hyperspectral imaging) which are under investigation for thermometry purposes in tumors and organs undergoing thermal therapies.

Keywords: Thermal therapies, tumor, thermometry, fiber optic sensors, fiber Bragg gratings, hyperspectral imaging

1. INTRODUCTION

Energy-based image-guided interventions provide a minimally-invasive treatment option, which is largely performed in interventional oncology for the treatment of liver, lung, kidney and bone tumors, as an effective alternative to not surgical candidates, and it is studied for treating tumors in other organs, such as pancreas and brain. These techniques offer low complications rate and high therapeutical efficacy, with limited systemic toxicity, and the potential to synergize with other therapeutic modalities. Among different technologies, we can list the thermal ablation therapies, such as radiofrequency ablation (RFA), microwave ablation (MWA) and laser ablation (LA). These techniques utilize increase of temperature in the tumor target, aimed at inducing necrosis of the cancer cells [1, 2]. Maximum temperature can reach and overcome 80-100 °C in specific location of the tumor. The energy conversion modalities related to the single technique and the heat transfer in the tumor, which are governed by the dieletric, optical, thermal and mechanical properties of the tissues, allow obtaining a spatial and temporal distribution of the temperature in the organs. These temperature values must be optimized in order to have the required therapeutic dose in the tumor (at least 50-60 °C for some minutes-seconds) able to induce irreversible thermal damage, while spearing the surrounding healthy tissue and structures. Thus, achieving optimal therapeutic outcomes relies on precise and conformal energy delivery localized to targeted tissues, as well as the real-time monitoring of the induced thermal effects in the tissue. Different modalities are presently in place for monitoring the temperature distribution in tissues undergoing minimally-invasive ablation treatments, like standard thermocouples embedded in the MW antennas or RF electrodes, or magnetic resonance imaging thermometry. These techniques, even tough usually selected by manufacturers of ablation devices, still present some drawback, such as: overestimation of temperature and artifact due to magnetic susceptibility [3]. For these reasons, the opportunity to identify performant measurement systems is still a major goal in the field of temperature monitoring of tumors undergoing thermal therapies [4].

A viable solution which has been increasingly studied in last decade is represented by optical methods. In particular, fiber optic sensors (FOSs) have proven to be a suitable technology for designing thermometers dedicated to the monitoring of temperature distribution in tumors and in organs undergoing thermal ablation procedures. Indeed, small-size and flexible FOSs are increasingly entering in the design of minimally invasive medical devices [5,6]. Technologies based on high-density Fiber Bragg Gratings (FBGs) or distributed sensing, based on Brillouin and Rayleigh scattering, allow for accurate and spatially resolved temperature measurement in the operative field. Other optical technologies have being recently proposed for correlating the change of tissue biomarkers with temperature [7], like hyperspectral imaging [8,9].

In the following paragraphs, the mentioned technologies and some of their applications in the specific field are presented.

2. OPTICAL TECHNOLOGIES FOR THERMAL EFFECTS MONITORING IN BIOLOGICAL TISSUES

Fiber Bragg Grating (FBG) sensors

An FBG is a spatial modulation of the refractive index inside the core of a single-mode optical fiber. This modulation, usually called grating, works as a selective mirror for specific wavelengths. When broadband light travels along the fiber, the grating reflects a small portion of it, in correspondence of a specific wavelength, which is called Bragg wavelength (λ_B), as shown in Fig. 1. This λ_B depends upon the effective refractive index of the fiber, n_{eff}, and periodicity of the modulation, Λ. FBGs are usable as thermometers, as the temperature ΔT cause a change of the optical properties of the grating, thus resulting in the change of λ_B:

$$\frac{\Delta\lambda_B}{\lambda_B} = \alpha\Delta T \qquad (1)$$

where α is the temperature sensitivity of the FBG, usually equal to 10 pm/°C [6]. Taking advantage from the multiplexing capability of the instrumentation, multiple FBGs can embed inscribed inside the core of a single fiber and allow quasi-distributed measurement. This feature is crucial for temperature monitoring during thermal therapies: it is desirable to have at least 10 gratings characterized by millimetric spatial resolution, in order to capture the thermal gradient generated in the target, which can be up to 50 °C/mm [5].

