LASERLAB-EUROPE

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WP 30–Laser and Photonics for Biology and Health
(BIOPTICHAL)

Deliverable D30.15
"Workstations for broadband TRS based on short pulse generated supercontinuum and advanced DCS instrumentation"

Lead Beneficiary: POLIMI

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Deliverable Nature	
R = Report, P = Prototype, D = Demonstrator, O = Other	R
Dissemination Level	
PU = Public PP = Restricted to other programme participants (incl. the Commission Services) RE = Restricted to a group specified by the consortium (incl. the Commission Services) CO = Confidential, only for members of the consortium (incl. the Commission Services)	PU

A. Abstract

Two prototypes for broadband Time-Resolved Diffuse Optical Spectroscopy (TRS) and Diffuse Correlation Spectroscopy (DCS) were developed and finalised for clinical use. The TRS system is based on a supercontinuum pulsed laser source and time-correlated single-photon counting detection, and permits continuous acquisition of absorption and reduced scattering spectra in the 600-1300 nm range for the assessment of tissue composition and structure. A complete spectral measurement can be taken automatically in about 10 minutes, compatible with in vivo use. The DCS system operates around 800 nm with high temporal coherence laser sources and avalanche photodetectors to retrieve changes in blood flow particular in neuromonitoring. A full acquisition requires few seconds of measurements, and is thus suitable for in vivo continuous monitoring of blood flow. The two prototypes are portable and suitable for use in a clinical settings. Extensive tests were performed on shared protocols and reference phantoms. The work was conducted in collaboration between POLIMI, UL, and ICFO.

B. Deliverable Report

1 Introduction

The study of light propagation through highly diffusive media is a powerful tool to investigate non-invasively the physiological and pathological status of biological tissues in vivo. Within the BIOPTICHAL JRA, two techniques were translated from the basic laboratory settings to movable prototypes apt to be used in a clinical environment.

The first technique is Time-Resolved Diffuse Optical Spectroscopy (TRS) based on the detection of the temporal broadening of a short laser pulse propagating through the biological tissue. The analysis of the photon temporal distribution with a proper model of photon migration permits to retrieve the absorption and reduced scattering coefficient of the traversed medium. When this technique is combined with a pulsed and broadly tuneable laser source, both the absorption and reduced scattering spectra of the visited medium can be assessed, leading to information on the tissue chemical composition (e.g. oxy- and deoxy-hemoglobin, water, lipids, collagen, …) and on the microstructure (size and density of scattering centres). LaserLab Europe has fostered the development of this approach at the laboratory level, with the first installations at the Lund Laser Centre and at POLIMI-CUSBO, and now is pushing the translation of prototypes to clinics.

The second technique is Diffuse Correlation Spectroscopy (DCS) that investigates the autocorrelation function of a high temporal coherent source propagated through the medium and detected at some distance (few cm) from the injection point. The motion of scattering centres within the medium – in particular red blood cells – causes a phase shift in the scattered field causing a deformation of the autocorrelation function dependent on the strength and speed of the scattering centres. The analysis of the autocorrelation function with a Diffusion based model yields information on the blood flow. This recent approach is particularly suited to monitor cerebral blood flow both in physiological (e.g. functional brain studies) and in pathological conditions (e.g. stroke, traumatic brain injury). The research group at ICFO has actively contributed to the proposal of this technique, and is now quite advanced on the design and application of clinically oriented instruments.

2 Objectives

The key objectives of the deliverable are:

1 – further development of two prototypes for broadband TRS and DCS in particular for what concerns light harvesting and measurement time.

2 – finalisation of the prototypes towards use in a clinical environment.

3 – validation at the laboratory level.

3 Work performed / results/ description

The two prototypes have been completed and are now fully operative. A description of the schematics of the two prototypes, together with the work performed and the first results on the use of the systems is provided in the following.

