

# HABILITATION THESIS

# MYOCARDIAL ISCHEMIA – FROM ATEROSCLEROSIS TO CLINICAL MANIFESTATIONS

DIANA ȚÎNȚ

2016

# CAREER OVERVIEW



# MEDICAL DEVELOPEMENT



**Cardiology senior MD  
2010**

**Internal medicine senior:  
2004**

**Cardiology specialist:  
2003**

**Internal medicine  
specialist 1999**

# MEDICAL DEVELOPEMENT



**Interventional cardiology  
Fellowship 02.2006-04.2006**



**Complex  
arrhythmia  
ablation  
03.2013-09.2013**



**2009-2011**

**EHRA  
TRAINING  
FELLOWSHIP**



# UNIVERSITARY TEACHING DEVELOPEMENT



**Universitatea  
TRANSILVANIA  
din Braşov**

**Associate Professor: 2009  
- present**

**University Lecturer: 2004  
- 2009**

**University Assistant:  
2000 - 2004**

**University Preparator:  
1995 - 2000**

# SCIENTIFIC ACHIEVEMENTS

# SCIENTIFIC ACHIEVEMENTS

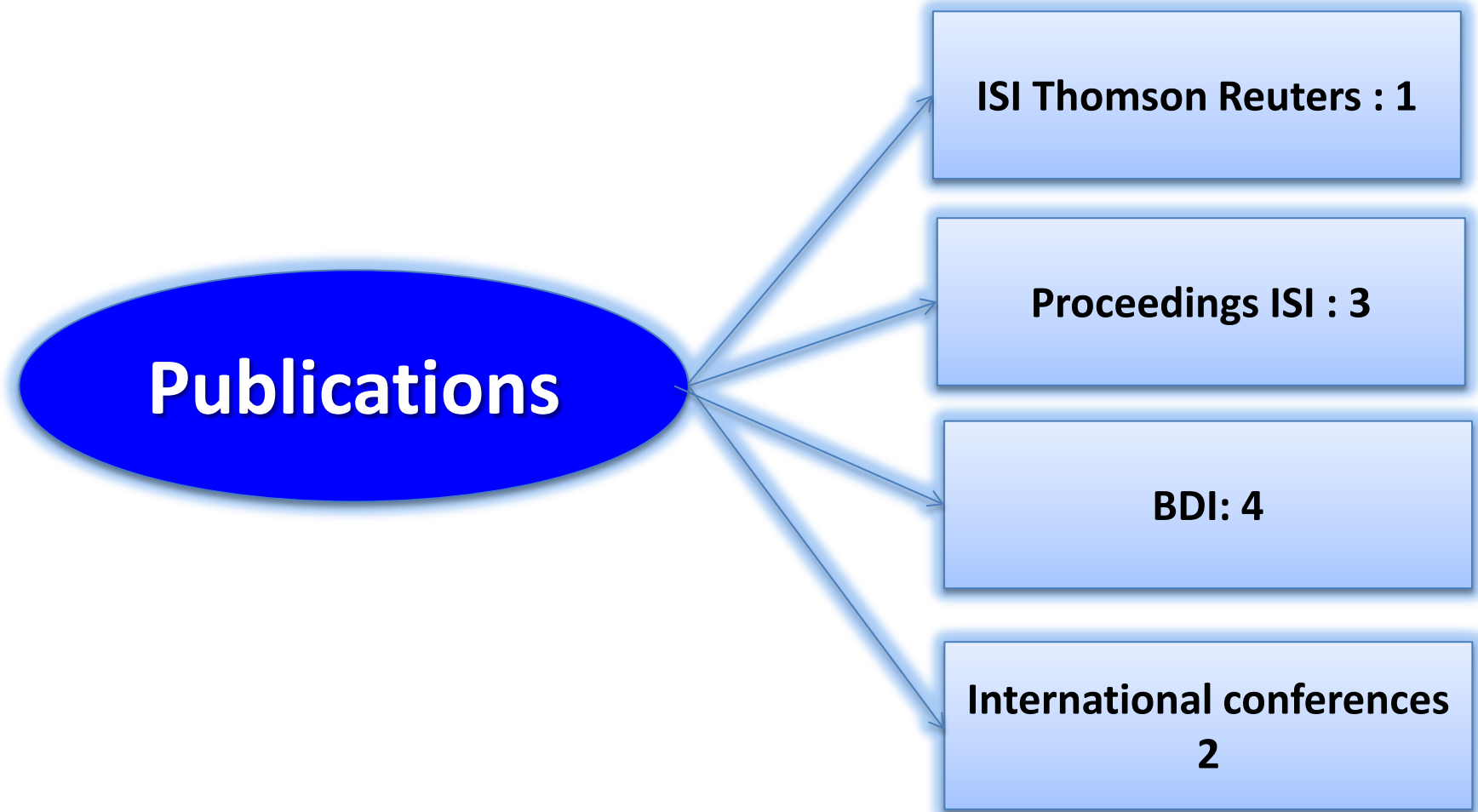
## Scientific developments in the field of

**myocardial  
infarction**

**atherosclerosis  
and metabolic  
syndrome**

**atrial  
fibrillation  
ablation  
therapy**

# 1. Scientific developments in the field of myocardial infarction





## „Long term prognosis in patients with acute myocardial infarction treated with fibrinolytic therapy”

**The aims** of my doctoral thesis were:

- To identify the risk factors for cardiovascular events post-infarction (death, post-myocardial angina/re-infarction and heart failure)
- To correlate the identified factors with the occurrence of these cardiovascular events tracked for a period of two years follow-up in patients with acute myocardial infarction treated with fibrinolytic therapy.
- To create an experimental predictive model based on identified risk factors and to evaluate the risk of death at to two years

## What was new

I tried to identify new prognostic factors

- peripheral arterial disease
- laboratory determinations (serum level of alpha hydroxybutyrate dehydrogenase) – for the assessment of myocardial damage

These new factors have not been studied at that time in relation with the outcome of patients with acute myocardial infarction treated with fibrinolysis.

## What was new

We developed a **clinical risk prediction model** for estimating the cumulative two years risk of death in patients with AMI who received pharmacological reperfusion therapy.

