Summary of Professional Accomplishments Appendix 4 to the request of Dr. Maciej Szkulmowski to conduct the habilitation procedure in the field of physical sciences in the discipline of physics. May 21, 2014.

### 1. Name.

Maciej Tomasz Szkulmowski

- 2. Held diplomas, degrees with the name, place and year of their acquisition and the title of the doctoral dissertation.
  - 2003 master's degree in physics, specialization Experimental Physics, Faculty of Physics, Astronomy and Informatics, Nicolaus Copernicus University in Toruń,
  - 2004 master's degree in physics, specialization Computational Physics, Faculty of Physics, Astronomy and Informatics, Nicolaus Copernicus University in Toruń,
  - 2008 doctor of physical science in physics, Faculty of Physics, Astronomy and Informatics, Nicolaus Copernicus University in Toruń, "Numerical methods of increasing the quality of the images in spectral optical tomography".

### 3. Information on previous employment in scientific/artistic institutions.

Since 2008 - Associate Professor, Faculty of Physics, Astronomy and Informatics, Nicolaus Copernicus University in Toruń.

4. Indication of the achievements resulting from Art. 16 paragraph. 2 of the Act of 14 March 2003 on Academic Degrees and Title and Degrees and Title in Art (Journal of Laws No. 65, item. 595, as amended.).

As a scientific achievement resulting from the act, I point monothematic series of publications on the spectral and time domain optical coherence tomography technique I developed, under the collective title:

## Spectral and Time domain Optical Coherence Tomography (STdOCT)

The achievements includes the following publications (numbering is identical to Appendix 5):

IB.1. M. Szkulmowski, A. Szkulmowska, T. Bajraszewski, A. Kowalczyk, M. Wojtkowski, "Flow velocity estimation using joint Spectral and Time domain Optical Coherence Tomography", Optics Express 16 (2008) 6008-6025.

Impact factor: 3.880, number of citations: 88, my involvement: 60%.

IB.2. A. Szkulmowska, M. Szkulmowski, D. Szlag, A. Kowalczyk, M. Wojtkowski, "Three-dimensional quantitative imaging of retinal and choroidal blood flow velocity using joint Spectral and Time domain Optical Coherence Tomography", Optics Express 17(13) (2009) 10584-10598.

Impact factor: 3.278, number of citations: 50, my involvement: 40%.

IB.3. M. Szkulmowski, I. Grulkowski, D. Szlag, A. Szkulmowska, A. Kowalczyk, M. Wojtkowski, "Flow velocity estimation by complex ambiguity free joint Spectral and Time domain Optical Coherence Tomography", Optics Express 17(16) (2009) 14281-14297.

Impact factor: 3.278, number of citations: 18, my involvement: 65%.

IB.4. M. Szkulmowski, I. Gorczynska, D. Szlag, M. Sylwestrzak, A. Kowalczyk, and M. Wojtkowski, "Efficient reduction of speckle noise in Optical Coherence Tomography", Optics Express 20(2) (2012) 1337-1359.

Impact factor: 3.587, number of citations: 18, my involvement: 70%.

IB.5. B. F. Kennedy, M. Wojtkowski, M. Szkulmowski, K. M. Kennedy, K. Karnowski, and D. D. Sampson, "Improved measurement of vibration amplitude in dynamic optical coherence elastography", Biomedical Optics Express 3(12) (2012) 3138-3152.

Impact factor: 2.333, number of citations: 6, my involvement: 35%.

IB.6. M. Szkulmowski and M. Wojtkowski, "Averaging techniques for OCT imaging", Optics Express 21(8) (2013) 9757-9773.

Impact factor: 3.587, number of citations: 3, my involvement: 95%.

IB.7. A. Bouwens, D. Szlag, M. Szkulmowski, T. Bolmont, M. Wojtkowski, and T. Lasser, "Quantitative lateral and axial flow imaging with optical coherence microscopy," Optics Express 21(15) (2013) 17711-17729

Impact factor: 3.587, number of citations: 1, my involvement: 20%.

Spectral and time domain optical coherence tomography (STdOCT) is a method of data acquisition and analysis that can be used in various embodiments of Fourier domain optical coherence tomography (FdOCT), which under one computational scheme allows for extraction of information about the structure, speed distribution, as well as elastic and spectroscopic properties of the sample under investigation.

Fourier domain optical coherence tomography is an interferometric imaging technique that uses partially coherent light to reveal the internal structure of almost transparent objects [1, 2]. Commonly used for this purpose is the light of near infrared range of approximately 700 to 1300 nm, due to the availability of light sources with wide spectral range, which is necessary to achieve a micrometer imaging resolution. FdOCT uses a Michelson interferometer which in one arm has a stationary reference mirror and in t-he second the imaged sample is placed. The light returning from the two arms is combined in the third arm, wherein the detection occurs. The registered light spectrum is modulated and the spectral fringes have the frequency that depends on optical path difference between the arms of the interferometer. In case of more scattering layers in one of the arms of the interferometer, the registered signal is the sum of the spectral fringes of different frequencies. Application of Fourier transform allows to recreate optical scattering layers distance relative to the reference mirror and, consequently, the internal structure of the sample.