3.1 – TRS PROTOTYPE (main partner: POLIMI)

3.1.1 – system setup

A schematic of the system is presented in Figure 1. The source is a supercontinuum fibre laser emitting pulsed white light radiation over the spectral range 450 nm to 1750 nm with an overall power of 5 W. A typical pulse duration is in the order of tens of picoseconds, with a repetition rate of 80 MHz. The white light is then dispersed by an F2-glass Pellin-Broca prism and light of the selected wavelength is focused onto an adjustable slit to achieve better spectral selection. Light is coupled into a 100 μm graded-index optical fibre and subsequently injected into the scattering medium. Diffused light at the distance of few cm from the injection point is collected using a 1 mm core multimode step-index fibre and separated into two beams by a 50/50 beamsplitter mirror. Half of the collected signal is sent to a home-made Silicon Photomultiplier (SiPM) detector, whereas the other half is sent to a photomultiplier tube (H10330A-25, Hamamatsu, Japan). The electronic signals arising from the detectors are connected to two different time-correlated single-photon counting (TCSPC) boards (SPC-130, Becker&Hickl, Germany) together with a synchronization signal derived from the laser. The set-up is also provided with a reference arm to compensate for the temporal drift of the laser.

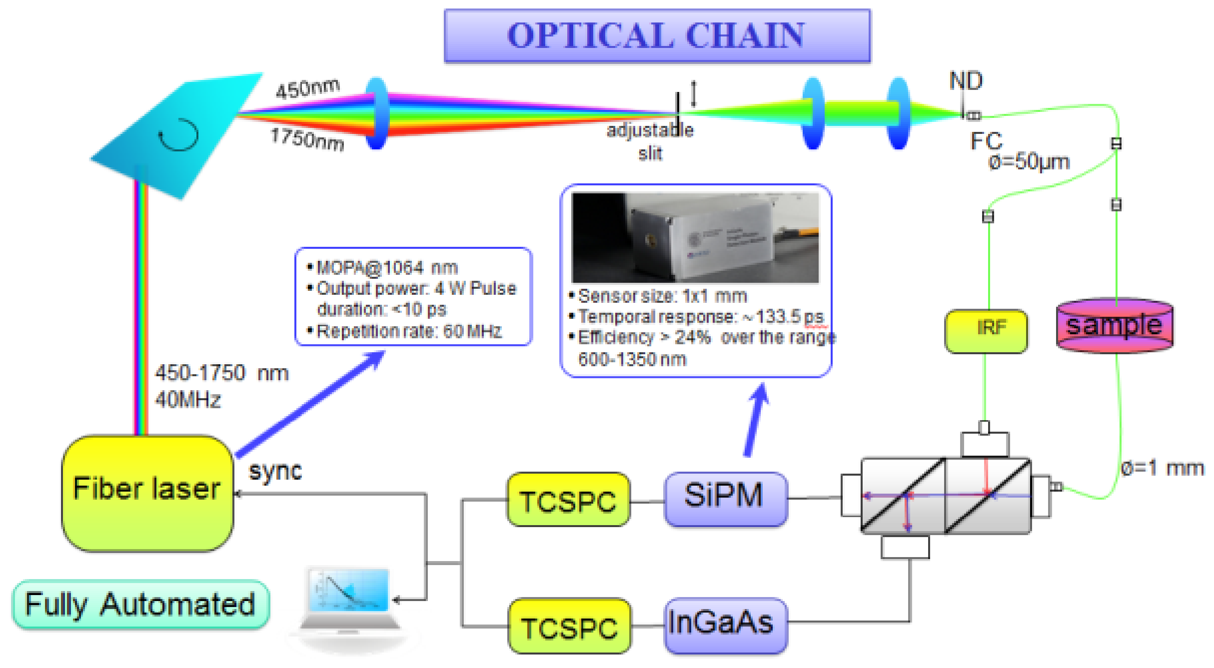

Figure 1 – setup of the broadband TRS prototype developed at POLIMI.