Hyperspectral imaging

Hyperspectral imaging (HSI) is a noninvasive optical sensing technique used for remote monitoring and increasingly investigated in the medical field [10]. HSI combines high-resolution spectroscopy with digital imaging: a camera acquires a series of images in multiple adjacent spectral bands, and the reflectance spectrum for each pixel in the image is reconstructed. Cameras working in the visible and the near-infrared (NIR) ranges are mostly used for medical applications. This imaging technique has already provided promising results as a tool for intraoperative guidance, in the diagnosis of disease, and in the prediction and classification of thermal damage induced by heat treatments [8,9]. HSI has proven to be an efficient method for monitoring tissue modifications induced by thermal therapies, as tissue biomarkers, like oxy-, deoxy- and met- hemoglobin, water, lipids, reveal temperature-related optical changes (Fig. 1).

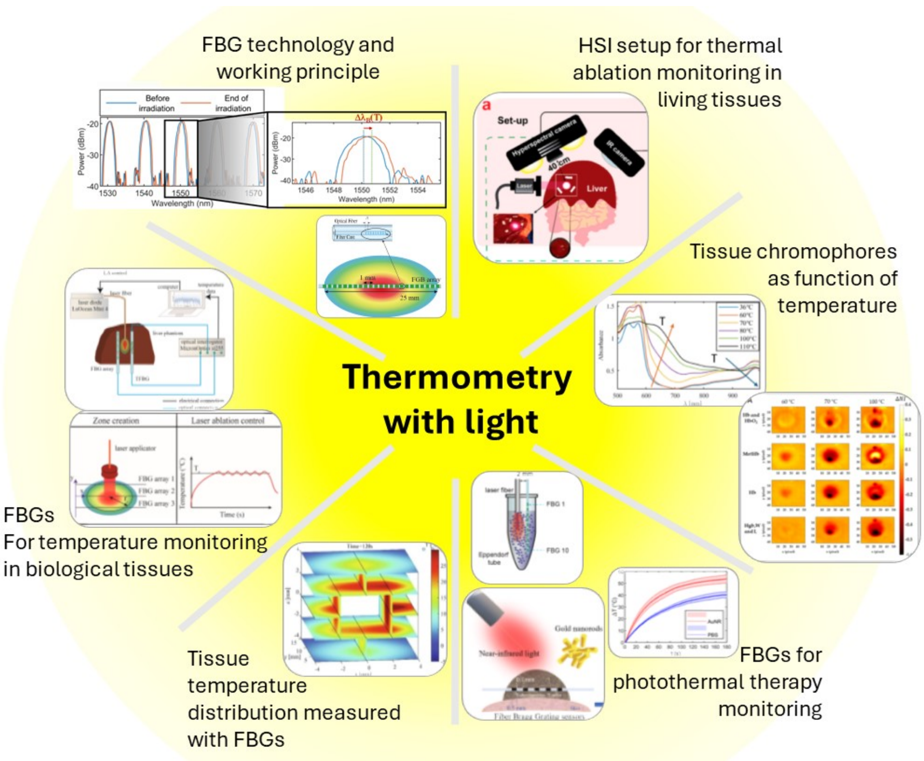

Figure 1. Overview of the applications of FBGs and HSI for monitoring thermal therapies.

3. OVERVIEW OF THE APPLICATIONS OF THE OPTICAL TECHNOLOGIES FOR THERMAL THERAPIES MONITORING

In the following paragraphs, the outcome of some studies using the mentioned technologies are reported.

FBG sensors for thermometry in biological tissues undergoing thermal therapies

The study by Morra et al. presents the comparison between FBGs and distributed sensing, based on Rayleigh scattering, for monitoring LA effects in biological tissues and tissue-mimicking phantoms [5], focusing on the effect of the sensor spatial resolution on the temperature measurements. Results show a low spatial resolution of the sensors (>1 mm) causes temperature underestimation with respect to 1 mm-long FBGs, which can reach up to 16 °C.