FdOCT can be divided into two main techniques differing in the way how the spectra fringes are detected. The first, so called spectral optical coherence tomography (SOCT), uses wideband light source and a spectrometer [3]. The second, swept source optical coherence tomography (SSOCT), exploits rapidly swept laser source and a photodiode as a detector to register spectral fringes in time [4]. Both techniques are competing in terms of speed of data acquisition. In the first, restriction is the speed of CCD or CMOS cameras placed in the spectrometer, and in the second the tuning speed of lasers. At present, the rate of spectra acquisition reaches hundreds of thousands of lines per second in SOCT [5], and several million in SSOCT [6].

The acquisition rate FdOCT techniques is thus two to three orders of magnitude greater than in the formerly common tomographs using time domain optical coherence tomography principle, where the interference signal was acquired by the photodiode during the mechanical movement of the reference mirror with speeds of acquisition reaching barely 4000 lines per second. Due to the very high speed of data acquisition, and thus the ability to collect in a short time the information about the three-dimensional structure samples to be tested as well as high sensitivity and high dynamic range [7] the FdOCT tomography has found a widespread use in medicine and biology [2], as well as an inspection tool for works of art and industrial materials [8]. Several companies offering commercial FdOCT devices for applications in medicine appeared on the market. Amongst them one constructed by Polish company Optopol Technology SA (now a wholly owned subsidiary of Canon Inc.) using the know-how of the Medical Physics Group NCU, of which I was at that time a member. SOCT Copernicus and Copernicus HR constructed by Optopol, were the world's first tomographs utilizing the FdOCT technique. I wish to note that the part of the software performing reconstruction of tomographic images from the recorded spectra was written by me using my proprietary software algorithms.

FdOCT as a non-contact and non-invasive technique is particularly suited to in vivo imaging of vulnerable tissue such as the human eye. Therefore, the next stage of development of technology

FdOCT is the development of methods for imaging not only the structure of tissues, but also their functions. So-called functional OCT allows for example quantitative determination of the velocity of movement as a function of depth [9], followed by the spatial distribution of the refractive index and the absorption spectrum as a function of wavelength of light [10, 11]. The aim of the work on the functional OCT is to develop optical methods for evaluation of the state of tissue in vivo. In particular, intensive work is conducted in the field of visualizing the blood flow velocity in major vessels and capillaries [12-14], what in the future might give information about tissue blood circulation. An important feature of this method is that no external application of fluorescent dyes (such as fluorescein or indocyanine green) is needed as the source of contrast is the movement of blood cells. Measurements of blood supply in conjunction with blood oxygenation (obtained from information about light absorption in the blood) will lead to imaging of metabolic processes in the tissues. As part of the development of techniques for functional FdOCT methods for visualizing the mechanical properties of tissues [15] and the distribution of the refractive index [16, 17] have also been developed. Imaging of mechanical properties of tissues seems to be of high importance, as changes in tissue stiffness often occur with pathological findings.

In 2008, on the wave of interest in the methods of functional FdOCT, I developed a novel method for determining the distribution of the projection of the velocity on the sample beam direction (longitudinal velocity), which I called spectral and time domain optical coherence tomography (STdOCT) [IB.1]. Previous methods of determining the longitudinal velocity were based on determination of the initial phase difference between the two registered spectral fringes. The phase difference is proportional to the change in the optical path difference that occurred between acquisitions of the two spectra. In practice, these techniques consisted of the determination of the phase differences between the Fourier transforms of the fringes, what gave the distribution of changes in the optical path as a function of depth. This is important in the case of samples composed of multiple dispersing layers moving at different speeds. Then, knowing the time between acquisitions of the two spectra the longitudinal velocity distribution as a function of depth could be determined. The problem began to appear when to increase the sensitivity of velocity measurement a moving object was observed during a larger number of acquisitions and the calculated phase differences between registered spectral fringes were averaged. Thus obtained velocity strongly depended on signal to noise ratio and the absolute value of the velocity. In order to solve this problem instead of calculating the phase differences I used two-dimensional Fourier transform of a set of spectral fringes collected in successive moments of time. As a result of such an operation the distribution of the longitudinal velocity is obtained as a function depth into the sample. This method uses the information contained in all the collected spectral fringes and at the same time takes into account the different signal to noise ratio in each of the spectra. Consequently, this technique has a higher sensitivity and allows to determine the longitudinal velocity with greater accuracy than previously known methods. In [IB.1] I introduced the so-called STdOCT diagram that shows all the possibilities for the implementation of the Fourier transform on the collected set of spectral fringes and is a convenient tool to design data analysis methods for functional FdOCT. STdOCT diagrams for the simple case of a moving mirror and a laminar flow of liquid in the capillary tube are shown in Figure 1, while Figure 2 shows the necessary numerical steps needed to obtain the tomograms using STdOCT and by using classical methods.



Fig. 1. STdOCT diagrams. The measured data are in the upper left corner of each diagram. Horizontal transitions are accomplished by Fourier transformation along wavenumber axis, vertical – by Fourier transformation along time axis. Amplitude of the complex signal is displayed for visualization purposes. Useful information can be easily extracted from the signal subjected to double Fourier transformation (panels in the lower right corner of the diagram). In this panel for each depth in the sample (within the available range) intensity of the scattered light and the Doppler frequency associated with the movement of scattering centers at this depth can be read (see also Figure 2). In this panel, the images are symmetrical with respect to a central point due to the fact that the original data is real valued. (a) STdOCT diagram for experiment with a moving mirror as the object. Red arrows indicate the position of the image and its conjugate mirror image. Position of the point simultaneously gives information about the position and velocity of the mirror relative to the reference mirror. (b) STdOCT diagram for experiment with scattering fluid flowing in a glass capillary. The parabolic velocity distribution as a function of depth is visible. Figure is taken from [IB.3].



