SUMMARY OF HABILITATION THESIS

Title: Integrative research in cardiology: from cardiac electrophysiology to heart failure
Author: dr. Frigy Attila

The habilitation thesis includes (1) the main themes and results of the research activity of the last two decades (a selection based on the most relevant publications), (2) the main data of the professional and academic career, and (3) the perspectives and plans for the development and diversification of the scientific, professional and academic activity of the author.

The scientific premises of the thesis are represented first of all by the PhD thesis, written under the supervision of Professor Simion Cotoi, and held publicly in January 2002. The PhD thesis dealt with a method of non-invasive cardiac electrophysiology - heart rate variability - and included several studies, performed on healthy subjects and cardiac patients, mainly for methodological purposes, with the primary objective of testing the feasibility of the method under various physiological and pathological conditions. The majority of the studies were carried out using a computerised rhythm analysis system, designed and manufactured in-house. In my interpretation and that of the evaluators, the thesis was a solid proof of the scientific and practical potential of non-invasive cardiac electrophysiology methods. Continuing research in this field was a natural consequence of my previous activity, but at a different level, in terms of the methodology used, the co-option of new topics and objectives more closely related to practice. Parallel to my professional training and my increasing involvement in the care of cardiac patients, especially those with heart failure, it became a necessity to develop clinical studies in this field, related to practical problems. These heart failure research studies have addressed several topics, among which I would just mention the issues of comorbidities, biomarkers and ultrasonographic imaging.

The **first Section** of the thesis presents the scientific, professional and academic achievements.

The **first Chapter** contains the main data and results of the research undertaken in the field of non-invasive cardiac electrophysiology, basically the continuation of my work contained in the PhD Thesis. The main research directions and the results of selected studies are presented below, most of them being materialized in articles and conference abstracts:

a. heart rate variability analysis
    - the influence of blood pressure measurement on short-term heart rate variability
    - the study of autonomic influences in the genesis of frequent premature ventricular beats in patients without structural heart disease

a. the study of the early repolarization electrocardiographic pattern
    - ECG and echocardiographic changes associated with the early repolarization pattern in young, healthy men

b. analysis of atrial depolarisation by P-wave analysis. Prediction of atrial fibrillation.
    - prognostic value of P-wave characteristics after electrical cardioversion in patients with atrial fibrillation.

c. ventricular repolarisation analysis - assessment of QT interval
    - effect of mental arithmetic on heart rate and QTc interval in young, healthy individuals

- study of the QT interval in heart failure with reduced ejection fraction, and in hypertension

d. miscellaneous studies

- estimation of exercise heart rate, based on resting ECG, in patients with permanent atrial fibrillation
- study of the Littmann-concept phenomenon in patients with severe aortic stenosis

The **second Chapter** contains the description and results of the main studies conducted in the field of heart failure. Similar to Chapter 1, the main research topics and the related, selected studies are presented, most of which being contained in articles and conference abstracts:

a. assessing the clinical importance of comorbidities in heart failure

- the study of anaemia in patients with acute heart failure, and in severe aortic stenosis
- the study of the importance of sleep apnoea in hospitalised patients with acute heart failure; the influence of sleep apnoea on circadian variation of ECG and blood pressure parameters in patients with acute heart failure
- association of negative psychical characteristics with cardiac morpho-functional changes in heart failure
- clinical significance of severe tricuspid regurgitation present at admission in patients with acute heart failure
- the study echocardiographic patterns in patients with heart failure and thyroid dysfunction
- the study of significance of clinical frailty in hospitalized patients with acute heart failure

b. biomarker studies in patients with heart failure

- the study of the correlation between total 25-hydroxy-vitamin D and left ventricular ejection fraction in heart failure patients with low and mildly reduced ejection fraction
- the study of the determinants of arterial stiffness, with a focus on biomarkers of calcium metabolism, in patients with heart failure with reduced ejection fraction
- the study of biomarker CA-125 in the assessment of heart failure patients

c. assessing the usefulness of chest ultrasound in heart failure patients, and in patients with COVID-19

- the study of the prognostic value of chest ultrasound in patients with aortic stenosis

Chapter 3 contains a summary of the main professional and academic (teaching) achievements, and a summary of the scientific activity in figures.

I am a primary (consultant) physician of internal medicine (since 2004) and cardiology (since 2006), and I do my clinical activity at the Clinical Department of Cardiology of the Mures County Clinical Hospital, being the head of the Department since its establishment (2013).

