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Multidistance time domain diffuse optical spectroscopy in the assessment of abdominal fat heterogeneity

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ABSTRACT

A periodic monitoring of the adipose tissue functions due to interventions, such as calorie restriction and bariatric surgery, or pathophysiological processes, has an increasing relevance in clinical diagnostics. Diffuse Optical Spectroscopy (DOS) is a valuable non-invasive tool that can be used in that direction. In this work, we present a pilot study based on Time Domain Broadband Diffuse Optical Spectroscopy (TD DOS) to characterize *in vivo* the subcutaneous fat tissue in the abdominal region. A first of its kind, portable TD DOS instrumentation, already enrolled in clinical studies, was used. Three healthy male volunteers were considered. Three source-detector separation distances (1, 2, and 3 cm) were used over the broad wavelength range of 600-1100 nm. The analysis was performed using a method based on a heterogeneous model to account for the multi-layered nature of the subcutaneous adipose tissue, and to obtain the optical properties specific to this fat localization. Inter-subject variation of tissue composition data was observed.

Keywords: abdomen, fat, diffuse optics, non-invasive, heterogeneous, time domain, adipose tissue, absorption

1. INTRODUCTION

Until recently, adipose tissue was thought to be an inert tissue, that stores energy-providing lipids (triglycerides). On the contrary, current research demonstrates that adipose tissue must be considered as a single, plastic organ in mammals, including humans [1]. A diffuse endocrine gland constituted by different cell types (white, brown, and beige adipocytes) with diverse properties. Fat, present in different parts of the body, has different biological characteristics and a tremendous influence on the metabolic function and energy balance. Especially for sedentary and aging societies as in Western countries, excess unwanted fat accumulation could lead to obesity and related disorders, including type 2 diabetes, with increased cardiovascular risk and overall accelerated aging process [2]. Therefore, a periodic monitoring of the “adipose organ" function (secretome) and plastic changes due to nutritional intervention, such as caloric restriction, disease state, physical exercise, or surgical treatments, has increasing relevance in medicine.

Diffuse optical spectroscopy (DOS) is a valuable technique that has been extensively used to probe non-invasively various organs of the human body, like breast, forehead, and bone [3–6]. In fact, a recent study has successfully demonstrated the use of this technique on the abdominal fat tissue of patients undergoing caloric restriction, by showing a strong correlation between diet control and variation in both the absorption and scattering properties [7].

However, the accurate monitoring of the fat layer using the DOS technique faces one major challenge - the complex multi-layered structure of human body. The fat layer is usually sandwiched between the thin layer of skin/dermis on the top and the underlying muscle layer. Both layers contribute to the absorption and scattering spectra obtained by means of DOS measurements, thereby contaminating the information on fat tissue, if not properly disentangled.

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In this paper, we use a Time Domain Broadband Diffuse Optical Spectroscopy (TD DOS) system for the non-invasive characterisation of subcutaneous fat tissue, specifically at the abdominal region. This system has been enrolled in various clinical and phantom studies in the past [5,8,9]. We consider a set of multidistance time-resolved measurements [10] and fit the data to a heterogeneous model to investigate the layered nature of the abdomen. Our aim is to build strong basic knowledge on the effect of experimental and anatomical factors, including probe location and superficial tissue thickness, on the spectral information gained from the abdomen tissue. This would be a useful first step for an upcoming clinical study.

2. MATERIALS AND METHODS

2.1 Instrumentation

A detailed description of the instrumentation used has been presented elsewhere [11]. A supercontinuum fiber laser (SC450, Fianium, UK), with a spectral range of 450-1750 nm generating picosecond pulses (60 MHz repetition rate), was used as the source, and a Silicon Photomultiplier (SiPM) [12], [13] detector with a good responsivity over the wavelength range 600-1100 nm was used as the detector along with a PC card for time-correlated single photon counting. The injection and detection fibers were plastic-glass fibers with 200 μm and 1 mm core, respectively. The system was designed to acquire the Instrument Response Function (IRF) for each measurement within the same temporal window, which could also be used for drift and distortion compensation [11].