GATA-model-nou-2

C6 : 560

Diana TINT		Two years risk of death prediction after acute myocardial infarction treated with fibrinolytics			
Risk factor	Data				
Gender	m	[M / F]	✓	0.00	
Age [years]	62	[31 - 79]	✓		
α-HBDH 72	560	[140 - 2000]	✓	-0.11	
PAD	y	[Y / N]	✓		
Admission BP	135	[70 - 200]	✓	-0.50	
Admission HR	74	[36 - 170]	✓		
LVEF	33	[18 - 63]	✓	-9.27	
Calculate	Results				
Complete data?	Y	[Y / N]			
Percent risk	80.016	[0 - 100]			
Estimated risk	very high				

GATA-model-nou-

C11 : Results

Diana TINT		Two years risk of death prediction after acute myocardial infarction treated with fibrinolytics			
Risk factor	Data				
Gender	m	[M / F]	✓	0.00	
Age [years]	65	[31 - 79]	✓		
α-HBDH 72	400	[140 - 2000]	✓	-0.08	
PAD	n	[Y / N]	✓		
Admission BP	115	[70 - 200]	✓	-0.43	
Admission HR	77	[36 - 170]	✓		
LVEF	32	[18 - 63]	✓	-8.99	
Calculate	Results				
Complete data?	Y	[Y / N]			
Percent risk	29.395	[0 - 100]			
Estimated risk	medium				

# STEMI national registry

## Active involvement in creation, development and analysis of the National Romanian Registry for Acute Myocardial Infarction RO-STEMI



Romanian Journal of Cardiology | Vol. 26, No. 1, 2011



### ARTICOLE ORIGINALE

Vârsta, factorii de risc cardiovascular, terapia și mortalitatea intraspitalicească la pacienții cu infarct miocardic acut cu supradenivelare de segment ST. Un subraport al Registrului Român pentru infarctul miocardic acut cu supradenivelare de segment ST (RO-STEMI).

Diana Ținț, Mariana Rădoi, A. Petriș, D. M. Datcu, Crina Sinescu, Elvira Craiu, D. Vinereanu, Maria Dorobanțu, D. D. Ionescu, C. Macarie, Carmen Ginghină, Cătălina Arsenescu-Georgescu, Luminița Șerban, P. Stănciulescu, I. Petrescu, L. Petrescu, A. Tase, Eugenia Nechita, Lăcrămioara Topolnițchi, I. Benedek, D. Dobreanu, Smaranda Gârbea, A. D. Gheorghe, Luminița Vida-Simiti, D. Olinic, C. Pop, G. Tatu-Chițoiu,  
*din partea investigatorilor RO-STEMI*

**This research took in consideration data of 10037 STEMI patients.**

# STEMI national registry

## What was new

Through the high volume of information coming from the centers spread throughout the country this Registry reflects the demographic and therapeutic characteristics, and the outcome of the STEMI patients hospitalized in Romanian hospitals over a decade.

# Mechanical reperfusion in patients with STEMI - Percutaneous transluminal coronary angioplasty (PTCA)

*Mol. Cryst. Liq. Cryst.*, Vol. 603: pp. 99–104, 2014  
Copyright © Taylor & Francis Group, LLC  
ISSN: 1542-1406 print/1563-5287 online  
DOI: 10.1080/15421406.2014.968072



## **Advanced Metallic Stents and Their Efficiency in Complicated Myocardial Infarction Treatment**

DIANA TINT,<sup>1,2,\*</sup> STEFANIA SIMA,<sup>1</sup> ILEANA RAU,<sup>3</sup> FLORIN  
OVIDIU ORTAN,<sup>2</sup> AND MARIUS ALEXANDRU MOGA<sup>1</sup>

# Mechanical reperfusion in patients with STEMI - Percutaneous transluminal coronary angioplasty (PTCA)

## What was new

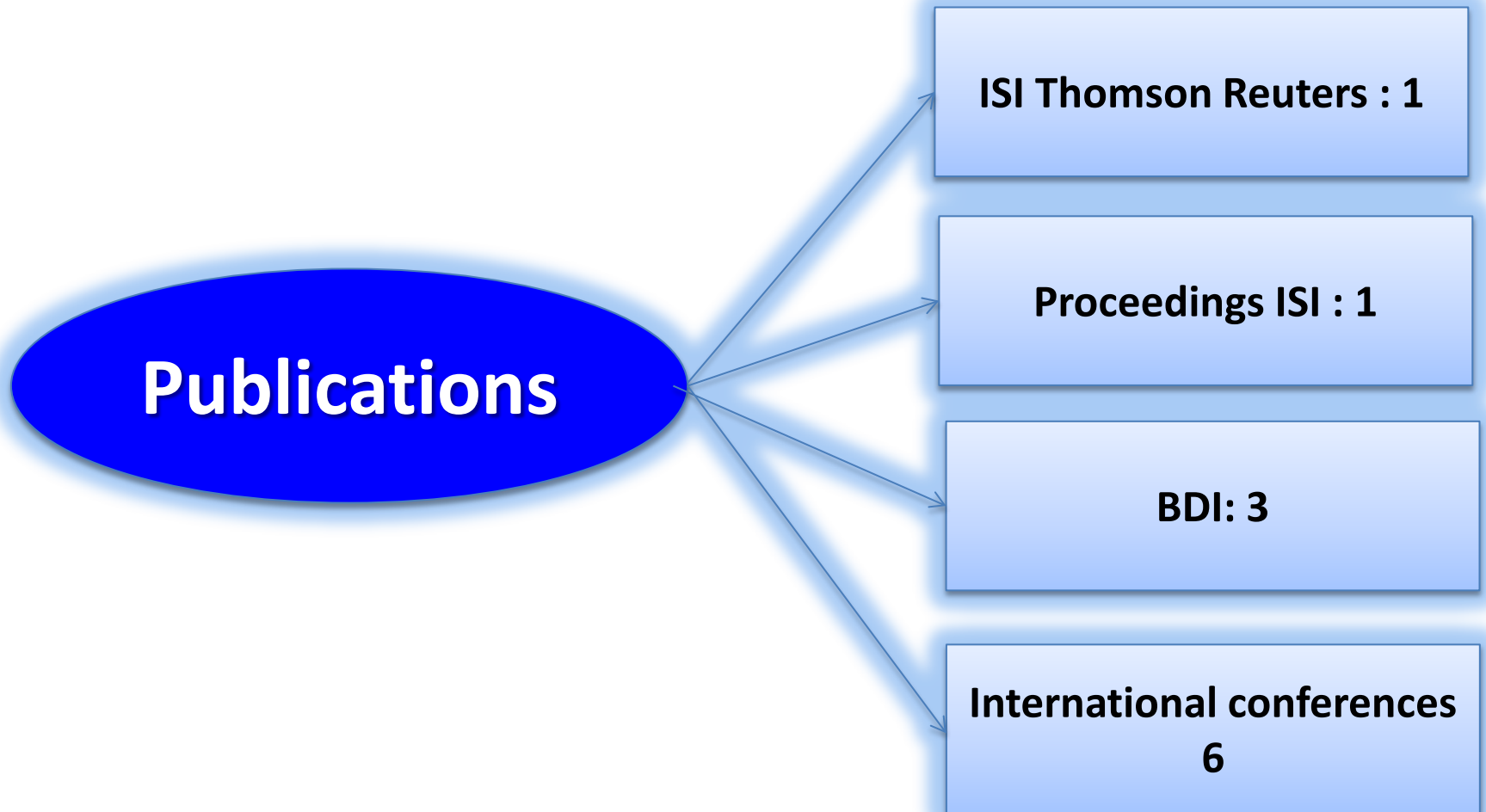
**Limited data are available regarding the outcome of patients with CAVB after primary PCI.**

- The incidence of CAVB in STEMI pts. was 6.5%
- The patients with CAVB were older, were female in greater proportion had more diabetes mellitus and had significantly higher mortality (14% vs. 2.4%) than patients without CAVB.
- The mortality in patients with CAVB and anterior infarction was even higher (43%).
- The resolution of CAVB after revascularization appeared in 76% of pts. with inferior myocardial infarction and in just 28% of pts. with anterior myocardial infarction ( $p = 0.019$ ).