The absorption and reduced scattering spectra of the medium are retrieved from the time-resolved curves measured at different wavelengths by means of a nonlinear least-square fitting procedure exploiting a model for photon migration in diffusive media based on the solution of the diffusion equation with extrapolated boundary conditions in the semi-infinite geometry.

The system is hosted in a standard rack cabinet mounted on wheels, as shown in Figure 2. A fully automated measurement procedure is implemented via a dedicated software, which permit smooth acquisition and analysis of the absorption and scattering spectra in the whole 600-1300 nm range in about 10 minutes with large flexibility and adaptability to different operating conditions (e.g. choice of source-detector distance, range of absorption and scattering coefficients covered).

Figure 2 – photo of the broadband TRS prototype developed at POLIMI.

3.1.2 – work performed

The specific contribution of the BIOPTICHAL JRA, that was favoured by fruitful interaction between POLIMI and ICFO where:

- Introduction of the SIPM detector – specifically optimised at POLIMI – which permitted to increase the overall system responsivity in the 600-1000 nm range, as compared to previous solutions, an thus to extend the range of applicability of the system and reduce the total acquisition time;
- Design of a proper spectral strategy with the combined use of two detectors and the reference to extend the spectral coverage continuously in the whole 600-1300 nm range with smooth automatic operation, and compensate for temporal drifts for increased reliability and reproducibility in a clinical environment.
- Adaptation of the system to a rack cabinet, to comply with requirements of portability and compactness needed for use in clinics.
- Implementation of proper electrical and laser safety issues to comply with use of the prototype in a clinical environment.
- Thoroughly test of the system performances using well established protocols for assessment of diffuse optics instruments such as the BIP (temporal response, non-linearity, stability, responsivity, noise) and the MEDHOP Protocols (accuracy, linearity, noise, stability, reproducibility). These tests were made possible also with the strong interaction between POLIMI, ICFO, and UL for the accurate characterisation of reference materials.

3.1.3 – results

The developed system was used for the optical characterization of different scattering materials at the laboratory level, namely: collagen, elastin, wood samples, food products, porous ceramics. Due to its outstanding performances in terms of spectral coverage, it was also used for the spectral characterisation of a new kind of switchable inhomogeneous phantom, which could be extremely simple and rugged for performance assessment and quality check of clinical instruments. An example of the measured absorption and scattering spectra of the reference homogeneous material is shown in Fig.3, which demonstrate also the wide-range capability and the quality of the recovered spectra.

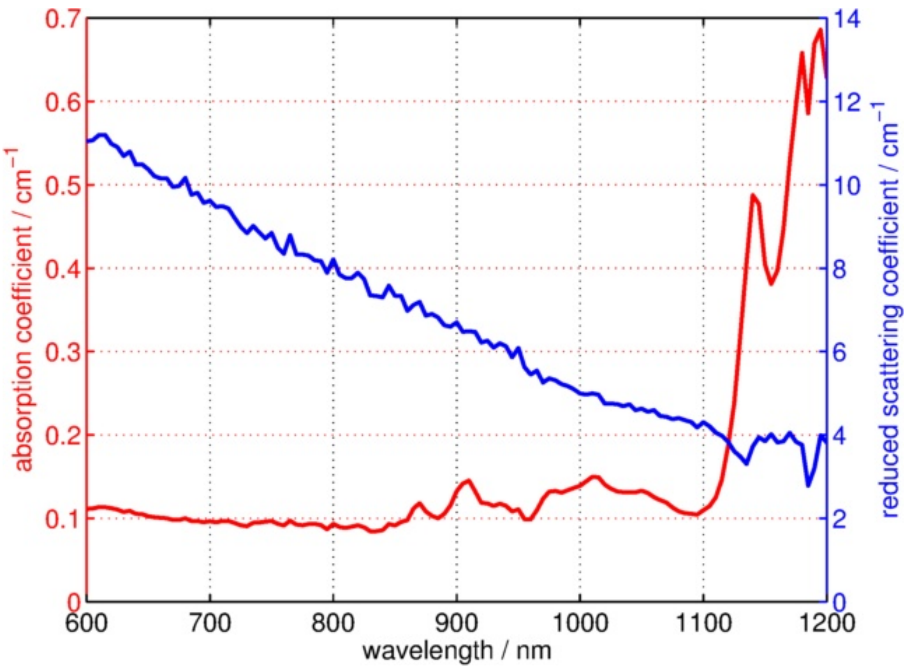

Figure 3 – absorption and scattering spectrum of the homogeneous matrix of a new concept of solid switchable phantom for use in performance assessment and quality check of clinical instruments.