Fig. 2. STdOCT diagram for the data obtained from the retina of the human eye with the sequence of actions needed to produce tomographic images by STdOCT. 1. Preprocessing (fixed-pattern noise reduction, resampling to wavenumber space, dispersion compensation). 2. Spatial Fourier transformation (FT) to in-depth position. 3. Classical methods for obtaining the structural and functional tomograms (averaging amplitudes of transforms in order to obtain the structural image and averaging the phase differences of transforms in order to obtain longitudinal velocity map). 3'. Temporal FT to Doppler frequency. 4'. Creating images in the STdOCT method. For each depth position the distribution is found. The central value of the distribution is proportional to the longitudinal velocity and used to create velocity maps, while the amplitude of the distribution is proportional to the intensity of scattered light and is used to create structural tomograms.

Figure is taken from [IB.6].

I have also shown quantitative differences in the quality of the estimation of velocity between STdOCT, and previously used methods of phase analysis [9]. I have also proved that it is possible to quantitatively determine of the longitudinal velocity in the human eye in vivo, with exposure times of the order of 1 µs. Taking advantage of these properties of the STdOCT method in combination with high-speed data acquisition offered by the SOCT, we showed in the following year its use in a three-dimensional structural and functional imaging of the retina of the human eye in vivo [IB.2]. This paper presents a three-dimensional map of the longitudinal velocity in the areas surrounding the optic disc and macula. These results are shown in Figure 3 and Figure 4 below. We have also developed a technique to suppress the effects of movement of the entire sample (which is

unavoidable in the case of the human eye imaging in vivo) using only the information provided by STdOCT. We have also shown that besides quantitative information about the distribution of longitudinal velocity in large and medium-sized blood vessels of the eye, angiographic maps showing with high sensitivity very weakly contrasting capillaries can be obtained.



Fig. 3. The STdOCT method imaging of the human eye in vivo. In the bottom row, fragments of images from the upper row are magnified 2.5x. Circles identify the location of large blood vessels. Each vertical line in the tomograms is formed as shown in Figure 2. (a) Structural tomogram. The intensity is proportional to the scattering ability of object. (b) Velocity map. The velocity is always parallel to the sample beam (light hits an object from the top of the image) Colors specify the direction of velocity of blood (blue indicates the movement away from the tomograph, and red towards the tomograph). Color saturation is proportional to the velocity of movement. (c) Tomogram with segmented blood vessels. Information from panels a nad b is used. Only those points of structural tomogram (a) are retained, for which the rate of velocity read from the map (b) is greater than the preset threshold. Figure is taken from [IB.2].



Fig. 4. Blood vessels in the region of optic nerve head. Imaging range 5mm x 5mm. (a) Red-free fundus photography. (b) ICG angiography. (c) En face image of the eye fundus obtained from 3D SOCT data (point of the image is obtained by adding up the total scattering of light in a single line from SOCT tomogram, Fig. 3(a)), to create the image 100 tomograms of 2200 lines each were used. (d) Reconstructed 3D velocity image overlaid onto structural SOCT data, Fig. 3(a-b). (e) En face longitudinal velocity map. Point of the map is created from a single line of velocity tomogram, Fig. 3(b). (f) En face view of segmented vessels (SOCT angiography). Point of the map is created from a single line of tomogram with segmented vessels, Fig. 3(c). Figure is taken from [IB.2].

Demonstrating the advisability of the use of this method in practical clinical ophthalmology has resulted in a post-conference papers and articles in which it has been applied [IIA.21, IIC.2, IIC.15, IIC.17, IIC.20, IIC.23-IIC.25, IIC.27, IIC.30-IIC.32, IIC.39, IIC.42]. It was also successfully used to evaluate the blood flow in the brains of rodents in vivo [IIA.24, IIC.33, IIC-34] and in the microchannels [IIA.27, IIC.21, IIC.25, IIC.28, IIC.38]. It was also combined with the techniques of determining the total flow rates and with methods of determining the absorption [IIC.19, IIC.21, IIC.29]. STdOCT method applied to the determination of blood flow in the human eye has also been commercialized and transferred to the industrial partner [IIIQ.3].

In the next step of the development of the method I used the STdOCT diagram to design a version of the technique in which, together with the assessment of the value of the longitudinal velocity, the typical for FdOCT problem of limited imaging range is solved [IB.3]. Limited imaging range is related to the fact that the recorded spectral fringes have real values. For this reason, the Fourier transform of fringes comprises symmetrical components ("mirror" components) relative to the point of equal optical paths in the arms of the FdOCT interferometer. Therefore, standard practice consists in positioning the sample relative to the position of the reference mirror, such that the mirror image is located entirely on the side of negative relative positions to the proper image positions, which means that the images do not overlap. This is at the expense of the available imaging range being halved. Solution to this problem is known and consist of introduction an additional longitudinal velocity using an optical delay line such as the movable mirror of the reference [18]. As a result of specific and welldefined delays for subsequent measurements of spectral fringes can be introduced and the free of mirror components complex spectral fringes can be calculated. The disadvantage of these algorithms was the need to input precise phase delays. There was also no possibility of estimating the longitudinal velocity. In the method proposed by me based on STdOCT an additional longitudinal velocity is also used, but it does not need to be precisely determined. It uses the fact that the introduced longitudinal velocity moves the entire object image on the velocity axis in the opposite direction to the movement of its mirror image. The change in the STdOCT diagrams as a result of the movement of the reference mirror can be seen on Fig. 5.



