

**BASIC AND CLINICAL RESEARCH IN
CARDIOLOGY**

Habilitation thesis

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Summary

My involvement in clinical research started already in the first years after I graduated the University of Medicine, when I initiated many research directions that I developed afterwards during my entire scientific and professional career.

Already in the 80's I observed and described for the first time in the literature the **architectonic modifications of the left ventricle** in cases with advanced heart failure and dilated cardiomyopathy, and I tried to explore the mechanisms that could contribute to maintenance of cardiac output in these circumstances: inter-relation between the mechanisms for preservation of cardiac output and those contributing to arrhythmia genesis, possible role of the stem cells injected in the diseased area, etc. The hypothesis of left ventricular architectonic modifications was demonstrated later with the help of three-dimensional echocardiography and 3D Angio CT in my Laboratory of advanced research in cardiac imaging, being communicated in the most prestigious international conferences (*European Congress of Cardiology, Euroecho, Heart Failure, etc*).

I also formulated the hypothesis that extension of the **myocardial fibers from the left atrium into the pulmonary veins could represent** a compensatory mechanism in cases with advanced heart failure and contribute to genesis of arrhythmia, hypothesis that I demonstrated and communicated in 1985, being recognized on international level in 2000, when these myocardial fibers have been proved to represent the substrate of common atrial arrhythmia in these cases and pulmonary vein ablation was introduced.

Following an intensive research activity dedicated to pulmonary hypertension I created a special catheter for transcatheter pulmonary puncture-biopsy and I performed for the first time in the world a **transvascular pulmonary puncture-biopsy** using right heart catheterization, as a measure to collect samples of pulmonary tissue in cases of pulmonary hypertension. For this invention I obtained a **patent** for the device and technique - *Patent OSIM nr. 100812/11.06.1990 – Endovascular Pulmonary Puncture Biopsy – method and device*.

As a measure of my intense research activity in these years I participated in **7 research contracts with the Romanian Academy of Medical sciences in the period 1980 - 1985**, in 4 of them as coordinator.

All these research priorities have been reflected in my PhD thesis entitled "**Contributions in diagnosis and treatment of Dilated Cardiomyopathy**" which I finalized in 1993 and since then I continued to explore them together with new

research hypotheses in the field of Dilated Cardiomyopathy, in parallel with diversifying my research activity in other fields of cardiology.

During my PhD studies I introduced in our center several new methodologies related to research of dilated cardiomyopathy such as **endomyocardial biopsy** or determination of ventricular volumes using cardiac catheterization. Even in the years of my doctoral studies, other major fields of interest were represented by acute coronary syndromes, study of vulnerable plaques, congenital heart diseases, diseases of the pericardium, peripheral arterial diseases or arrhythmia.

In 2000 I created the Clinic of Cardiology in the County Clinical Emergency Hospital Targu Mures, and a laboratory of research of excellence in cardiovascular diseases, which succeeded to win **4 CEEEX research grants under my leadership**, followed by **3 research grants in the national Partnership (PNCD II) programme**, 2 in the IMPACT programme, and **one research grant in the FP7 programme**, financed by the European Commission. One of these grants, dedicated to stem cell transplantation post acute myocardial infarction, received two awards from the Romanian Ministry of Education and Research and the Romanian Academy of Medical Sciences.

One of my main achievements on professional level was the **introduction of new methodologies** in clinical practice, such as

- Starting with the year 2001 I introduced **excimer laser angioplasty** in peripheral arterial diseases and also in the treatment of coronary artery diseases and in acute coronary syndromes.

- In 2007 I started a research project dedicated to **stem cell transplantation in postacute myocardial infarction patients and also in critical limb ischaemia** (CEEEX grant TRANSCARDIOSTEM, contract no. 172/2006, financed by the Romanian Ministry of Research and Romanian Academy of Medical Sciences), and within this project I performed in 2007 the first intracoronary stem cells injections in patients with previous acute myocardial infarction, and several months later the first intraarterial and intramuscular stem cells injections in patients with critical limb ischaemia.

- I performed in 2007 the **first intracardiac echocardiography** to assist implantation of an atrial occluder in a young patient with atrial septal defect.

- In 2007 I performed the **first CARTO ablation** in a patient with atrial fibrillation, as a live case demonstration during the international congress of cardiology.

- In 2008 I performed the **first intravascular echography associated with virtual histology** for assessment of atheromatous coronary plaque composition and in 2012 I introduced in the clinical practice the technology of **Optical Coherence**

Tomography, useful for intracoronary assesment of plaque vulnerability and also for assesment of coronary stents.

-In 2013 I performed the first **Renal denervation** in refractory hypertension, a new methodology which starts now to be implemented in Europe for treatment of severe cases of hypertension

The **most representative research directions that I developed in the recent years are:**

-**Research dedicated to vulnerable plaque**, describing for the first time the quantification of the vulnerable core of atheromatous coronary plaque with the help of cutting-edge imagistic technologies - published in *Canadian Journal of Cardiology* - **IF 3.1**, *International Heart Journal* - **IF-1.2**)

-Research dedicated to **stem cells** - results published in and was reflected in many publications in high-impact journals (*Nature Clinical Practice CV Medicine* - **IF 5.9**, *Stem Cell Review and Reports* - **IF 3.7**, *American Heart Journal* - **IF 4.5**, *Journal of Molecular and Cellular Cardiology* - **IF 5.1**). In 2013 I described for the first time in the literature the long-term protective effect of the stem cells against progression of atherosclerosis (*Journal of Atherosclerosis and Thrombosis*, **IF 2.7**).

-Research dedicated to different applications of cutting-edge technologies in cardiac imaging - results published in *European Heart Journal* - **IF 14.1**, *European Heart Journal - Cardiovascular Imaging* - **IF 2.4**, *Heart and Vessels* - **IF 2.1**.

-Especially my activity in the field of **STEMI networks** received a large appreciation on international level, the results being published in the prestigious journal "American Heart Journal" - **Benedek Imre**, Gyongyosi Mariann, Benedek Theodora. *A prospective regional registry of ST-elevation myocardial infarction in Central Romania: Impact of the Stent for Life Initiative recommendations on patient outcomes. American Heart Journal* 2013, 166 (3):457-465, ISSN 0002-8703, **IF 4,497**. In this study I demonstrated that the intervention of the appropriate logistic measures in the network had a significant impact and led to a more substantial increase in the total number of patients treated for STEMI, in parallel with a significant reduction in mortality from 22% at the initiation of the study to 6.35% in 2011. Also, our results received extremely positive appreciations from the American scientific community, as proved by the editorial published by this journal in the same number, where the prestigious editors of American Heart Journal appreciated, in the editorial entitled "Regional systems of care in ST-elevation myocardial infarction – do they save lives?" by T. Henry, that "**The impressive results from the de-novo development of a regional STEMI system in Central Romania reminds us the impact of regional systems and should lead us**

to focus our attention on implementing strategies to provide our life-saving, evidence-based and guideline-recommended therapy”

The international nature of my research activity is reflected by the large cooperation with many research groups activating in different European countries, resulting in common publications and pan-european grants, and also by the numerous publications in high impact journals from Europe, USA and Japan, most of them as principal author (American Heart Journal, Canadian Journal of Cardiology, European Heart Journal, Nature, International Heart Journal, Journal of Atherosclerosis and Thrombosis, Heart and Vessels, etc), totalizing an **impact factor of >50**. This proves the high level and the European dimension of my research and professional activity.