3.2 – DCS PROTOTYPE (main partner: ICFO)

3.2.1 – system set-up

A schematic of the system is presented in Figure 4. On the left, one of the ICFO DCS platforms is shown. This system consists of eight independent detector channels and four switchable source positions powered by a single 785 nm laser. The intensity auto-correlation functions are calculated in real-time by a eight channel hardware correlator and the results are fitted by a correlation diffusion model. The live display shows the relative blood flow as it is calculated. The system is controlled by a touch screen laptop and a user-interface that is suitable for clinical use. One feature of the hardware is that most major functions can be controlled by external hardware signals (digital and analogue) and they report about their functioning as an output. This enables the system to be used either as a “master” or as a “slave” when it is being connected to a TRS system. The data can be acquired either sequentially or in a parallel fashion with properly designed optical probes.

3.2.2 – work performed

The specific contribution of the BIOPTICHAL JRA, that was favoured by fruitful interaction between POLIMI and ICFO where:

- ❑ Introduction of the professional user-interface;
- ❑ Introduction of software modules that allow communication and display of TRS data.
- ❑ Adaptation of the system to an enclosure to comply with requirements of portability and compactness needed for use in clinics.
- ❑ Implementation of proper electrical and laser safety issues to comply with use of the prototype in a clinical environment.
- ❑ Detailed tests of the system in novel new phantoms.