Thanks to their performances, FBGs can be used to evaluate the temperature distribution induced by different kind of laser applicators (characterized by different light emission patterns) and wavelengths, and can be also used to validate numerical models aimed predicting the laser-tissue interaction phenomena [11,12].

Our research group has devised the first temperature-based control strategy for modulating laser light based on temperature measured by FBGs, as described in the works of Korganbayev et al. [6,13,14]. Several strategies have been proposed, aimed at controlling the laser power according to the temperature measured at certain tissue locations, with the aim to confine the thermal damage within a specific tissue region, and to avoid inducing excessive and dangerous temperature increase in the organs.

The laser light can be used in combination with nanoparticles (NPs) delivered inside the tumor, to enhance the therapeutic effect and safety of the treatment, delivering a modality which is known as photothermal therapy (PTT). Also in this specific application it is pivotal to verify which is the temperature induced by the combined effect of laser and NPs. To this aim, our research group has carried out the first study for multipoint FBGs-based thermometry of gold nanorod-enhanced PTT in *in vivo* breast tumor model [15]. We could measure internal tumor temperature in 5 different locations, with sub-millimetric (0.5 mm) sensing length. The method has allowed also to assess the temperature rise caused by different combinations of gold NPs and laser wavelengths for tumor treatment, *i.e.*, a mean value of 13 °C *vs* 6 °C after 3 minutes of LA at 2.6 W, at 940 nm and 1064 nm, respectively.

In this application, before adopting NPs for PTT, it is mandatory to evaluate NPs thermal enhancement capability and potential release of NPs in cells from nano-carries due to the heating effects. Thus, we have carried out a large experimental campaign for assessing the thermal response of NPs made of different materials (*e.g.*, gold, copper oxide, silicon) and characterized by various features (black porous silicon NPs, spheres, rod, biodegradable nano-architectures). Also in this case, FBGs were employed, because we could use a chain of sensors in small tubes containing solutions of NPs undergoing NIR-laser irradiation. [16-19].

Hyperspectral imaging for thermal effect investigation in biological tissues undergoing thermal therapies

Different studies have been carried out, exploring the performances of HSI commercial systems for assessing the ability of the systems to detect the spectral variation of relevant temperature-dependent tissue chromophores, like deoxyhemoglobin, methemoglobin, lipids, and water, and the methods for extracting valuable information from HSI data. Experimental studies were conducted during thermal ablation procedures on pigs, with the focus to detect thermal damage induced in vital organs (such as the liver, pancreas, and stomach) during laser thermal therapy. Other studies have been carried out in *ex vivo* models undergoing LA and RFA [8,9,20]. In all works, the visible and NIR ranges were considered. The studies provided that, in general, a temperature of 70 °C causes a detectable change of the measured reflected spectrum, which might be related to the formation of methemoglobing at 65 °C [21].

4. DISCUSSION AND CONCLUSIONS

Several characteristics of the measurement systems must be taken into account before electing them as suitable technology for thermometry and thermal damage monitoring in biological tissues. FOSs and, in particular, FBGs, hold a long list of advantages which make them suitable for thermometry during thermal ablation procedures, *i.e.*, the high signal-to-noise ratio, the small size, the immunity to electromagnetic fields, the biocompatibility and the inertness [22]. Moreover, the wavelength-division multiplexing capability allows measuring the tissue temperature distribution on tens of locations with a spatial resolution at the millimetric scale. The femtosecond laser inscription is the most recent technique for inscribing FBGs in the fiber core, and enable high customization of the gratings length and spatial resolution. FBGs have been used to monitor tissue temperature during many thermal ablation techniques, including LA, RFA and MWA. One of the main challenges is the cross-sensitivity of FBGs to strain (e.g., breathing motion, body tremor during procedures), which can be mitigated by solution for embedding the fiber and limiting the strain transfer. HSI is still at the investigation stage, especially for the mentioned purpose, but holds the main feature to become a prospective technique. Due to the limited light penetration in tissues in the visible and NIR ranges, it is effective for monitoring superficial thermal effects [8-10, 20]. Dedicated protocol for data acquisition, reduction and processing are under development, with the aim to manage the huge amount of data produced with a single acquisition.

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