Fig. 5. STdOCT diagrams of scattering fluid flow in a glass capillary. (a) data collected in a standard configuration with a fixed reference mirror; (b) with an additional velocity  $v_{ref}$  set by the mirror in the reference arm. Additional velocity causes movement of the image and its complex conjugate in opposite directions along the axis of frequency and allows them to be easily separated, even if the images overlap along the depth axis. Figure is taken from [IB.3].

In the diagrams shown in Figure 5 it can be seen that that the mirror images are spaced in the frequency domain and do not overlap in the spatial domain. If the applied reference mirror velocity is equal to the half of the maximum velocity possible to record by the FdOCT system, the velocity components connected with the sample (eg. movement of blood in the eye) are also separated from the corresponding components of the mirror image. Thus, at the same time doubling the imaging range and access to information about the sample longitudinal velocity is achieved. The method was applied to of the human eye retinal imaging in vivo [IB.3], as well as structural imaging to obtain the first in the world image of the entire anterior segment of the human eye in vivo (from the rear wall of the lens to the cornea-tear film) with the standard tomography SOCT [IIA.19]. Both examples are presented in Figure 6.



Fig. 6. Images of the human eye in vivo with a mirror image removed by STdOCT. (a) Structural tomogram of the area surrounding the optic disc; (b) velocity map of the image corresponding to tomogramow a. (c) Structural tomogram of the entire anterior chamber of the human eye in vivo. The tomograms present structures of the eye from the front layer of the cornea to the posterior wall of the lens. Figures a and b are derived from [IB.3], Figure c. from [IIA.19].

The results of the work on this variation of the STdOCT method have also been commercialized by transferring the know-how to the industrial partner Optopol Technology SA [IIIQ.2]. The delay line presented in the publication has received patent protection [IIB.1], and the method of measuring the longitudinal velocity in full range FdOCT was submitted in the form of a patent application [IIB.5].

The next stage of work was to use STdOCT to improve the quality of structural imaging. In the simplest and most common approach, a single line of structural tomogram is computed as a module of Fourier transform of spectral fringes [19]. Due to the fact that modern FdOCT techniques are characterized by a great acquisition speed of spectral fringes, the natural tendency is to try to maximize the quality of tomographic images by averaging. Most often this is done by averaging the Fourier transforms of spectral fringes before or after the calculation of module of complex tomogram line (respectively complex or amplitude averaging). During the work on STdOCT I showed that STdOCT can be considered as a weighted averaging of spectral fringes. I presented the first qualitative comparison of STdOCT with other averaging techniques at a conference [IIJ.6] and published in conference proceedings [IIC.32]. In the publication [IB.6] I showed theoretically and experimentally that the best contrast-to-noise ratio (CNR) in OCT imaging, compared to the results obtained by complex and amplitude averaging, can be achieved by forming structural images from intensity values after two Fourier transforms, as is done in the STdOCT method. I determined the distributions of OCT signal intensity after averaging by different methods and analyzed the image quality (as measured by contrast, the contrast-to-noise ratio, signal-to-noise ratio and dynamic range) as a function of the number of averaged spectral fringes. The result of the study was to demonstrate advantage of STdOCT approach over the other averages for both types of objects found in of OCT: reflecting and scattering. Figure 7 shows the increased quality of the images obtained by STdOCT for the human eye in vivo. I have also showed that it is reasonable to apply STdOCT for averaging images in procedures of numerical speckle noise reduction, where complex averaging completely fails.



Fig. 7. Comparison of methods for data averaging for Fourier domain OCT. Tomogram of the area surrounding the optic nerve head of the human eye in vivo. Compared are the classical methods of averaging the measured data (averaging complex transforms or their amplitudes - complex and amplitude averaging, respectively) with averaging using the STdOCT method (STdOCT averaging). See also Figure 2. Inserts are enlarged 1.7x and show respectively: 1 vitreous; 2 large retinal blood vessel; 3 choroid. Figure is taken from [IB.6].

Paper [IB.4] is entirely dedicated to the problem of averaging speckle noise. Most frequently the problem of reducing the speckle noise in OCT is solved by averaging a set of tomographic images collected from almost identical positions of the sample, but shifted by a distance comparable to the diameter of the sample beam [20, 21]. Assuming that the elements of the imaged structures are larger than the spot size, averaging of these images leaves the structural details and reduces the contrast of speckle noise. A major problem with this approach in vivo imaging are movement artifacts. As a result of eye movements the tomograms are shifted more than required, which sometimes leads to a drastic reduction of resolution. Techniques using tomograms averaging are so sensitive to movement of the sample, because the interval between averaged lines is equal to few dozen or a few hundred milliseconds, what is the exposure time of the whole tomogram consisting sometimes of thousands of lines. Movement artifacts can be addressed by using a numerical

correction of images, but it does not always give sufficient results, and always leads to a significant prolongation of the resulting tomogram generation. In the paper [IB.4] I proposed an innovative approach to the way data acquisition in OCT, in which the problem of motion artefacts was almost completely eliminated. In this method, the time between the acquisition of the spectral fringes used in the averaging is minimized and averaged lines are collected in successive acquisitions. In other words, before collecting the information necessary to produce the next line of averaged tomogram all the information needed to create the previous line is gathered. This approach requires almost no numerical corrections of collected images, so it is fast enough to be used in real-time imaging of the human eye in vivo. No numerical interference with the image, and the lack of motion artefacts allows the use of STdOCT technique which leads to two additional advantages: improved quality of structural images (in accordance with the results obtained in [IB.6]) and access to the longitudinal velocity [IB.1, IB.2, IB3], which is not feasible with other known techniques for reducing speckle noise in FdOCT. An example of longitudinal velocity estimation simultaneously with reducing speckle noise is shown in Figure 8. It is worth mentioning that this technique has been commercialized [IIIQ.4] and is the subject of patent application [IIB.9].