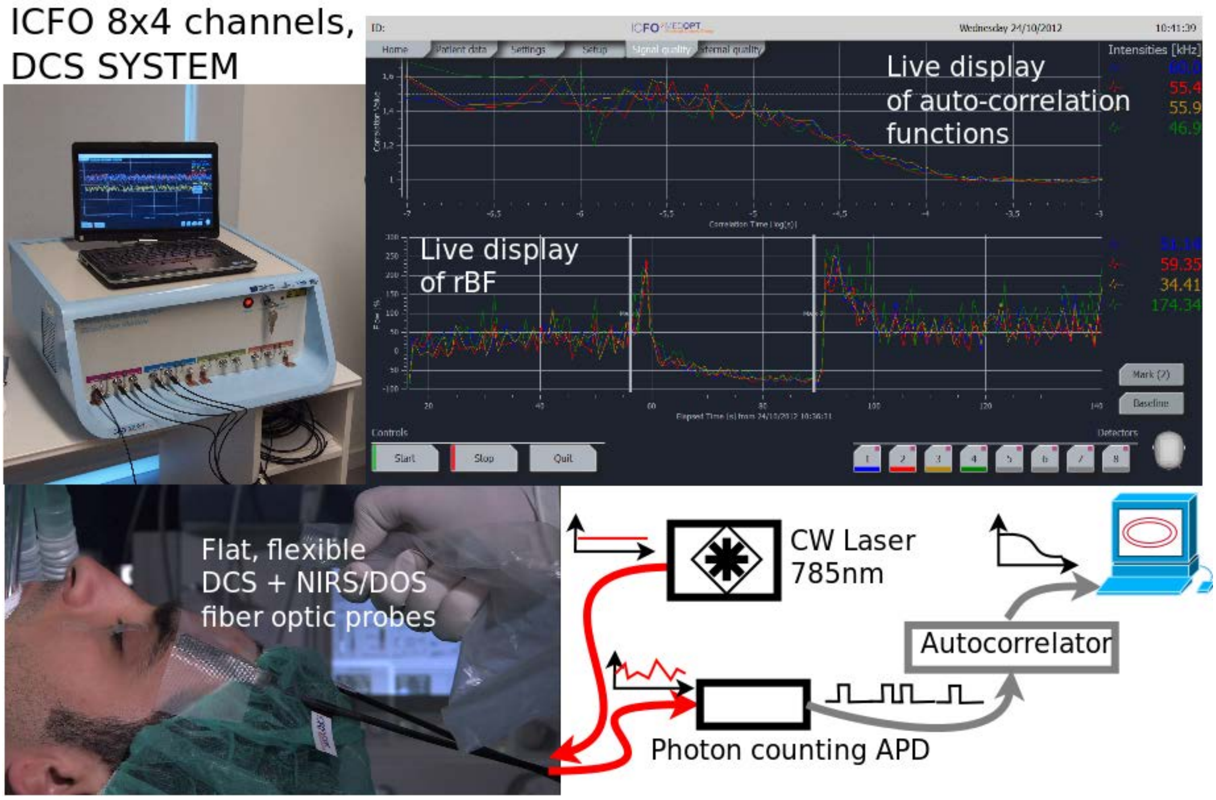

Figure 4 Schematics, photos and screenshots of the ICFO DCS system.

3.1.3 – results

The new system was used in studies on healthy subjects, flow phantoms and in industrial applications. One indicative result is shown in Figure 5. Here we show the measured Brownian diffusion coefficient of scatterers in a tissue phantom over ~10 hours. The variability is very small (~1.16%). The fitted auto-correlation curves showed variability less than 0.01% in the instrument coefficient and the tail and its characteristic decay is reflected in the variability of the Brownian diffusion coefficient variability of ~1.16%. This translates to excellent performance potential for physiological measurements where the intrinsic variability of blood flow over few minutes is greater than ~3%.

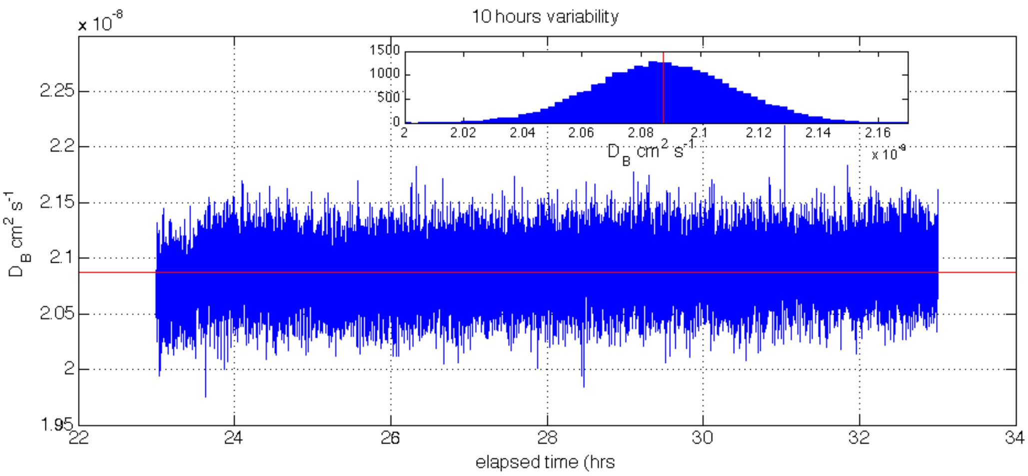

Figure 5 Brownian diffusion coefficient (DB) values recorded on a liquid phantom; in the small box, distribution of the values recorded is shown. Red line represents the average of data

4 Conclusions

In conclusion a broadband TRS prototype and a DCS prototype were fully developed and finalised for clinical use. Both instruments stem from the excellence of LaserLab Europe facilities on these two specific techniques at the laboratory level and now are ready for use in a clinical environment. The work was conducted in collaboration between POLIMI, ICFO, and UL.

5 Publications

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