In conclusion

**CAVB in patients with acute myocardial infarction remains a severe condition associated with high in-hospital mortality despite prompt and efficient revascularization.**

## 2. Scientific developments in the field of atherosclerosis and metabolic syndrome







**Research Article**

**Open Access**

## Low dose Flaxseed Oil Supplementation Alters the Fatty Acids Profile and the Progression of Metabolic Syndrome in Men without Adequate Medical Treatment

Tint D<sup>1</sup>, Anghel M<sup>1</sup>, Lupu DS<sup>2</sup>, Fischer LM<sup>3</sup> and Niculescu MD<sup>2,3\*</sup>

<sup>1</sup>School of Medicine, Transilvania University in Brasov, Brasov, Romania

<sup>2</sup>UNC Nutrition Research Institute, Kannapolis, NC, USA

<sup>3</sup>Department of Nutrition, School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

# The study

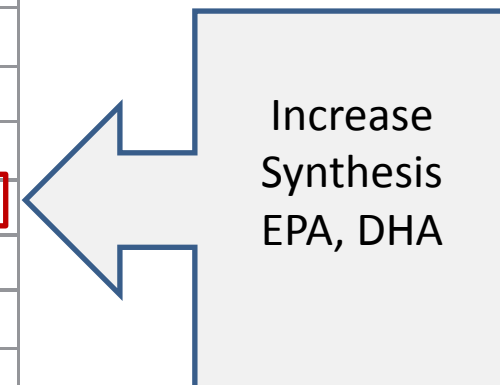
A double-blind, placebo-controlled, randomized intervention trial, designed to determine secondary clinical and biochemical outcomes related to changes in the phenotypic presentation of the metabolic syndrome during the intervention after supplementation with ALA for 3 months.

## What was new

- The administration of a supplement rich in ALA - since most of the research on  $\omega$ -3 fatty acids has been focused on dietary interventions using DHA
- Subjects with a lower probability of significant  $\omega$ -3 fatty acids intakes - the two main types of cooking oils that contain ALA (canola and soybean oil) are not generally used by the majority of Romanians.

# Fatty acid composition of the supplements

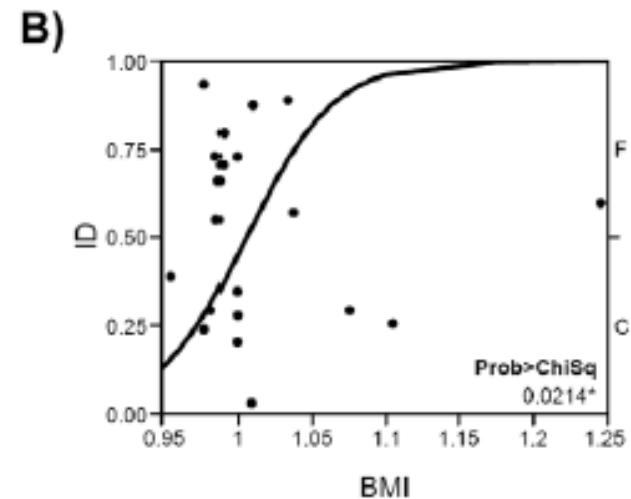
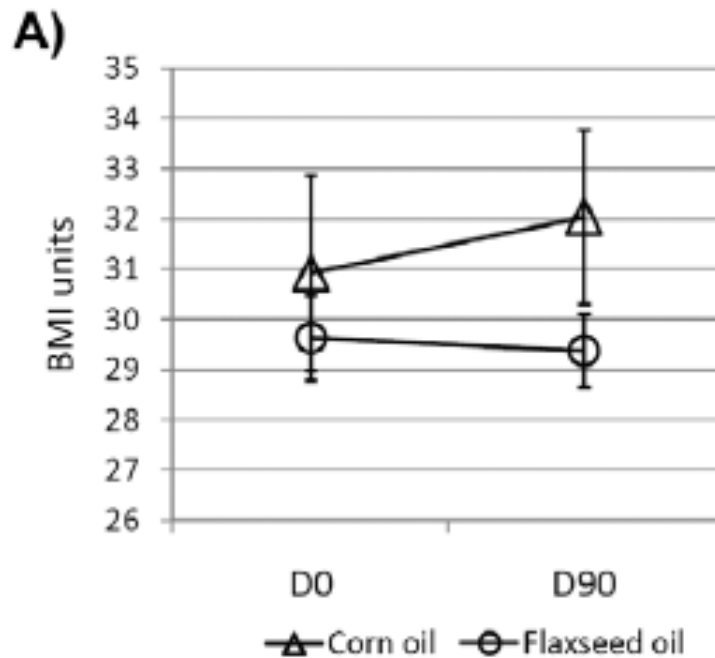
FA species		FA concentration $\mu\text{mol/mL}$	
		Corn oil	Flaxseed oil
14:0	myristic	ND	1.26
16:0	palmitic	368.51	200.44
16:1n7	palmitoleic	3.78	3.26
18:0	stearic	55.47	119.01
18:1n9	oleic	844.36	528.58
18:2n6	linoleic	1653.74	554.79
18:3n3	linolenic	13.51	1638.40
20:0	eicosanoic	25.24	ND
20:1n9	11-eicosenoic	9.31	5.79
20:2n6	11,14-eicosadienoic	ND	1.27
20:3n3	11,14,17-eicosatrienoic	ND	1.53
22:0	behenic	3.62	3.93
22:1n9	erucic	ND	1.28
22:5n3	7,10,13,16,19-docosapentaenoic	1.66	1.06
24:0	lignoceric	5.42	3.69