Fig. 8. Speckle noise reduction with simulataneous creation of maps of the longitudinal velocity. (a) Structural tomogram from the area surrounding the optic nerve head of the human eye in vivo. Imaging range 7 mm. (b) Structural tomogram from the area surrounding macula of the human eye in vivo. Imaging range 3 mm. (c) Longitudinal velocity map for tomogram a.; (d) Longitudinal velocity map for tomogram b. (e-f) Enlargements of areas from z d. Figure is taken from [IB.4].

In contrast to the classical methods of assessing longitudinal velocity FdOCT, the STdOCT method gives the whole spectrum of Doppler frequencies, and not only the mean value. This allows to widen the scope of available functional measurements using FdOCT. In the paper [IB.5] in collaboration with scientists from the University of Western Australia we showed that using STdOCT method the frequency and amplitude of the mechanical vibrations as a function of depth within the sample can be determined with far greater sensitivity than it was possible to that time. We used the fact that the frequency spectrum of spectral fringes modulated in the time due to oscillatory motion can be presented as the sum of the harmonic frequencies of modulation frequency. The amplitudes of these

harmonics depends on the Bessel function of the first kind with argument dependent on the amplitude of oscillatory motion. We proposed a method of determining the amplitude and frequency of oscillation as a function of depth in the sample based on the Doppler spectrum calculated using STdOCT. In the presented case the Doppler spectrum is a set of peaks corresponding to the consecutive excitation frequency harmonics, which allows to determine the vibration amplitude as a function of depth. Analyzing the change in the oscillation amplitude we determined the distribution of stiffness in test samples: a phantom with known mechanical properties and animal tissue ex vivo. In the paper we showed that, in both cases, the approach based on the STdOCT technique is more sensitive than traditional methods based on spectral analysis of the fringes phase and allows to obtain reliable results in the case of low signal to noise ratio. The results obtained for the phantom are shown in Figure 9



Fig. 9. Application of STdOCT to measure the elasticity of the sample: (a) Structural tomogram OCT; (b) Map of vibration amplitudes obtained by STdOCT. (c) Elastogram – map of elastic properties of the sample (dark color indicates high stiffness) obtained by STdOCT; (d) single line from tomogram a. marked by arrow. (e) Vibration amplitude plots for STdOCT (blue) and standard phase-sensitive OCE (red) at the lateral position indicated by the red arrow in (a), (f) Vibration amplitude image obtained using standard phase analysis (g) elastogram for image f. Figure is taken from [IB.5].

Another application of the STdOCT technique is a method for determining the velocity transverse to the direction of incidence of the light beam shown together with scientists from the Ecole Polytechnique Fédérale de Lausanne in Switzerland [IB.7]. Methods for determining the longitudinal velocity for FdOCT are known and used for over 10 years. The problem is to determine the motion component perpendicular to the beam (the lateral velocity). It is well known that the value of the center of mass of the Doppler spectrum is proportional to the longitudinal velocity, the broadening of the spectrum is proportional to transverse velocity [22, 23]. In the article [IB.7] we have developed a theoretical model that combines the Doppler broadening of the spectrum with longitudinal and lateral velocities and with the optical parameters of the probing beam and properties of the sample. The model has been experimentally verified under controlled conditions in glass capillaries with exactly known flow of liquid. As mentioned previously, the STdOCT technique gives a Doppler spectrum for each depth position within the sample and has been used to experimentally find the

Doppler spectrum parameters, which served to determine both velocity components. The theoretical model in combination with STdOCT proved to be valid for the two sample illumination configurations used commonly in FdOCT: standard system with the Gaussian beam, and in the system with the Bessel beam.

In summary, the method STdOCT is an universal tool for generating tomograms in FdOCT. Within a single computing paradigm allows to obtain structural tomograms of a higher quality than other methods, as well as tomograms mapping longitudinal flow velocity, transverse flow velocity and mechanical properties. It also allows you to obtain these results, together with the procedure of doubling the imaging range. The development of STdOCT method is still in progress. Yet unpublished results show that it can be used for the assessment of the spectrum of light extinction as a function of depth into the sample, and also to evaluate the spatial distribution of the refractive index. The ability of the STdOCT technique to image of structure and function in FdOCT resulted in 12 publications in peer-reviewed journals, 18 conference proceedings, two patent applications and three commercializations. At the moment, at the end of the edition process is a book in the field of optical tomography OCT, where I am a co-author of one chapter about methods for measuring flow in the human eye which is partly devoted to the STdOCT technique [IID.1].