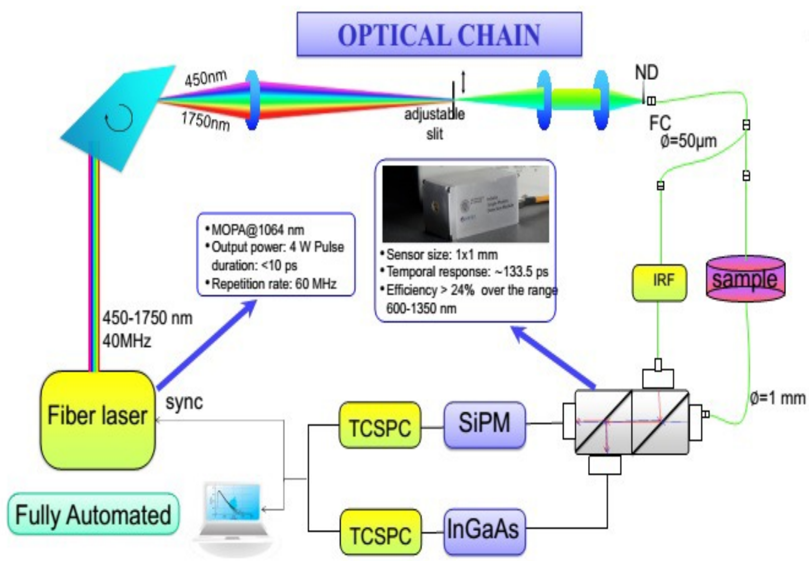

Fig. 1. Layout of the clinical prototype.

2.2 In vivo study

The study is presently on-going. At present, 3 male volunteers were enrolled. The demographics are summarised in Table 1, where “Thickness” refers to the subcutaneous adipose layer thickness measured using the skinfold technique. The measurements were performed on the right of the navel, at a distance of 4 cm from it, with the subject lying supine. For each position, the temporal point spread functions (TPSF) were obtained at three source-receiver distances ρ = 1, 2, and 3 cm, spanning the broad wavelength range of 600-1100 nm in steps of 10 nm. At each wavelength, 4 repetitions of 1 s each were acquired. Informed written consent was obtained from all subjects prior to the study.

Table 1 – Demographics of the subjects involved in the study.

Subject	Age (y)	Height (m)	Weight (kg)	Body Mass Index (kg/m^2)	Thickness (cm)
#1	50	1.75	82	26.8	2.3
#2	44	1.84	100	30.0	2.3
#3	74	1.74	66	21.8	1.2

3. DATA ANALYSIS

3.1 Homogeneous Model

The reduced scattering and absorption coefficients (μ'_s and μ_a) at each wavelength were obtained by fitting the experimental curves (shown in Figure 2) to a diffusion approximation of the radiative transport equation for a homogeneous semi-infinite medium under the assumption of an extrapolated boundary [14], [15]. The theoretical curves were convolved with the IRF and normalized to the area under the experimental curve [16]. The μ_a and μ'_s values were then retrieved by achieving a best fit between the theoretical and experimental curves using a Levenberg-Marquardt minimization algorithm. This method was performed for each source-detector separation, giving us 3 absorption and scattering spectra per subject.

3.2 Heterogeneous Model

The data was also fit to a bilayer model to extract the optical properties of the superficial dermal layer as well as the underlying fat layer. All the three source-detector separation data were simultaneously fit to a bilayer model of the transport equation using the same minimization algorithm described above [17], [18]. Since different source-detector separation data probe different layers of the tissue, such a simultaneous fit would give a more accurate description of the layered nature of the tissue under investigation. The bilayer model used typically retrieves 5 parameters in total: the absorption and scattering of the top and the bottom layers and the thickness of the top layer. Of these, two parameters were fixed. The thickness of the top layer was not exactly known. So, it was fixed for all subjects to 7.5 mm, a value which is expected to overestimate actual values, in such a way that the second layer probed would predominantly be the fat layer. Also, the bottom layer's scattering coefficient was assumed to be the scattering coefficient of the largest source-detector separation. This helps stabilize the fit and lead to a faster convergence. In this way we obtain two sets of absorption and scattering spectra per subject, for the top and the bottom layers, respectively.