ND. not detectable

# MS-related parameters

**BMI assessment between the start (day 0) and the end of the study (day 90)**



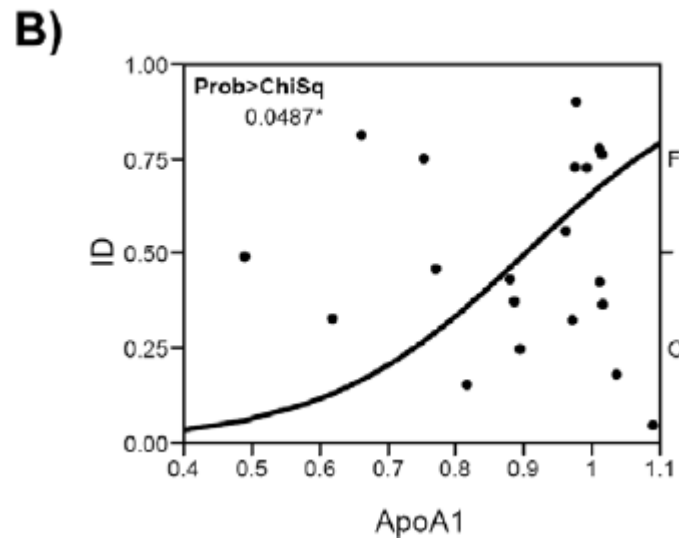
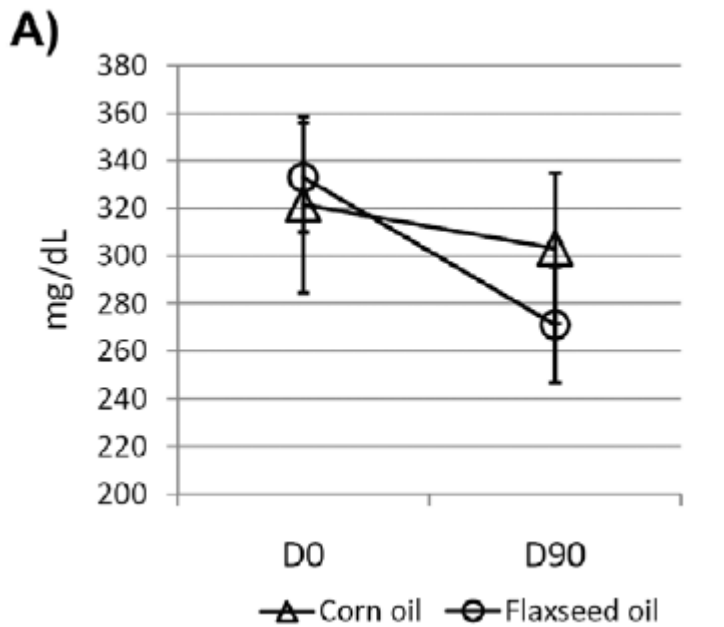
# MS-related parameters

**Insuline resistance assessment between the start (day 0) and the end of the study (day 90)**

Variable	Corn oil		Flaxseed oil	
	D90/D0 ratio	D90/D0 bivariate model (Prob > F)	D90/D0 ratio	D90/D0 bivariate model (Prob > F)
AST	0.90 ± 0.10	NS	0.84 ± 0.11	0.0096
ALT	1.26 ± 0.35	NS	0.97 ± 0.14	0.0017
Col	1.03 ± 0.04	0.0146	0.98 ± 0.04	NS
TG	1.05 ± 0.10	0.0057	0.93 ± 0.09	NS
Insulin	2.11 ± 0.79	NS	1.12 ± 0.17	0.0359
HOMA	2.00 ± 0.66	NS	1.16 ± 0.20	0.0243
TNFα	1.20 ± 0.70	NS	0.75 ± 0.19	0.0188

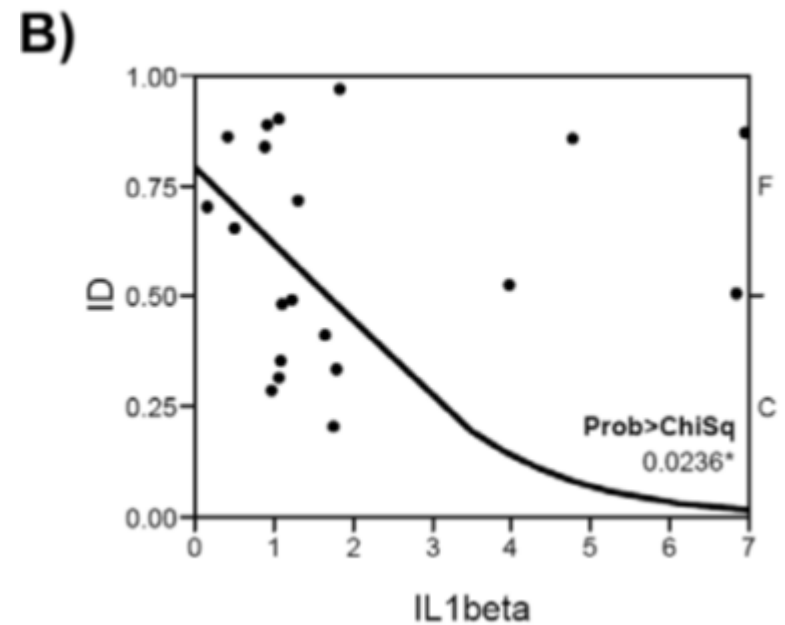
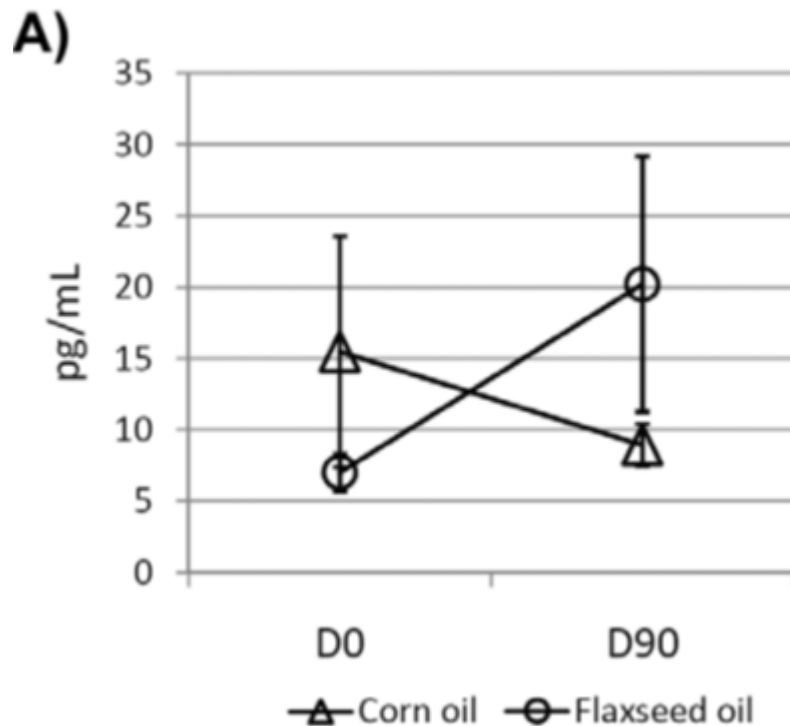
# MS-related parameters

Serum ApoA1 assessment between start and end of study.