# 5. Discussion of the other scientific (artistic) achievements.

My main research tasks were related to the analysis of data obtained by optical coherence tomography (OCT). Until obtaining the degree of doctor I dealt with the development of efficient numerical procedures for processing recorded spectral fringes to the final lines of tomograms. I developed a number of algorithms that solve efficiently problems in FdOCT. The first is a dramatic decrease in resolution due to non-linear registration of the spectral fringes as a function of wave number. In order to obtain the maximum resolution it is necessary to find an accurate relation connecting points of the detector with the wave number of light, using only the sampling light of OCT. Methods must be sufficiently rapid and simple to make it possible to be performed in the laboratory during the single minutes. I developed a universal calculation procedure, which can use the data obtained by different measurement procedures. It has been successfully applied to both swept source OCT and spectral OCT [IIA.2, IIA.20]. After solving this problem, I developed a computational path of transforming the spectral fringes to the lines of the tomogram, which consists of removing artifacts associated with reflections in the interferometer, the correction of non-linear light measurement, correction of uncompensated dispersion in the arms of the interferometer and Fourier transform. All steps are crafted to the number of necessary calculations and allow to convert about 40,000 spectral fringes per second on a single core CPU. This solution has been commercialized [IIIQ.1] and optical scanners SOCT Copernicus and SOCT Copernicus HD offered by the Polish company Optopol Technology SA generate tomograms based on algorithms developed by me. Moreover, they are used in everyday practice in the Optical Bioimaging Imaging Group, where I work and in ophthalmic examinations conducted by the doctors cooperating with the Group [IIA.6-IIA.8, IIA.11, IIA.14-IIA.23, IIA.28, IIC.6-IIC.9, IIC-13-IIC.14, IIC.16, IIC.22, IIC.41] as well as material studies [IIA.9, IIC.10-IIC.12]. My algorithms are also implemented in software of SOCT tomograph built for co-workers of Madrid's Instituto de Óptica "Daza de Valdés" [IIA.24]. Due to the ease of scaling and parallelization of computations in these algorithms have adapted them to perform on GPU graphics cards, which allowed to reach speeds of one million lines of calculations per second [IIA.26, IIC.26, IIC.36, IIC.40].

As part of the exploration numerical techniques to improve the quality of OCT images I have attempted to apply deconvolution to the tomographic image in order to increase the resolution beyond the constraints set by the coherence length of the light used [IIA.2, IIC.3]. For this purpose, I have developed a technique which makes use of the specific for OCT symmetry in deconvolution matrix and uses Fourier transformations in place of matrix multiplication. As a result, I have dramatically increased the speed of calculation, which led to the then world's fastest deconvolution methods for applications in OCT.

Another area of interest was the development of techniques to increase the imaging range for FdOCT. I participated in the development of techniques based on well-known multi frame methods from holography [IIA.1, IIA.3, IIC.1, IIC.4, IIC.5] and developed a versatile technique for removing residual artifacts from images obtained by the multi frame methods [IIA.5]. The culmination of the work in this field was to develop a variant of the STdOCT method as described previously, which allows of doubling the range in both structural and functional imaging [IB.3, IIA.19].

Regardless of the work on the STdOCT method for imaging flow velocity I was developing existing methods using the phase difference of spectral fringes. In [IIA.13] we showed a favorable data averaging method, which gives the correct result for the estimated velocity value for lower signal to noise ratio and is devoid of artifacts occurring in the prior techniques for velocity approaching the theoretical velocity limit for given FdOCT system. I also supported the work of the group on the development of techniques for the visualization of blood vessels using both phase and intensity information [II.C35, IIC.37].

Another problem solved by me in the context of work on increasing the quality of OCT images was a method of correction of geometric distortion of the imaged objects resulting from the refraction of light on the surfaces separating volumes of the sample with different refractive indices. The lines that make up the of OCT image show the boundaries of the structures along the sample beam. Refracted rays are visible as straight lines, and the distances are distances optical. I developed a method which basing on the knowledge the refractive indices of media in which the beam moves, calculates the angles of refraction of the beam at the borders between the volumes and so transforms the tomogram that in the resulting image the actual geometrical dimensions of the imaged sample are presented. The method has been used for the correction of ophthalmic images [IIA.3], as well as in material studies [IIC.11]. I have also developed a method to reorient a three-dimensional images of the human eye, with respect to the axis perpendicular to the plane of the pupil. The method was used to generate quantitative maps of thickness and corneal topographic maps of the human eye [IIA.23].

In 2007, I developed a technique of semi-automatic segmentation of retinal layers for quantitative evaluation of the progression of diseases of the eye. The method is described in [IIA.10], and then used in clinical trials [IIA.14, IIA.16, IIA.18, IIA.22, IIC.18].

In total I have published 78 research papers, in 15 of which I was the first author. According to the Web of Science database, my work has been cited more than 760 times (more than 620 times without self-citations) and h-index is 17.

Since 2005 I have participated in nine research grants, including two times as a manager [IIH.1-IIH.9]. In 2011, I headed a grant from the Ministry of Science and Higher Education "Iuventus Plus" [IIH.8],

and now (2013-2015) I am the head of the grant in the Programme for Applied Research of the National Research and Development Centre [IIH.9, IIIE.1], which is implemented by a consortium composed of five research institutions: Nicolaus Copernicus University, Poznan University of Technology, Nencki Institute of Experimental Biology, Poznan University of Medical Sciences and Warsaw University.

Since completing PhD in 2008, my employment at the university is financed exclusively from research grants. Therefore, didactic work is limited to the period of doctoral studies, in which I carried out exercises to lecture on advanced methods of data analysis and virtual studio instruments [IIII.1, IIII.2]. Despite the absence of an obligation of teaching arising from the employment as a full-time scientific assistant professor, I was a supervisor in one engineering project [IIIJ.1], reviewer in 5-five master's theses [IIIJ.2] and in one Bachelor's [IIIJ.3]. I was also an auxiliary dissertation supervisor in one PhD project, in which a graduate student applied the STdOCT method to extract information about the properties of optically inhomogeneous liquids [IIIK.1]. The PhD thesis was defended with distinction.

