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### OPINION

of Prof. Dr. Dimitar Kadiysky, Doctor of Medical Sciences,

Institute of Experimental Morphology, Pathology and Anthropology with Museum (IEMPAM) at BAS, Sofia

of a dissertation work for the award of a scientific degree "Doctor of Sciences" field 4. Natural sciences, mathematics and informatics, Professional field 3. Biological sciences, Scientific specialty "Anthropology" (01.06.01).

Author: associate professor SILVIYA YANAKIEVA NIKOLOVA, doctor

## Dissertation topic:

MEDICO-BIOLOGICAL ASPECTS OF CRANIAL SUTURES: MICROSTRUCTURE, PHYSIOLOGICAL CLOSURE, METOPISM

# 1. General presentation of the author, the procedure and the materials.

The set of materials presented to me on an electronic form by associate professor Silvia Nikolova, PhD, includes a dissertation, a project for an abstract and all the required documents according to the Law on the development of the academic staff in the Republic of Bulgaria (LDAFRB), incl. Regulations for its application, necessary for conducting the defense of a dissertation for the acquisition of the scientific degree "Doctor of Sciences".

Associate Professor Silvia Nikolova has a bachelor's degree in Biology and Chemistry since 2003 at Sofia University "St. Kliment Ohridski", and since 2005 she has a master's degree in General Anthropology, majoring in Biology at the University of Sofia "St. Kliment Ohridski". Since 2011, the author of the dissertation has been a doctor in the scientific specialty of Anthropology at the Institute of Experimental Morphology and Anthropology with a Museum, BAS.

The scientific indicators of Silvia Nikolova, beyond those included in her previous registrations at National Agency for Information and Documentation (NACID), are sufficient and exceed the requirements of the Law and the Regulations for opening a procedure for the defense of a dissertation for awarding the academic degree "Doctor of Sciences".

The dissertation work of Silvia Nikolova is laid out on 251 pages, illustrated with 71 figures - diagrams, graphs, microphotographs of high quality and with 28 tables. 378 literary sources are cited.

## 2. Relevance of the topic of the dissertation.

The genesis of closing the sutures of the cranial vault, traced during the development of the individual, as well as the morphology of the bone system in the head area are the main objects of the author's scientific search, which served to write the work. The relevance of the results

included in the dissertation is complemented by a screening of some cellular and molecular mechanisms of this natural ontogenetic process in humans. The study of the essence of the phenomena of metopism in the development of the skull (in general, a relatively little studied anatomical phenomenon!) complements the relevance of the conducted studies, laid down in the dissertation.

**3. The author's literary awareness** is good, to which the active scientific collaboration with national anatomical units and with leading specialists in virtual technologies for computer 3D visualization and scanning definitely contributes.

The bibliographic reference includes the most recent scientific publications, while the historical aspect of the studies related to the morphology of cranial sutures and metopism is not omitted.

# 4. Construction and scope of the dissertation work. Scientific approaches, presentation of results.

The goal in creating the dissertation work, as indicated by the author, is to summarize newly obtained data related to the microstructure and physiological closure of the cranial sutures, as well as to evaluate the specifics of the cranial morphology in metopism.

The volume and variety of the researched material are impressive, including objects from the osteological collection of IEMPAM-BAN (medieval male and female cranial series and a sufficient number of single finds) and extensive material from the ossuary at the National Military History Museum, Sofia.

The morphometric studies and analyzes creating the basis for the construction of the dissertation were realized entirely virtually after generating two-dimensional and three-dimensional images of skulls. These include digitization of the examined material, digital radiography, generation of volumetric three-dimensional images and polygonal three-dimensional models, and finally digital morphometry. The analysis was performed through classical statistical analyses, geometric morphometrics, use of artificial intelligence solutions, through machine learning for modeling and extracting results from the processed data.

