GDAŃSK UNIVERSITY OF TECHNOLOGY

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**OPINION**

**on the PhD Dissertation by MSc Mounika Rapolu entitled**

**„Contrast enhancement in optical coherence angiography for brain imaging"**

Supervision:
Prof. dr hab. Maciej Wojtkowski

This opinion of the doctoral dissertation has been prepared at the request of the Chairman of the Institute of Physical Chemistry of the Polish Academy of Science in Warsaw, prof. dr hab. Jacek Gregorowicz, expressed in the cover letter of September 9th, 2021, attached to the dissertation.

**The description of the dissertation**

The opinioned doctoral dissertation is 127 pages long. It consists of an abstract in English, a list of figures, 5 chapters.

The first chapter is an introduction, the second delivers the theoretical background on Optical Coherence Microscopy (OCM)– Angiography. There is a detailed description of the methodology which was used by the Author in experiments. Optical Coherence Microscopy hardware set-ups are indicated as well as software that was applied for data acquisition. The results of experimental work were included within chapter fifth. The last part of the dissertation presents conclusions and ideas for further research. There is also a list of correctly selected literature references, including 185 items.

**The scientific problem of the dissertation**

The thesis presented in the reviewed dissertation is as follows:

*Introduction of new biomarkers in angiographic imaging of the rodent brain vasculature in the presence of pathological changes by optical coherence microscopy (OCM) can be accomplished by varying the physical experimental conditions affecting any of the following parameters:*
*1. amplitude of light scattered from blood;*
*2. geometry of illuminating beam;*
*3. timing and settings of the raster scan.*

The thesis of this dissertation has been correctly formulated and it has given the opportunity to precisely estimate the goal of the research work related to this thesis. From the scientific point of view, the thesis focuses on important and current problems.

**Critical state-of-the-art analysis**

The dissertation includes 185 references. Mostly there are now-a-day papers. The theoretical background of the scientific problem is presented in the first chapter – "Introduction", and in the second chapter titled "Theory: Optical Coherence Microscopy – Angiography". In both chapters, the Author has focused on an in-depth analysis of the current state of knowledge. She presents the brain imaging technologies with a cranial window as well as the application of the OCT and OCM techniques for brain imaging. Consequently, one after reading this chapter can meet the motivation of the Author to focus on the scientific problem included in the thesis.

The second chapter is dedicated to the critical state-of-the-art analysis focusing on OCM and techniques which can improve the OCM image quality, such as the use of the shape

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spectra of the low coherence source or application of the scattering centres in the biological tissue.

**Scientific problem**

In the fourth chapter, the methodology of solving the scientific problems has been comprehensively described. This chapter contains a description of works that tune the OCM system parameters for brain imaging. In order to verify the thesis, the Author of the dissertation conducted a series of research works. The Author focused not only on the hardware of the system by choosing the optimal focusing of the light beam which interacts with tissue, but also on the optimal field view and the optimal shape of the spectra of the source. On the other hand, the candidate tested representative processing algorithms to optimize the OCM image. Furthermore, the Author used two different scattering centers to enhance the contrast of biological tissue during *in-vivo* imaging. As a result of the conducted work, the Author could compare and contrast a broad representative set of methods that can be used to enhance the contrast in the OCM-A. The candidate analysis outlines the best method to achieve that goal. The Author of the dissertation solved the scientific problems and used the appropriate method to complete established tasks. During these works, MSc Mounika Rapolu showed that she has the ability to plan and conduct research. The Author chose appropriate methods to achieve the contrast enhancement in the optical coherence angiography for brain imaging.

Based on the analysis of the results, it can be concluded that the scientific problem presented in this dissertation has been solved.

**Originality of the dissertation**

The topic of the presented dissertation is the object of the interest of many research groups. This proves that this topic is a present-day problem in biophotonics.

The originality of the dissertation mainly lies in the development of the method of contrast enhancement in the imaging of biological objects. The doctoral student demonstrates that the application of the averaging of sans can be as effective as the implementation of scattering centers into the body of the patient. The candidate proves the ability to average by comparison images which were acquired by the use of the representative methods of contrast enhancement such as shaping the source spectra, the application of the scattering center, and the scan post-processing.

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Taking into consideration the rapid growth of the applications of photonics in life science, especially in the field of biomedical imaging, this dissertation can have a social impact. The dissertation presents an innovative method of contrast enhancement in optical coherence angiography for brain imaging. Taking into consideration that the elaborated method lies mainly in the software part of the imaging system, this solution can be adopted by another research group to increase the resolution of imaging. Furthermore, such a simple and sufficient method can be introduced in the procedures that are currently used during medical investigations to increase the resolution of imaging.

The candidate is the first author of 3 published articles. One of them is published in the journal from JCR list with a high impact factor – Biomedical Optic Express. She was very active in presenting her research results to the public. Within her PhD study, she delivered 6 oral and poster presentations during international research conferences.

This proves that the investigated topic is up-to-date and interesting for the broad group of researchers whose study focuses on bioimaging.

**Comments and questions to the Author**

***Major comments***

- Please explain why did you use *in-vivo* imaging in place of *in-vitro*? *In-vitro* measurements with the use of phantoms mimicking tissue seems to be more accurate for such a preliminary study. It is because the investigation can be repeated and all the parameters of the investigation procedure can be tuned and are stable.
- Please explain more clearly your motivation for selecting such geometrical parameters of the micro fluids system, such as the dimension and shape of the channel.
- Please explain the method of choosing the best algorithm for scan proccessing. (page 71)
- Why did Author state that LGNRs were difficult and unattractive for brain imaging? The LGNRs are widely known as powerful tools for contrast enhancement in blood flow imaging, so the Author's motivation should be explained.
- Please clarify why do you choose the 1300 nm OCM system for *in-vivo* imaging?

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**Minor comments**

- The Author used imprecise terms in this dissertation, which can be confusing in the text focused on physical science e.g.:
  "...the sharpest vessels." (page 67)
  " ...a simple algorithm ..." (page 73)
  "...the larger vessels...", "...smaller vessels...", "...almost zero background noise..." (page 74)
  "...change significantly..." (page 77)
  "...it is not very huge ..." (page 97)
  "...hugely improved ..." (page 115)
- There are different colors in the figures (b) and (c) as well as (e) and (f) which makes it impossible to compare and contrast both figures. Furthermore, figures (c) and (f) have different scale values (Figure 4-13 in page 77).
- It would be useful to include all references in a separate chapter.
- There is a lack of a list of the acronyms which are used in the text.

**Conclusion**

The Author of the dissertation proved the truth of the thesis: *"Introduction of new biomarkers in angiographic imaging of the rodent brain vasculature in the presence of pathological changes by optical coherence microscopy (OCM) can be accomplished by varying the physical experimental conditions affecting any of the following parameters:*
*1. amplitude of light scattered from blood;*
*2. geometry of illuminating beam;*
*3. timing and settings of raster scan."*

The reviewed dissertation is a description of the original solution to a scientific problem provided by the Author. On the other hand, the dissertation demonstrates her general theoretical knowledge in a scientific discipline and the ability to independently conduct scientific work.

I confirm that the thesis submitted for evaluation by MSc Mounika Rapolu meets the requirements of the Act on Academic Degrees and Academic Title.

Taking into consideration the achieved results and the legal regulations, I recommend the Scientific Council of the Institute of Physical Chemistry of the Polish Academy of Science in Warsaw to admit M.Sc Mounika Rapolu to further stages of her doctoral procedure.

M. Szczerbe

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