During the whole period of research activity from 2004 to the present, I presented the results of my work nationally and internationally. I actively participated in 10 international conferences in the USA [IIIB.1-IIIB.8, IIIB.10, IIIB.11] and two in Poland [IIIB.9, IIIB.12] delivering a 7 speeches and presenting five posters. Four times I gained financial support for travel to conferences [IIID.1-IIID.4], including once conference scholarship for young scientists from Foundation for Polish Science.

I run a scientific collaboration with centers in Poland and abroad. Since 2003 to the present, together with ophthalmologists from Nicolaus Copernicus University Medical College, I lead the work on the use of OCT for imaging structural and functional anterior and posterior segment of the eye. The cooperation resulted in a number of papers and articles conference proceedings [IIA.6-11, IIA.14-18, IIA.20, IIA.22-23, IIA.29, IIC.6-7, IIC.9, IIC.13, IIC.18, IIC.22, IIC.42] and a patent application [IIB.8]. In 2008-2009, I participated in collaboration with the Visual Optics and Biophotonics Lab, Instituto de Óptica "Daza de Valdés" (Madrid, Spain). Cooperation related to design and build an OCT tomograph to study the anterior segment of the human eye, especially the cornea. My contribution was to create and implement methods for image reconstruction from the measured data. In September 2009, during a stay in Madrid [IIIL.1] the device has been activated and is used to this day. The result of this collaboration was the number of publications, including two of my participation [IIA.19, IIA.24]. Since 2011, I cooperate with scientists from The Optical + Biomedical Engineering Laboratory, University of Western Australia (Perth, Australia). The theme of cooperation is the development of methods for optical elastography using the STdOCT method I developed. Result of the collaboration is the publication in an international peer-reviewed journal [IB.5]. From 2012, I cooperate with researchers from the Laboratoire d'Optique Biomedical, École Polytechnique Fédérale de Lausanne (Lausanne, Switzerland). The theme of cooperation is the development of methods for measuring the total flow using the STdOCT method. Cooperation resulted in a stay in EPFL in October 2012 [IIIL.2] to demonstrate the possibility of STdOCT method and plan joint research projects. The result of this collaboration is the publication in international peer-reviewed journal on the use STdOCT method for determining the total flow in the liquid samples [IB.7]. I participate also in collaboration with researchers from the Nencki Institute of Experimental Biology in the examination of applications of the STdOCT method for the analysis of blood flow in the vessels of the brain of rodents. Collaboration resulted in a series of joint publications [IIA.25, IIC.33, IIC.34] ] And is continued on in a joint project [IIH.9, IIIE.1].

Since 2007, I made a review of more than 40 publications in ten national and international journals with IF index from 1.4 to 4.3 [IIIP.1IIIP.10] one international conference submission [IIIP.11] and one grant of the Foundation for Polish Science [IIIO.1].

My activity in the field of science has been recognized with numerous awards and scholarships [III.1III.10], and in particular I was granted the Ministry of Science and Higher Education scholarship for outstanding young scientists, twice the scholarship "START" by Foundation for Polish Science, once individual reward of Rector of Nicolaus Copernicus University first degree and twice team reward of Rector of Nicolaus Copernicus University.

In addition to the scientific work also participated in the commercialization of research. In 2006, I participated in the transfer to the industrial partner, Polish company OPTOPOL Technology SA, knowhow on the SOCT tomograph. The tomograph has been deployed to production and subsequent versions are sold to date. Numerical procedures leading to the creation of tomograms from the measured data in these devices are developed and implemented by me. In the period from 2006 to 2008 I supported the development of these devices by combining doctoral studies with the work in the research and development office of the company OPTOPOL Technology SA. This collaboration resulted in two patents and five patent applications regarding SOCT [IIB.3-IIB.7]. After finishing work in the R & D office I maintained the cooperation with OPTOPOL Technology SA by participating in commercialization of the technical solutions concerning SOCT, in particular by passing the know-how regarding the use of STdOCT method for determining total flow of liquid samples [IIIQ.3], speckle noise reduction in SOCT imaging [IIB.9, IIIQ.4] and numerical correction of phase distortions [IIB.10, IIIQ.6]. Also participated in commercialization of research results in collaboration with ophthalmologists in project on optical measurement of intraocular pressure [IIB.8].

In 2011, together with the members of the Medical Physics Group: Prof. Andrzej Kowalczyk, Prof. Maciej Wojtkowski, Dr. Anna Szkulmowska and Dr. Iwona Gorczyńska I founded spin-off company AM2M Ltd. L.P. dedicated to the commercialization of scientific results obtained in the Optical Biomedical Imaging Group. In 2013, the company was awarded the title of Leader of Innovation of Kujawsko-Pomorskie voivodship in the category of microenterprises.