I perform a number of routine and special explorations and therapeutic procedures, among them I would highlight: advanced transthoracic echocardiography techniques, transesophageal echocardiography, chest ultrasound, non-invasive cardiac electrophysiology techniques, cardiovascular autonomic testing, nocturnal polygraphy, non-invasive ventilation techniques, central venous catheterisation, transvenous

temporary pacing and pericardial puncture. I have acquired by examen the diploma of competence in general and transesophageal echocardiography and the European certification in transthoracic echocardiography.

I am a member of several professional societies, including the European Society of Cardiology (ESC, Fellow since 2015), the European Association of Cardiovascular Imaging (EACVI, Fellow since 2021), the European Heart Failure Association (HFA, Fellow since 2022, member of the Study Group on Heart & Brain, 2022-2024).

I am currently associate professor (since 2022), member of the Department of Internal Medicine IV of the Department M4, Faculty of Medicine, UMFST "G.E. Palade", Tg. Mureș, with 24 years of university teaching experience.

My actual teaching activity includes lectures, clinical internships and practical work with students, and the development of various teaching materials. The work with students also involves (1) coordinating and supervising graduating theses (110 since 2000), (2) coordinating students` research studies (96 since 2000, TDK and Marisiensis conferences), and (3) organising workshops at student conferences.

Since 2020 I am residency coordinator in cardiology. I am lecturer in the course for obtaining the certificate in general echography (module II, echocardiography). I have been coordinator and lecturer for a number of postgraduate, continuing medical education (CME) courses (36).

I have been the vice-dean of the Faculty of Medicine between 01.11.2012 - 30.04.2014, and 11.04.2016 - 20.04.2018, respectively, member of the Council of the Faculty of Medicine in the same period, member (period 2012-2023) in various Working Committees of the Faculty of Medicine (e.g. Residency Training Committee, Medical Committee). I have been a member of the Alumni Department and CEIPSCU since 2020.

I have participated several times in various committees for the elaboration of subjects for the admission exam, graduating exam (specialist committee) and residency exam (delegate in the central committee).

The scientific activity included in this thesis has materialized in numerous articles (original papers, reviews, case presentations), presentations (abstracts) at various conferences (regional, national, international) and student scientific papers (conference presentations, undergraduate and dissertation theses).

Summary of my scientific activity in figures:

- no. papers published in extenso: 79 (main author: 52, first author: 29)
    - o indexed in Web of Science (ISI): 32 (main author: 22, first author: 8)
    - o listed in Web of Science (ISI): 27 (main author: 18, first author 6)
- No. of conference papers (first author, co-author): 167
    - o published in ISI-indexed abstract volumes: 31
- Hirsch index: 6
- Web of Science citations: 126
- Cumulative IF: 59,268
- book chapters: 8
- books/courses for students (author, co-author): 7
- research grants: 9 (project director: 7)

The **second section** of the Thesis details the plans of scientific, academic and professional career development. In the development of the scientific activity, the emphasis will be on continuity (main areas), but also on addressing new research directions, involving advanced, complex, high-end imaging and laboratory explorations (molecular biology, genetics, specific biomarkers). Obtaining the habilitation certificate would facilitate the continuation of research at a higher level, and the status of PhD supervisor, by co-opting young researchers, PhD students and future PhD students, would greatly contribute to building of a high-performance, motivated research team. On the teaching side, in addition to the development of new teaching materials, I will focus on increasing the efficiency of the teaching process by promoting student-oriented approach, with the main purpose of developing medical/clinical thinking and practical skills and competences. Professionally, the essence of career development is the acquisition of new expertise and skills, mainly in interdisciplinary areas, like cardio-oncology, cardio-nephrology and cardio-diabetology.

The thesis concludes with a list of bibliographical references (total 222) related to the two sections.

My scientific, professional and academic work reflected in this thesis would not have been possible without the guidance, support and de facto contribution of mentors and close collaborators. Being deeply grateful to all these wonderful people, to avoid being exhaustive, I would mention Prof. Dr. Simion Cotoi, Prof. Dr. Alexandru Incze, Prof. Dr. Emilian Carașca, Prof. Dr. Nagy Előd, Dr. Kocsis Ildikó, Dr. Fehérvári Lajos, Dr. Szabó István Adorján and Dr. Vass (Szabó) Tímea Magdolna. Sincere thanks to all the young people, PhD students, residents and students, who over the years, in addition to their thorough research work, have provided me with a continuous source of inspiration, energy and motivation.

Warm thanks to my family, especially my wife Gerda, for their support and trust.

Dr. Frigy Attila