In the Results and discussion section, these data from the author's research are summarized and related to the existing scientific data regarding the microstructure of the cranial sutures and their physiological closure, incl. the correlation of the process with the age of the individual. Closure of cranial sutures and skull configuration in metopism, pneumatization of the frontal sinus, and anatomical variations such as supernumerary bones are the next subject of discussion in the study. A place is devoted to the appearance and morphology of the rarely studied bregma, worm bones and the function of fragmented ossification centers. Separate sections cover case studies such as supernumerary bones in the cranial vault and occipital region and the existence of a relationship between metopism and occipitalization of the atlas. The sequence of presentation of the results in the dissertation work and their discussion do not betray the stated research tasks and the title of the scientific work.

### 5. Conclusions and contributions.

The conclusions of the dissertation are six. These generally concern the morphology of sagittal suture closure, the correlation between physiological sagittal suture closure and the age of the individual, the peculiarities of sagittal suture closure in metopic skulls, the association of persistent metopic suture with reduced frontal sinus pneumatization, and the presence of supernumerary bones in the cranial vault.

Seven original contributions of a scientific applied nature stem from the author's research work, and to a significant extent they are related to results of modern research approaches - generation of three-dimensional images, introduction of specific methods of scanning objects, creation of a virtual collection of three-dimensional images with high resolution, introduction of a scale for reporting the degree of suture closure, computerized comparative analyzes of size and shape in metopic and non-metopic cranial series. Contributions related to the morphometry of the skull and data on the degree of closure of the cranial sutures, incl. models for predicting an individual's age at death.

Six original contributions of a theoretical nature stem from the dissertation work. They are related to the anatomy, morphology and some physiological and age-related features of the cranial sutures and the bony system of the skull. Part of the presented contributions concern the specifics of the process of pneumatization of the frontal bone and, in general, the features of metopism.

I accept the original nature of the presented 13 scientific and scientific-applied contributions to the work and consider them to be a natural assessment of the importance of the dissertation.

## 6. Evaluation of publications and impact among the scientific community.

The publication activity related to the dissertation work is proof that the author has included in her work interesting results for the scientific community. In its significant part, it represents scientific works referenced in international databases (Web of Science, Scopus) with an impact factor. Over 118 citations of articles related to the dissertation to date are a true indicator of the importance of the work.

7. The submitted abstract project (in a volume of 59 pages) reflects the results, is well illustrated with graphs, diagrams, color and black-and-white microphotographs and gives an accurate picture of the content of the dissertation.

### 8. Critical notes and recommendations.

I have no objections to the structure of the dissertation. The volume of work is sufficient and represents a synthesis and processing of obtained interesting results. The author complied with my small terminological recommendations related to the title of the paper before finalizing it.

#### 9. Conclusion.

Knowledge, skills and a scientific approach were invested in the compilation of Silvia Nikolova's dissertation. It enriches the national anthropological science, mainly developed in IEMPAM, with

modern computerized approaches. The dissertation successfully complements the anatomical view on the peculiarities of skull formation, its spatial geometry, suture closure and metopic deviations during ontogenesis. The scientific and scientific-applied results that formed the conclusions and contributions of the author's dissertation work are of interest to both preclinical and clinical biomedical science. The competent modern analysis of the data from Silvia Nikolova's many years of research suggests that the presented dissertation serves as a basis for further technologically modern visualizations of the morphology and pathology of the skull.

In connection with the above, I confidently give my positive assessment of submitted work and propose the second open meeting of the appointed scientific jury, after hearing the author's presentation, to decide on awarding the scientific degree "Doctor of Sciences" in the specialty "Anthropology " 01.06.01, Professional direction 4.3. "Biological Sciences", by Associate Professor Silvia Yanakieva Nikolova, Ph.D.

The submitted dissertation work is fully suitable in structure, content and significance for the award of this type of academic degree.

Prepared the opinion:

Prof. Dr. Dimitar S. Kadiysky, MD, PhD, DSci

Sofia