Optical methods for imaging of morphology and functions of the human eye for diagnostics of neurodegenerative diseases

Project goals

- To develop a multimodal optical setup consisting of the Scanning Laser Ophthalmoscope (SLO), the Optical Coherence Tomography (OCT) imager and the retinal tracker for comprehensive examinations of human subjects in clinical environment.
- To design experimental protocols for human subject examination using the device.
- To conduct experiments with human subjects in clinical environment.
- To create data analysis tools for finding potential biomarkers of various neurodegenerative diseases from data acquired from human subjects using the optimized device.

Outline

The doctoral project consists of two main research objectives. **The first research objective will be to develop methods for assessment of the structure and dynamics of the living human eye**. The methods will be based on the multimodal optical device comprised of the ultrafast retinal eye tracking module (FET – FreezEye Tracker), the optical coherence tomography (OCT) imager, and the scanning laser ophthalmoscope (SLO). The project will be carried out alongside a larger multidisciplinary team consisted of physicists, engineers, mathematicians and software developers that has recently developed one of the fastest and the most precise retinal trackers in the world [1]. Information provided by the tracker will be used also for image stabilization purposes of the other eye imagers enhancing significantly the quality of the registered images. The multimodality of the platform under development will provide comprehensiveness of the registered information about a patient. This leads to **the second objective which will be to attempt to apply the developed methods for diagnostic use of neurodegenerative disorders**, such as multiple sclerosis (MS), Alzheimer disease (AD), Parkinson disease (PD) or Huntington disease (HD) in clinic environment.

The retina and the optic nerve are considered to be the outermost part of the central nervous system (CNS). They are also the only part of CNS that is accessible with optical methods, in completely non-invasive manner due to the fact that the layer of retinal nerve fibers (RNFL) is composed of the unmyelinated axons of ganglion cells (which allows for better penetration of light to deeper structures of the retina down to the retinal pigment epithelium), the relatively low density of the glia cells and the transparency of the vitreous humor. In the literature there are reports that confirm the manifestation of neurodegenerative diseases in the condition and behavior of the eye. The initial set of the candidates for biomarkers are:

1. The thickness of the retinal layers, especially retinal nerve fiber layer (RNFL). It will be accessed with structural OCT imaging which provides 3D images of the retina [2]. The decreased number of the retinal ganglion cells and their axons in the nerve fiber layer (RNFL) was observed in AD subjects via postmortem histopathology [3]. There are numerous examples of application of OCT imaging to quantitatively show that the RNFL and thickness is reduced in AD populations [4] and PD populations [5].
2. Dynamics of the flow in retinal vessels. It can be measured with functional OCT imaging using techniques of OCT angiography as well as assessed with SLO device. In AD patients it was observed an overall reduction of vessel response, which mostly affected the vasodilatation of the arteries [6].
3. Characteristics of the eye movements. Eye movements deficits and abnormalities play a key role in many neurodegenerative diseases as they affect brain circuits responsible for eye

movement control. Saccadic dysfunction, fixation instability, and abnormal smooth pursuit are among the most common abnormalities. Eye movement abnormalities are known to be part of diseases such as PD, AD, HD and MS [7]-[8], therefore can be important and promising biomarker of the disease on its early stages as well as biomarker for cognitive decline in patients. The parameters of the eye dynamics will be accessed with the use of ultrafast retinal tracker based on MEMS scanning device.

Work plan

1. Systematic organization of the state-of-the-art knowledge in the field of diagnosis of the neurodegenerative diseases of interest with the use of optical methods,
2. design and construction of multimodal optical setup adapted for work in clinical environment,
3. adaptation and development of the data acquisition software,
4. development of the data analysis tools providing access to the parameters having the potential to be used as biomarkers,
5. test measurements on healthy subjects, evaluation of the measurement protocols,
6. systematic measurements on the cohorts of patients suffering particular disorders,
7. development of the tools for efficient and safe handling of big data,
8. synthesis of the results providing correlation between the stadium of the disease and the range of values of the chosen parameters.

Literature

[1] Maciej Bartuzel, Krystian Wrobel, Szymon Tamborski, Maciej Nowakowski, Krzysztof Dalasiński, Michał Meina, Anna Szkulmowska, Maciej Szkulmowski, High-resolution, ultrafast, wide-field retinal eye-tracking for enhanced quantification of fixational and saccadic motion, Biomedical Optics Express, Vol. 11 No. 6, accepted on 7.05.2020
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[3] Hinton, D. R., Sadun, A. A., Blanks, J. C. & Miller, C. A. Optic-Nerve Degeneration in Alzheimer's Disease. N. Engl. J. Med. 315, 485–487 (1986).
[4] Marziani, E. et al. Evaluation of retinal nerve fiber layer and ganglion cell layer thickness in Alzheimer's disease using spectral- domain optical coherence tomography. Invest. Ophthalmol. Vis. Sci. 54, 5953–8 (2013).
[5] Tsironi EE, Dastiridou A, Katsanos A, Dardiotis E, Veliki S, Patramani G, et al. Perimetric and retinal nerve fiber layer findings in patients with Parkinson's disease. BMC Ophthalmol 2012; 12: 54.
[6] Kotliar, K. et al. Altered neurovascular coupling as measured by optical imaging: A biomarker for Alzheimer's disease. In Scientific Reports 7 (2017).
[7] MacAskill MR, Anderson TJ. "Eye movements in neurodegenerative diseases" Curr Opin Neurol. 2016 Feb;29(1):61-8.
[8] Roberto Rodriguez-Labrada, Luis Velazquez Perez, Eye Movement Abnormalities in Neurodegenerative Diseases, Eye Motility, 2019

Required initial knowledge and skills of the PhD candidate

1. basics in optics
2. basics in computer programming (preferably Python, Labview, Matlab, C/C++/C#)
3. eager to learn

Expected development of the PhD candidate's knowledge and skills

The PhD candidate will gain skills in design, assembly and tests of optical systems for imaging the human retina in vivo. She/he will also gain knowledge on how to operate the systems in clinical environment when performing the data acquisition from healthy subjects as well as ophthalmic and neurological patients. She/he will also learn how to process the image data and will use data science methods to extract parameters that will serve as potential biomarkers.