

STATEMENT

On dissertation: “**FIBROTIC ACTIVITY IN PATIENTS AFTER PERMANENT PACEMAKER IMPLANTATION**” for the award of the degree of Doctor of Education and Science, Doctoral programme "Cardiology", field 7. Health and Sport, Professional field 7.1. Medicine of the full-time Doctoral student **Dr Ivaneta Dimitrova Yoncheva Biserova** in doctoral program "Cardiology", Faculty of Medicine, Medical University Varna.

Author of the statement: Assoc. Prof. Katerina Dimitrova Vitlianova, MD, PhD, DSc. - Department of Internal Medicine, Pharmacology and Clinical Pharmacology, Pediatrics, Epidemiology, Infectious and Skin Diseases, Faculty of Medicine, Sofia University "St. Kliment Ohridski" - External member for MU-Varna

I. Procedure for defence

The opinion was prepared on the basis of Order No. RD-38-357/05.07.2024 of the Rector of MU Varna in accordance with the report No. 102-2027/18.07.2024 by Assoc. Prof. Dr. Atanas Angelov Atanasov, PhD. - Head of the First Department of Internal Diseases, in accordance with the decision under Protocol No. 25/29.07.2024 of the Faculty Council and the report with Inv.No. 103-3752/30.07.2024 from Prof. Dr. Yoto Trifonov Yotov, Ph.D. - Dean of the Faculty of Medicine at Medical University - Varna, and on the basis of Art. 24 para 6, art. 30 par. 3 of Academic Staff Development Act in the Republic of Bulgaria (ASDA), on the basis of Art 68 par. 1, Art 71 par 1, 2 and 4 of the Regulations for the Development of Academic Staff at Medical University Varna on, I have been appointed to give a statement on the dissertation of Dr. Ivaneta Dimitrova Yoncheva Bisserova entitled "Fibrotic activity in patients after implantation of a permanent electrocardiac pacemaker" for the award of the educational and scientific degree "Doctor" in the doctoral programme "Cardiology" in the field of higher education 7.3 Health and sport, professional field 7.1 Medicine.

The statement complies with the requirements for the formulation of opinions for the award of the degree of Doctor of Education and Research.

The documents were submitted electronically within the statutory deadline,.

The set of materials submitted by the candidate in electronic form for the preparation of the review, as well as the dissertation and the abstract in paper form are in accordance with the requirements of the Academic Staff Development Act in the Republic of Bulgaria (ASDA), and the Regulations for the Conditions and Procedures for the Acquisition of Scientific Degrees and for Holding Academic Positions at the Medical University of Varna.

II. Brief biographical data

Dr. Yoncheva was born in 1976 in Sofia. In 2000 she obtained a Master's degree in medicine. From 2009 to 2012 Dr. Yoncheva specialized in cardiology at the University Hospital "St. Ekaterina". Dr. Yoncheva is a certified cardiologist with expert level in "Echocardiography" (2014) and "Cardiac Pacing" (2017). Since 2019 she is enrolled as a PhD student (part-time) at the Department of Internal Medicine - Medical University Varna. From 2013-2022 she was successively Head of the Intensive Cardiology Sector and Head of Department at the University Hospital "Virgin Mary" - Burgas. Since 2022 and at present Dr. Yoncheva is Assistant Professor of in Internal medicine and Cardiology at the Faculty of Medicine, University "Prof. Asen Zlatarov.

III. Structure of the dissertation

The dissertation is written in 135 pages: introduction 1 p., literature review 56 p., aim and objectives 1 p., patients and methods 14 p., results and discussion 32 p., conclusions 1 p., contributions 1 p.. Bibliography includes 409 references in Latin. The work is illustrated with 5 tables and 34 figures. The study was carried out in the cardiology department of the University Hospital " St. Virgin Mary", Sofia. The study was carried out in the research laboratory of the St. Mary's Hospital, Burgas. The procedure for inclusion of patients and controls was initiated after approval of the Research Ethics Committee of the Medical University of Varna 82/28.03.2019 and the Research Ethics Committee of the University Hospital "St. Virgin Mary", Burgas 502/21.03.2019.

IV. Actuality of the dissertation

The actuality of this dissertation is determined by the increasing number of patients with implanted pacemakers and the technological development of medicine in this direction. The development of HF in patients after permanent pacemaker implantation (PECS) with right ventricular apical pacing

within 2 years is a significant social, medical and scientific problem. Right ventricular apical pacing-induced electrical and mechanical dyssynchrony leads to changes in cell metabolism and left ventricular remodeling.

Determinants of the need and relevance of this dissertation are the lack of sufficient data regarding dynamic changes in extracellular matrix fibrosis status and collagen deposition in the myocardium of patients with PECS, and the need for an effective non-invasive method to diagnose them.

V. Essence of the dissertation

The aim is well defined and the tasks are well systematized and meet the objective. As a summary of the results, Dr. Yoncheva found a significant increase in the major regulatory molecules (transforming growth factor beta - TGF- β 1, connective tissue growth factor - CTGF and carboxy terminal propeptide of procollagen type I - PICP) responsible for collagen synthesis during the follow-up period correlated with increased synthesis of cardiac interstitium-specific collagen type I. Another important result was the establishment of a relationship between the dynamics in the levels of Amino-terminal propeptide of procollagen type III (PIIINP) and perioperative tissue trauma as a possible source for the increased collagen type III synthesis. She found a worsening electrical asynchrony and slowing of conduction velocity with increasing LV volume and prolongation of the paced QRS complex in the myocardium in the studied group of patients.

The thesis concludes with five specific and well-articulated contributions of an original nature.

The fibrotic process after PECS implantation was studied for the first time, The dynamics in the levels of the main regulatory molecules of collagen synthesis after PECS implantation was established. It has been shown that by the 6-th month after PECS implantation the development of structural and electrophysiological changes in the myocardium begins. The results obtained in this thesis provide an opportunity to search for new therapeutic options to influence myocardial remodeling.

VI. Publications and research.

On the basis of her dissertation work Dr. Yoncheva has 4 full-text publications in foreign journals in 3 of them she is the first author and 4 participations in congresses symposia and conferences.

In conclusion, Dr. Yoncheva's dissertation work fully meets the requirements for the award of the scientific and educational degree "Doctor" in terms of structure and content

All this gives me a reason to vote positively and to propose the members of the Scientific Jury at the Medical University "Prof. Dr. Paraskev Stoyanov"-Varna to vote positively for the award of the educational and scientific degree "Doctor" in the doctoral program "Cardiology to Dr. Ivaneta Dimitrova Yoncheva Bisserova.

13.09.2024 г.

Sofia

Assoc. Prof. Katerina Vitlianova, PhD, DSc.

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