# Markers of inflammation

Serum IL $\beta$ 1 assessment between start and end of the study



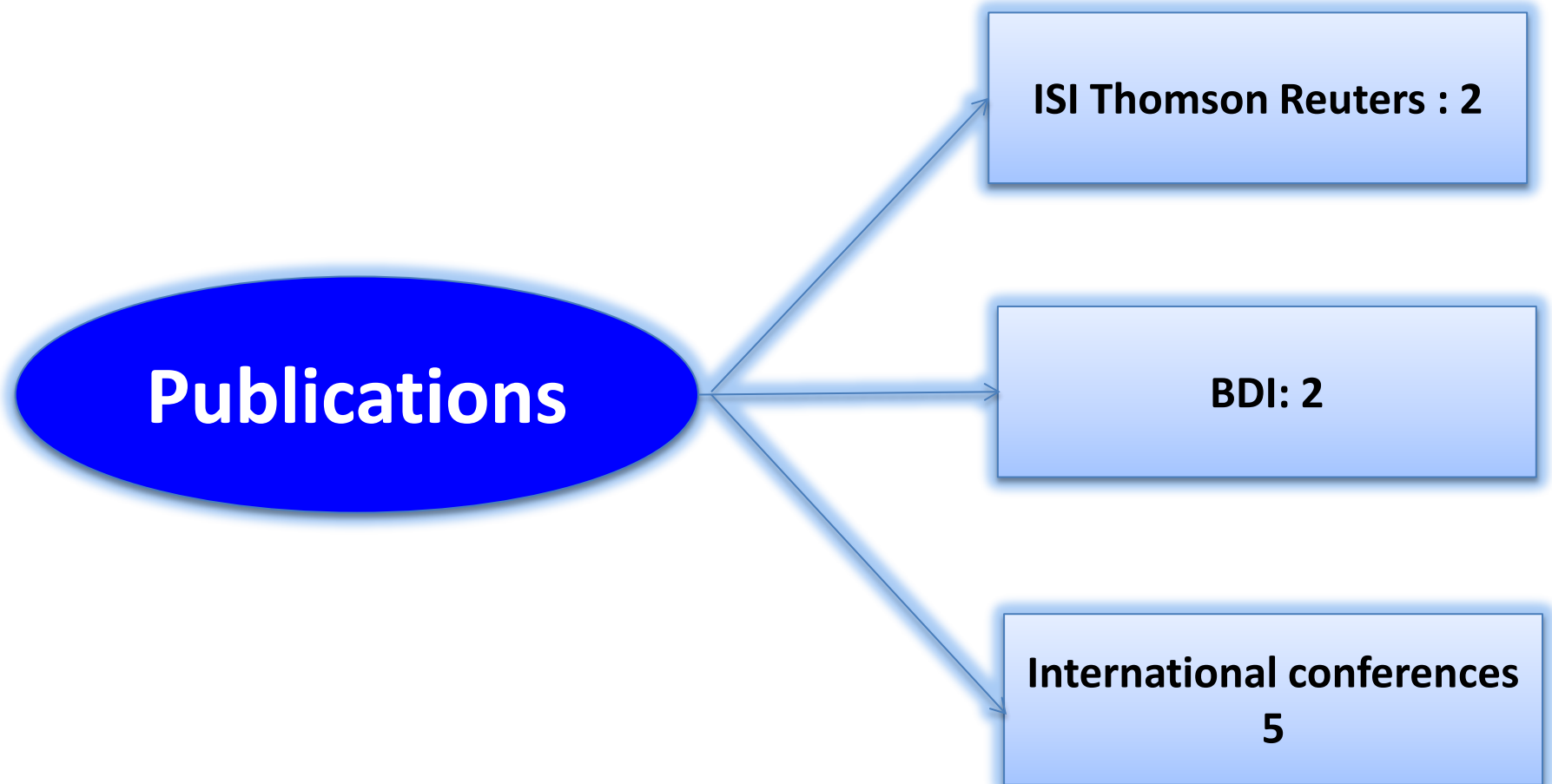
# Conclusions

1. Low daily doses of flaxseed oil may improve clinical and metabolic parameters in middle-aged men without adequate treatment for metabolic syndrome.
2. Low daily doses of flaxseed oil may alter the profile of inflammation markers, apolipoprotein A1, and plasma fatty acid composition.

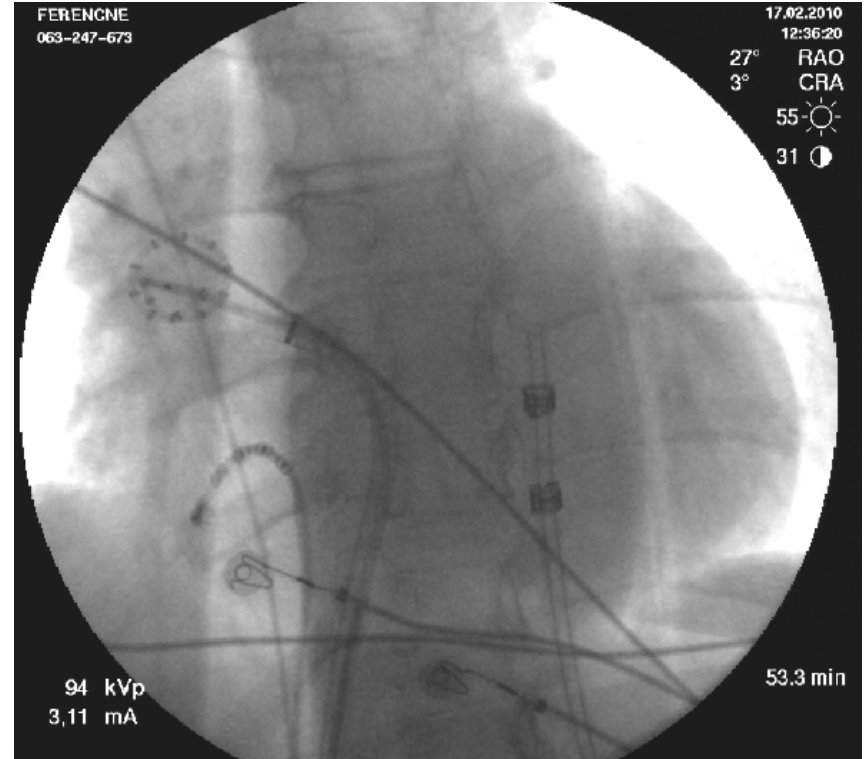
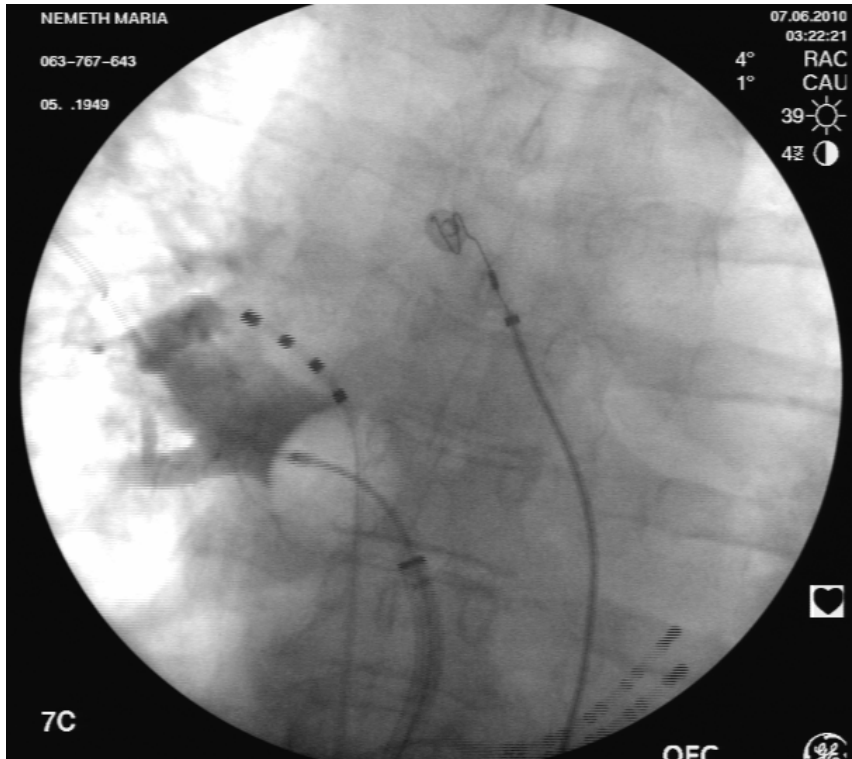
We hypothesize that these outcomes **could be the result of  $\alpha$ -linolenic acid supplementation**, in accordance with previous similar studies indicating its role in improving insulin sensitivity.