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### **References:**

- 1. A. F. Fercher, C. K. Hitzenberger, G. Kamp, and S. Y. Elzaiat, "Measurement of Intraocular Distances by Backscattering Spectral Interferometry," Opt Commun 117, 43-48 (1995).
- 2. M. Wojtkowski, "High-speed optical coherence tomography: basics and applications," Appl Optics 49, D30-D61 (2010).
- 3. M. Wojtkowski, R. Leitgeb, A. Kowalczyk, T. Bajraszewski, and A. F. Fercher, "In vivo human retinal imaging by Fourier domain optical coherence tomography," J Biomed Opt 7, 457-463 (2002).
- 4. M. A. Choma, M. V. Sarunic, C. H. Yang, and J. A. Izatt, "Sensitivity advantage of swept source and Fourier domain optical coherence tomography," Opt. Express 11, 2183-2189 (2003).
- 5. B. Potsaid, I. Gorczynska, V. J. Srinivasan, Y. L. Chen, J. Jiang, A. Cable, and J. G. Fujimoto, "Ultrahigh speed Spectral/Fourier domain OCT ophthalmic imaging at 70,000 to 312,500 axial scans per second," Opt. Express 16, 15149-15169 (2008).
- 6. W. Wieser, B. R. Biedermann, T. Klein, C. M. Eigenwillig, and R. Huber, "Multi-Megahertz OCT: High quality 3D imaging at 20 million A-scans and 4.5 GVoxels per second," Opt. Express 18, 14685-14704 (2010).
- 7. R. Leitgeb, C. K. Hitzenberger, and A. F. Fercher, "Performance of Fourier domain vs. time domain optical coherence tomography," Opt. Express 11, 889-894 (2003).
- 8. P. Targowski, M. Iwanicka, L. Tyminska-Widmer, M. Sylwestrzak, and E. A. Kwiatkowska, "Structural examination of easel paintings with optical coherence tomography," Accounts of chemical research 43, 826-836 (2010).
- 9. R. A. Leitgeb, L. Schmetterer, W. Drexler, A. F. Fercher, R. J. Zawadzki, and T. Bajraszewski, "Real-time assessment of retinal blood flow with ultrafast acquisition by color Doppler Fourier domain optical coherence tomography," Opt. Express 11, 3116-3121 (2003).
- 10. R. Leitgeb, M. Wojtkowski, A. Kowalczyk, C. K. Hitzenberger, M. Sticker, and A. F. Fercher, "Spectral measurement of absorption by spectroscopic frequency-domain optical coherence tomography," Optics letters 25, 820-822 (2000).
- 11. F. E. Robles, C. Wilson, G. Grant, and A. Wax, "Molecular imaging true-colour spectroscopic optical coherence tomography," Nature Photonics 5, 744-747 (2011).
- 12. B. R. White, M. C. Pierce, N. Nassif, B. Cense, B. H. Park, G. J. Tearney, B. E. Bouma, T. C. Chen, and J. F. de Boer, "In vivo dynamic human retinal blood flow imaging using ultra-high-speed spectral domain optical Doppler tomography," Opt. Express 11, 3490-3497 (2003).
- 13. L. An and R. K. Wang, "In vivo volumetric imaging of vascular perfusion within human retina and choroids with optical micro-angiography," Opt Express 16, 11438-11452 (2008).
- 14. A. Szkulmowska, M. Szkulmowski, D. Szlag, A. Kowalczyk, and M. Wojtkowski, "Three-dimensional quantitative imaging of retinal and choroidal blood flow velocity using joint Spectral and Time domain Optical Coherence Tomography," Opt. Express 17, 10584-10598 (2009).
- 15. B. F. Kennedy, S. H. Koh, R. A. McLaughlin, K. M. Kennedy, P. R. Munro, and D. D. Sampson, "Strain estimation in phase-sensitive optical coherence elastography," Biomed Opt Express 3, 1865-1879 (2012).
- 16. G. Min, W. J. Choi, J. W. Kim, and B. H. Lee, "Refractive index measurements of multiple layers using numerical refocusing in FF-OCT," Opt Express 21, 29955-29967 (2013).
- 17. J. Binding, J. Ben Arous, J. F. Leger, S. Gigan, C. Boccara, and L. Bourdieu, "Brain refractive index measured in vivo with high-NA defocus-corrected full-field OCT and consequences for two-photon microscopy," Opt Express 19, 4833-4847 (2011).
- 18. M. Wojtkowski, A. Kowalczyk, R. Leitgeb, and A. F. Fercher, "Full range complex spectral optical coherence tomography technique in eye imaging," Optics letters 27, 1415-1417 (2002).
- 19. P. H. Tomlins and R. K. Wang, "Digital phase stabilization to improve detection sensitivity for optical coherence tomography," Measurement Science & Technology 18, 3365-3372 (2007).
- 20. T. M. Jorgensen, J. Thomadsen, U. Christensen, W. Soliman, and B. Sander, "Enhancing the signal-to-noise ratio in ophthalmic optical coherence tomography by image registration method and clinical examples," J Biomed Opt 12, (2007).
- 21. R. J. Zawadzki, B. Cense, Y. Zhang, S. S. Choi, D. T. Miller, and J. S. Werner, "Ultrahigh-resolution optical coherence tomography with monochromatic and chromatic aberration correction," Opt. Express 16, 8126-8143 (2008).
- 22. D. Q. Piao, L. L. Otis, and Q. Zhu, "Doppler angle and flow velocity mapping by combined Doppler shift and Doppler bandwidth measurements in optical Doppler tomography," Optics letters 28, 1120-1122 (2003).
- 23. S. G. Proskurin, Y. He, and R. K. Wang, "Determination of flow velocity and spectrum broadening with vector based on Doppler shift optical coherence tomography," Optics letters 28, 1227-1229 (2003).