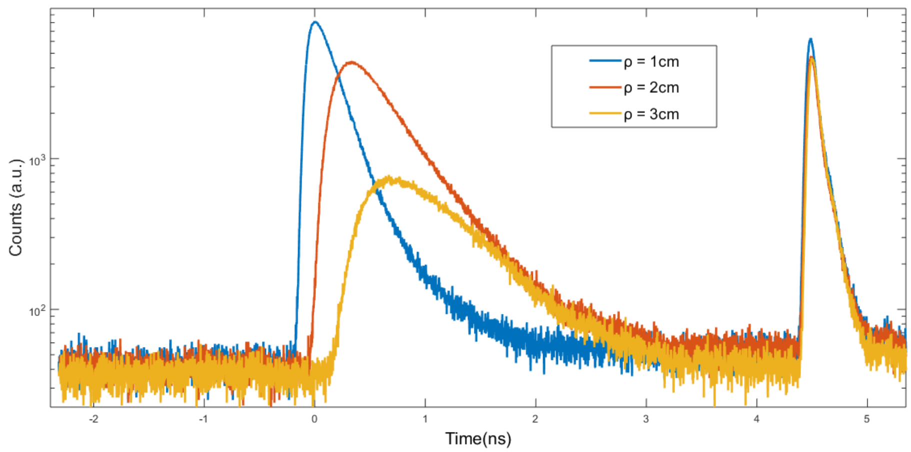

Fig. 2. Typical time dispersion curves for different source-detector separations (ρ) at the same wavelength. The sharp peak on the right corner is the Instrument Response Function (IRF).

4. RESULTS AND DISCUSSION

Figure 3 shows the absorption spectra from the abdominal region of the 3 subjects recovered from the standard homogenous analysis (left) and the novel multidistance based bilayer model (right). The analysis with the homogeneous model shows an increasing influence of the absorption properties of the bottom layer (adipose tissue dominated by lipid absorption at 930 nm) upon increasing source-detector distance, but only a qualitative trend can be obtained. The bilayer model clearly disassociates the two layers of this tissue in terms of spectral trends and absorption coefficient values. A closer observation reveals that the top layer for each of the subjects displays a predominant spectral signature beyond 950 nm. This indicates the presence of water (peak around 970 nm) in the superficial (dermal) layer. This peak is most pronounced for subject #2, who is expected to have thicker dermis, based on his high Body Mass Index (BMI). Clearly, this peak is absent in the bottom layer spectrum, which shows for each of the subjects only the sharp lipid peak at 930 nm as its dominant feature.

Figure 4 compares the reduced scattering and absorption spectra of the bottom layer amongst the 3 subjects. It can be observed that the scattering spectrum flattens with increasing age of the subject. Notably, this data could give valuable insights into the size and the kind of adipose cells present in this region, in addition to their dynamics. Also variation of the absorption spectra among subjects is another important observation. Here we can see that the spectral trends mostly remain unchanged for different subjects irrespective of their age and BMI. This confirms that, independent of thickness and composition of the superficial layer, we are probing the same underlying fat layer for all 3 subjects.

While the two layers have been disentangled spectrally, a reliable estimation of the absorption coefficients still faces a significant challenge: an over estimation of the optical properties of the top layer, which in turn leads to an under estimation in the properties of the bottom layer. This could be attributed to the bilayer model. A future step in this direction will be to perform an accurate phantom based study to understand and improve the minimization algorithm.