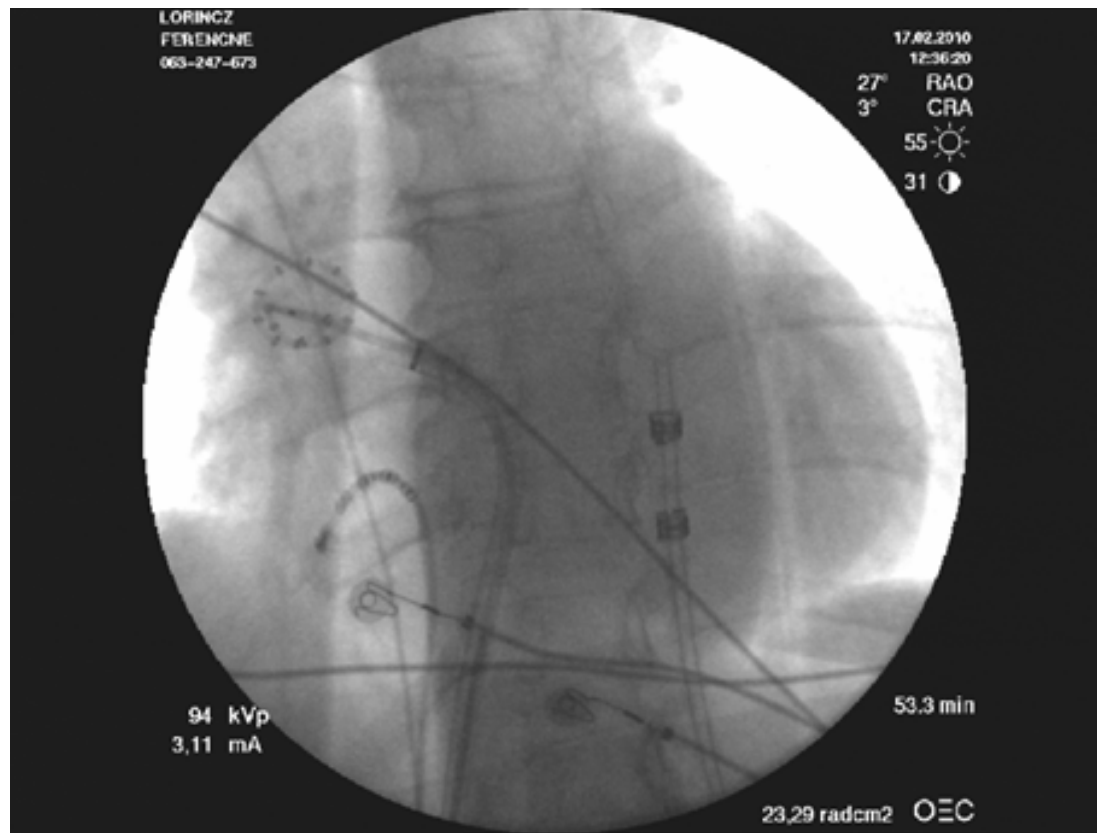
### 3. Scientific developments in the field of atrial fibrillation ablation therapy



# Pulmonary vein isolation using cryoballoon



# Pulmonary vein isolation using PVAC



## **Transcranial Measurement of Cerebral Microembolic Signals During Pulmonary Vein Isolation A Comparison of Two Ablation Techniques**

Edina Nagy-Baló, MD; Diana Tint, MD, PhD; Marcell Clemens, MD; Ildikó Beke, MD;  
Katalin Réka Kovács, MD; László Csiba, MD, PhD, DSc; István Édes, MD, PhD, DSc;  
Zoltán Csanádi, MD, PhD

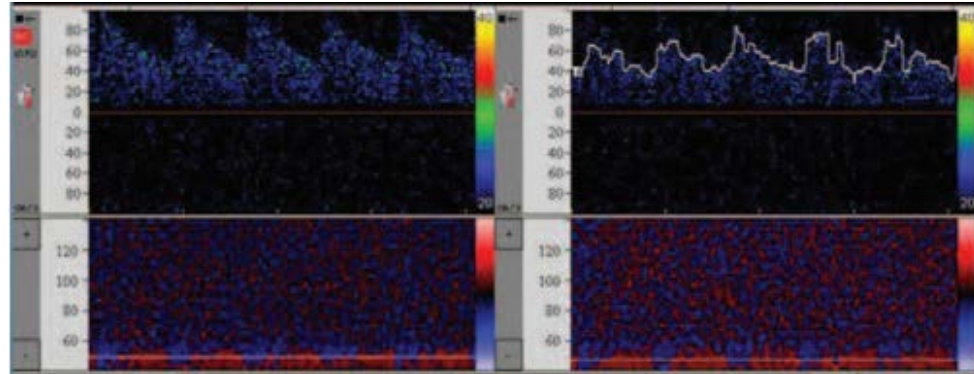
### **What was new?**

Characterization of the cerebral microembolization during AF ablation using

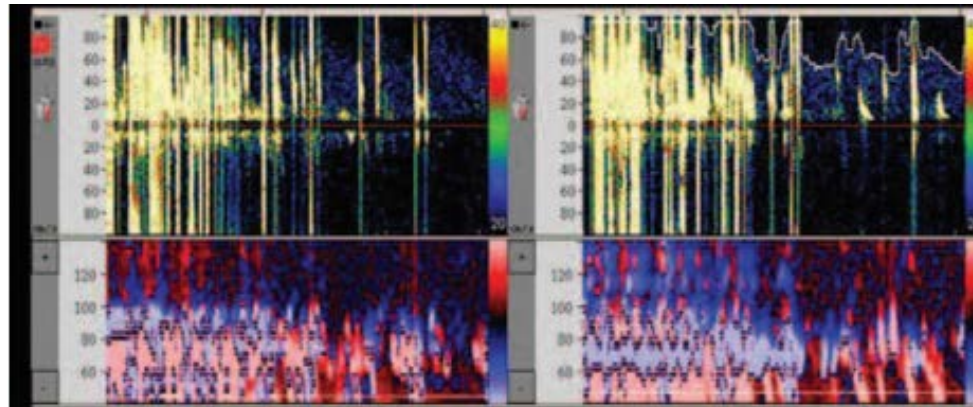
- Two different ablation techniques
- Two different methods for the microembolization assessment
- Two different anticoagulation regimens

