

Review of the doctoral dissertation for the degree of
Doctor of Philosophy

Entitled:

**A Hybrid Method for Tractography in Neurosurgery
Using Artificial Neural Networks and Path Search
Algorithms**

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The Author, in his dissertation analyzed the important, timely and interesting problems of tractography and the implementation of artificial neural networks and path search algorithms for its interpretation. The complex and multidisciplinary approach presented by the Author, adds great value to this important research problem.

The summary of the dissertation that I received is interestingly and well written both in English and Polish languages with respect to the typical scientific publication structure.

The list of contents is clearly presented followed by the list of figures, tables, abbreviations and a list of mathematical symbols used in the manuscript.

In the introduction, the Author briefly and precisely presented knowledge about brain tumours and its neurovisualisation. The classification of brain tumours quoted by the Author from the paper (dated 2013) is not topical. The new WHO classifications of brain tumours were published respectively in 2016 and 2021. Some differences in the classification are noticeable like Roman numerals do not apply anymore (should be Arabic numerals) (pages 1,11). In the same paragraph it might be added that besides neural tissue, the glial tumours do infiltrate the surrounding glia. Likewise in the following paragraph should be added that those invasive neoplasms beside cortical regions do infiltrate subcortical (white and gray matter) structures as well.

The motivation and aims of the dissertation are clearly and synthetically presented. Besides the dynamic development of neuroradiology, the Author underlined the remaining lack of efficient and objective method of preoperative planning, especially for individuals with brain tumours located in the eloquent areas. The aims of the study were to develop a method for creating labels based on tractograms. Additionally the aims were to design and train the artificial neural network (ANN) for processing of the data, and implementing a modified variant of the A* algorithm based on the ANN output, and implementing an automated pipeline to compute tractograms based on data obtained from an analyzed group of subjects.

For easier analysis of the manuscript, the Author included a subchapter where parallel to the list of contents, he precisely presented the structure of the dissertation.

In the following chapter, the Author briefly presents an introduction to neurophysiology. This chapter is substantial for the readers who do not have a medical background. Besides the peripheral and central nervous system, the autonomic nervous system is a third pillar of the human nervous system that might be highlighted. For semantic reasons, diencephalon (Latin) can be called interbrain as the rest of the elements of central nervous system are quoted in English. In the central nervous system supporting role of the neurons carry glial cells (mainly astrocytes and oligodendrocytes) whereas in the peripheral nervous system that role is carried by Schwann cells (neurolemmocytes) and myelin sheath (page 6 and 7). Likewise, it should be stated more clearly that in the central nervous system, neurons form tracts whereas in the peripheral nervous system those form nerve fibres (pages 6,9). It might be added that beside the cortex, the neural cells (gray matter) are also localized in the basal nuclei. Those complexes of neural structures are visible on MRI, as the Author stated.

Presented illustrative, artistic graphs give additional value to the dissertation. It has to be stressed that the majority of those graphs were prepared by the Author himself.

In the following chapter the Author clearly presents a treatment strategy for gliomas. It has to be stressed that those neoplasms (gliomas) are not cancers according to the pathological classification (pages 10,11). Gliomas do metastasize extremely rarely. The most common symptoms of brain tumours are morning headaches followed by nausea (usually without lateralization). The second most common symptoms are neurological deficits like motor weakness, aphasia and cerebellar symptoms. The application of corticosteroids is the key conservative treatment strategy for brain tumours. The usage of corticosteroids will cause adverse effects regardless of pathology of brain tumours. While using corticosteroids, the results of brain biopsies of cerebral lymphoma usually give false negative results. This section is followed by the description of MRI. The Author describes the mechanism of MRI, functional MRI and DWI- MRI that is essential for understanding the aims of the study as long as the research combines medical and non-medical aspects. As mentioned before implemented illustrations and graphs (both medically and non-medically related) prepared by the Author undoubtedly add scientific

and educational value to the dissertation. The introduction to neuroradiology is followed by a clear description of tractography.

In the following chapters, the Author precisely and clearly describes artificial neural networks and their applications in medicine. Similarly, the descriptive graphs allow the reader who is not familiar with the application of artificial networks to confirm the rationality of the study. The following subchapters present perceptron and feedforward networks, convolutional neural networks, recurrent neural networks, attention mechanism, training neural networks with backpropagation, activation and loss functions. In the following chapter, the Author describes previous applications of machine learning in genomics and proteomics. The Author describes attempts to involve computerized clinical decision support systems in diagnosis and treatment. As the Author states those attempts were undertaken in radiology as well which is being followed in the analyzed study.

In the following section, the Author describes path search algorithms that include the Dijkstra algorithm and A* algorithm. This section is followed by a section where the Author describes more precisely tractography. He describes methods of taxonomy that include mathematical (deterministic and probabilistic) and learning (classical machine and deep) models. In the following chapter, the Author describes the hybrid method for tractography, where he describes an automated tracking pipeline, neural network for diffusion data processing (minimal and two-fold input model with input attention weights, and convolution). Subsequently, the Author implements the Modified A* algorithm. In this chapter, he describes the problem with splitting fibres, and tract smoothing.

Afterwards, the Author described DWI analysis and processing that have been used in his study. He describes the method, how the scans were coregistered, brain masks and tractograms were commutated for training labels, and labels created.

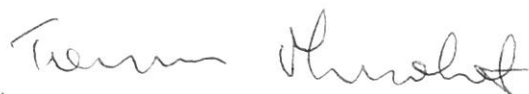
In the next chapter, the Author describes precisely the experimental dataset used for training and validating the HyTract ANN. The tools described in previous chapters are appropriately used in this research study. The results of experiments conducted in the research are described that is followed by a brief summary and discussion of the results. In the subsequent chapter, the Author focuses on the HyTract as a whole.

Similarly to the previous chapter, the experimental setup and dataset on real data are described, followed by the results. Those are followed by a brief summary and discussion of the results.

The last chapter of the manuscript consists of synthetic conclusions. The Author finds that the study revealed that ANN combined with a path search algorithm allowed for determining neural tracts with satisfying accuracy. The implemented HyTract method provided a novel technique to compute tractograms, which could be successfully used in the preoperative planning for brain tumour surgery. Implementation of the path search algorithm could be replaced by allowing to obtain additional features of the white matter using the artificial neural network. Finally, the Author identifies that an artificial neural network combined with a path search algorithm is an efficient method for determining the topology of nerve fibres that is crucial for tractography and planning of brain tumor surgeries.

I believe that the presented dissertation is an important step in the AI application to the diagnostic and treatment process of brain tumours. The Author demonstrated theoretical and multidisciplinary knowledge and has the ability to conduct research independently. In addition, the Author has proven that he can independently access and analyze collected data. The Author has correctly analyzed the literature and fulfilled the goals he set, which is why I kindly request and I ask the High Council to accept the dissertation and allow him to continue his PhD course.

Kind regards,



Tomasz Mandat

Warsaw, October 14, 2023