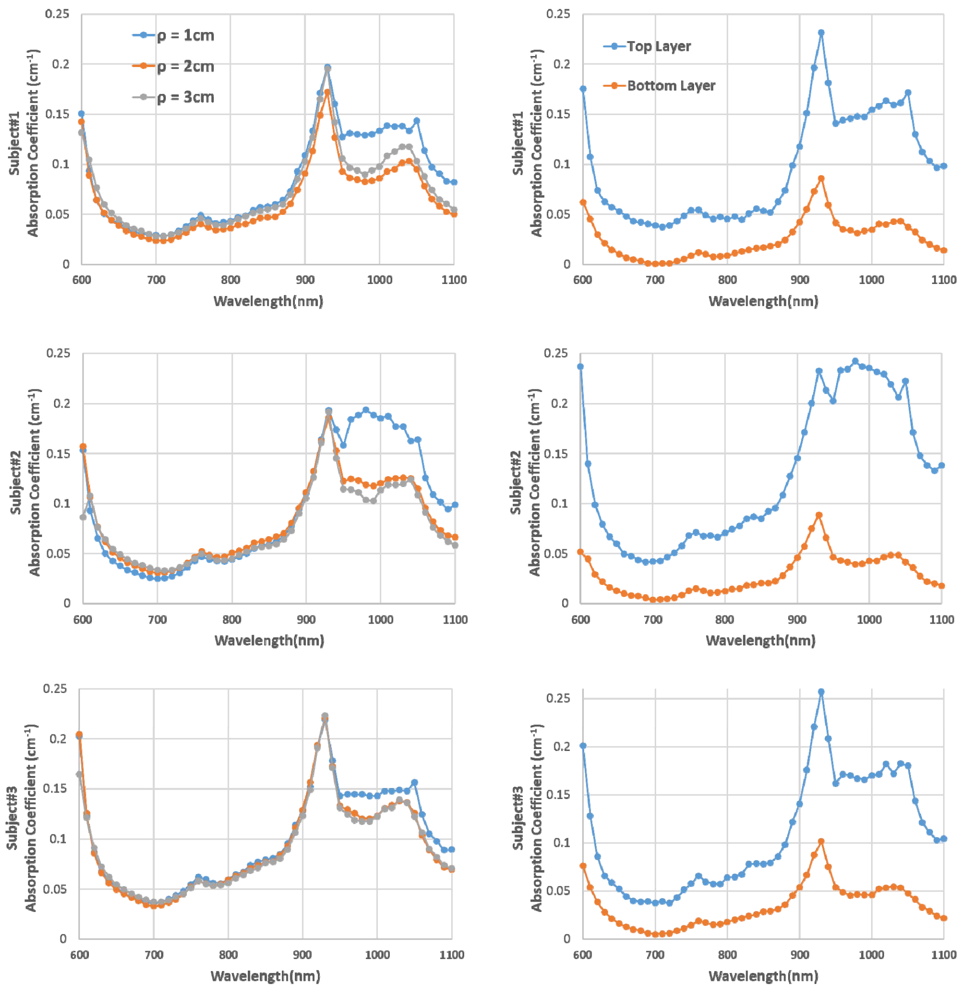

Fig. 3. Absorption spectra for the 3 subjects obtained at multiple source-detector separations using a homogeneous model (left), and for the top and bottom layers using a bilayer model (right).

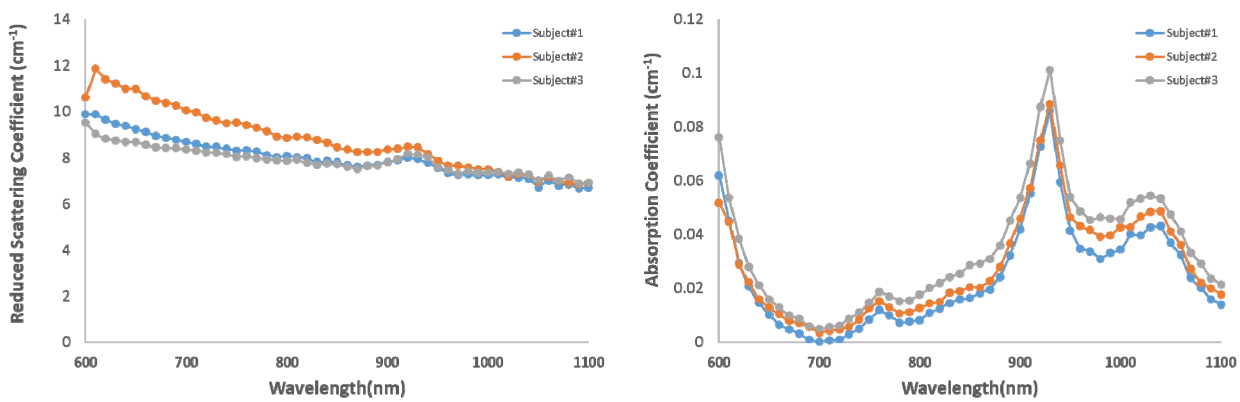

Fig. 4. Reduced scattering and absorption spectra of the bottom layer for the 3 subjects, showing the inter-subject variation.

5. CONCLUSIONS

Here we have reported, for the first time to the best of our knowledge, a complex study performed *in vivo*, on a broad wavelength range (600-1100), using time domain diffuse optics to analyse abdominal subcutaneous adipose layers. We have succeeded in extracting specific spectra for the fat layer in the abdominal region of 3 male subjects, and in disentangling fat layer from contaminations caused by the superficial dermis. Some preliminary inter-subject trends in the absorption and scattering spectra have been shown as well.

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