# Bilateral multifrequency transcranial Doppler monitoring of middle cerebral arteries.

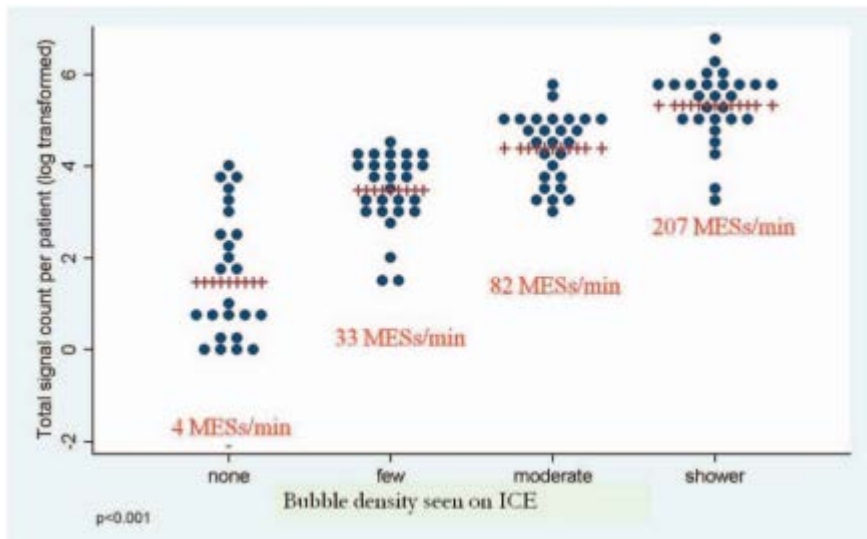
baseline  
curve



burst of  
microembolic  
signals (right;  
high-intensity  
transient  
signals)

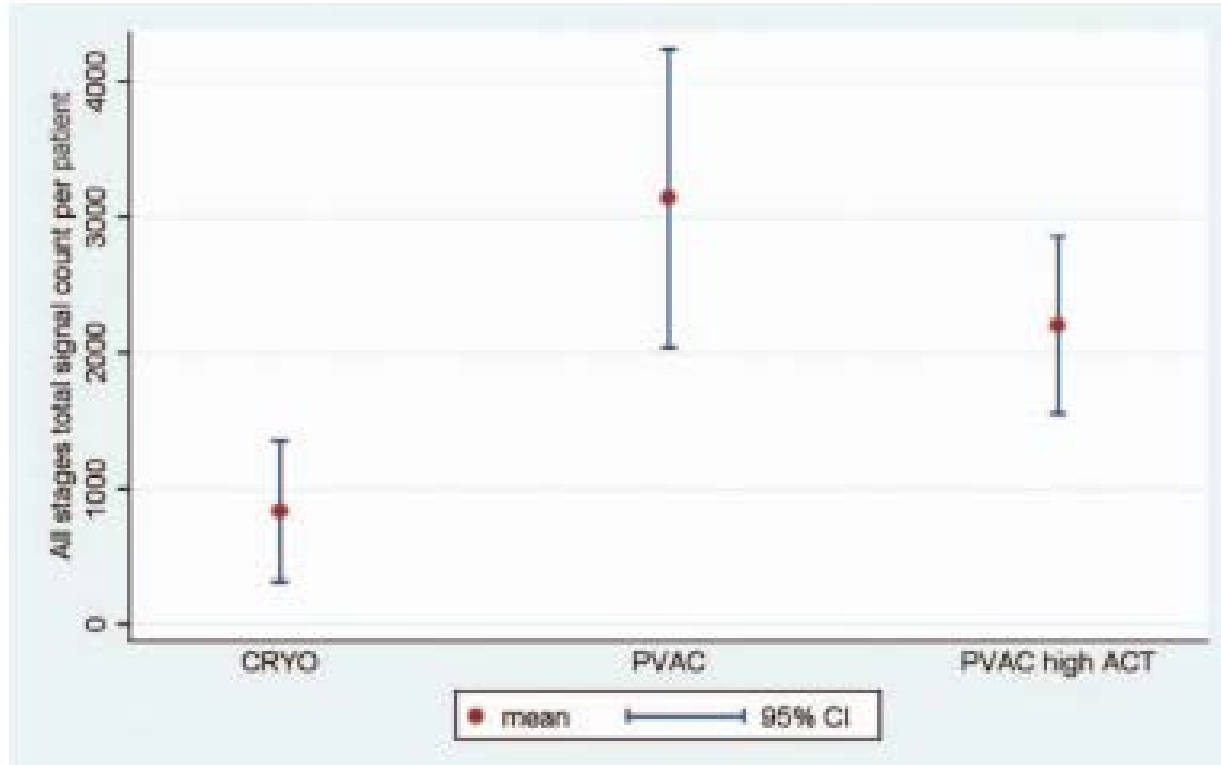


# Assessment of microbubble formation



Correlation between degree of microbubble formation on intracardiac echocardiography (ICE) and the number of microembolic signals (MESSs) detected by transcranial Doppler.

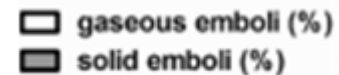
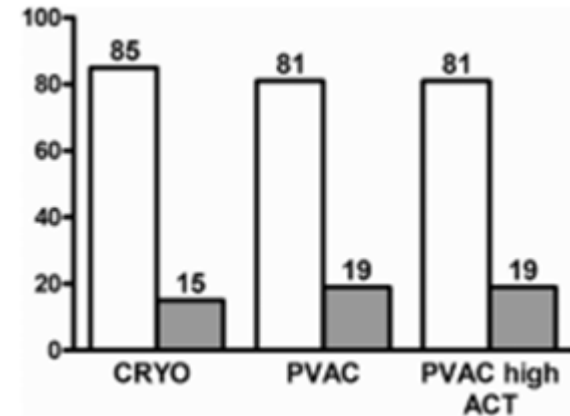
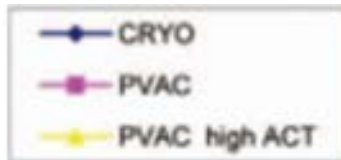
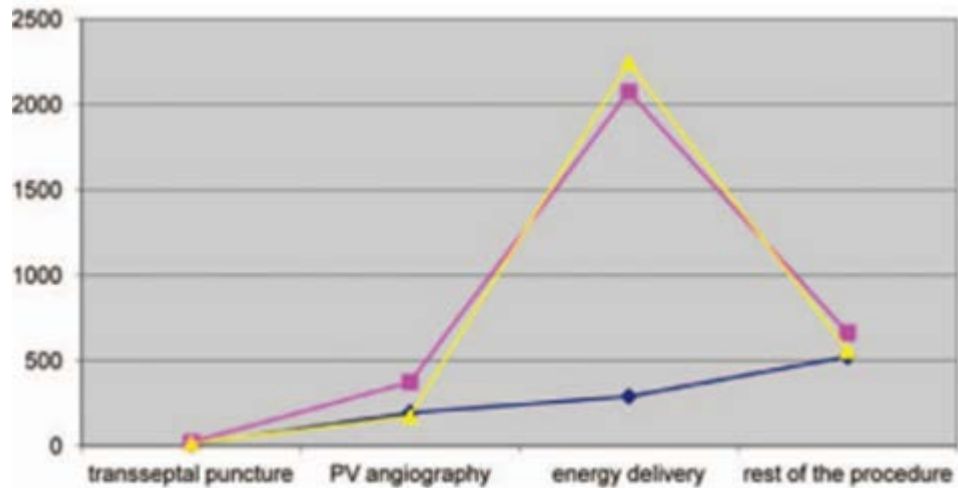
# Total microembolic signal count in the 3 treatment groups



Graph depicting mean number of microembolic signals (MESs) per patient in each treatment group.



# Trend of microembolus formation during different stages of the procedure





# Transcranial Measurement of Cerebral Microembolic Signals During Pulmonary Vein Isolation

## Conclusions:

- Phased RF ablation was associated with significantly more MESs than CB ablation.
- Use of higher ACT target for intraoperative heparinization during PVAC ablation resulted in a trend to a lower MES count that did not reach statistical significance at the size of our patient cohort.
- Although the occurrence of MESs exhibited an even distribution during CB ablation, it was concentrated during RF delivery with phased RF technology.
- The majority of MESs were gaseous, regardless of the ablation technique and the phase of the procedure.

# **FUTURE RESEARCH DIRECTIONS**

# Future research directions

**Autonomic changes and endothelial function in patients with ischemic heart disease. The role of preconditioning in patients undergoing cardiac surgery revascularization.**

**The concrete objectives of this research are:**

- To assess the influence of the autonomic nervous system on endothelial function and clinical prognosis in patients with documented ischemic heart disease with and without revascularization
- To assess the influence of the preconditioning in reduction of the endothelial dysfunction in patients undergoing coronary artery by-pass.

# Future research directions

**Autonomic changes and endothelial function in patients with ischemic heart disease. The role of preconditioning in patients undergoing cardiac surgery revascularization.**

**The concrete objectives of this research are:**

- To evaluate the correlation between urinary neurotransmitter levels and endothelial dysfunction in patients with acute and chronic coronary syndrome.
- To determine the correlation between neurotransmitters, inflammatory markers (cytokines), oxidative stress markers in patients with acute and chronic coronary syndrome prior and after intervention.

# Future research directions

## **Nanotopographic control of mesenchymal stem cell adhesion and proliferation on stent metal surfaces: towards a novel bioactive coating - STEMSTENT**

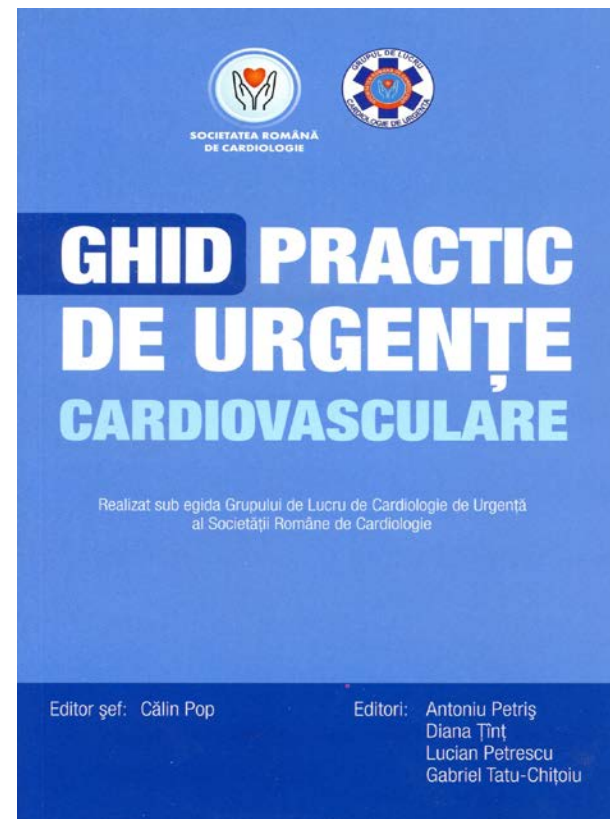
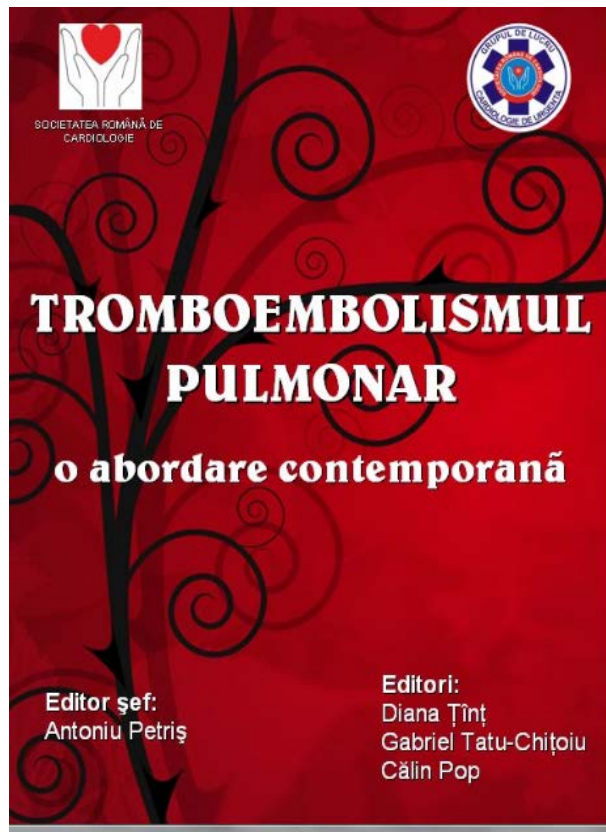
**The concrete objectives of this research are:**

- To develop on the overall properties and biocompatibility of metal stents used in interventional cardiology by covering them with MSCs using an effective strategy for precise control and patterning of the local Nano - roughness on stent surfaces, in order to mitigate ISR.
- To control the mechanisms and pathways that regulate stem cell growth and differentiation on the machined surfaces and to improve the immune tolerance of the developed coating.

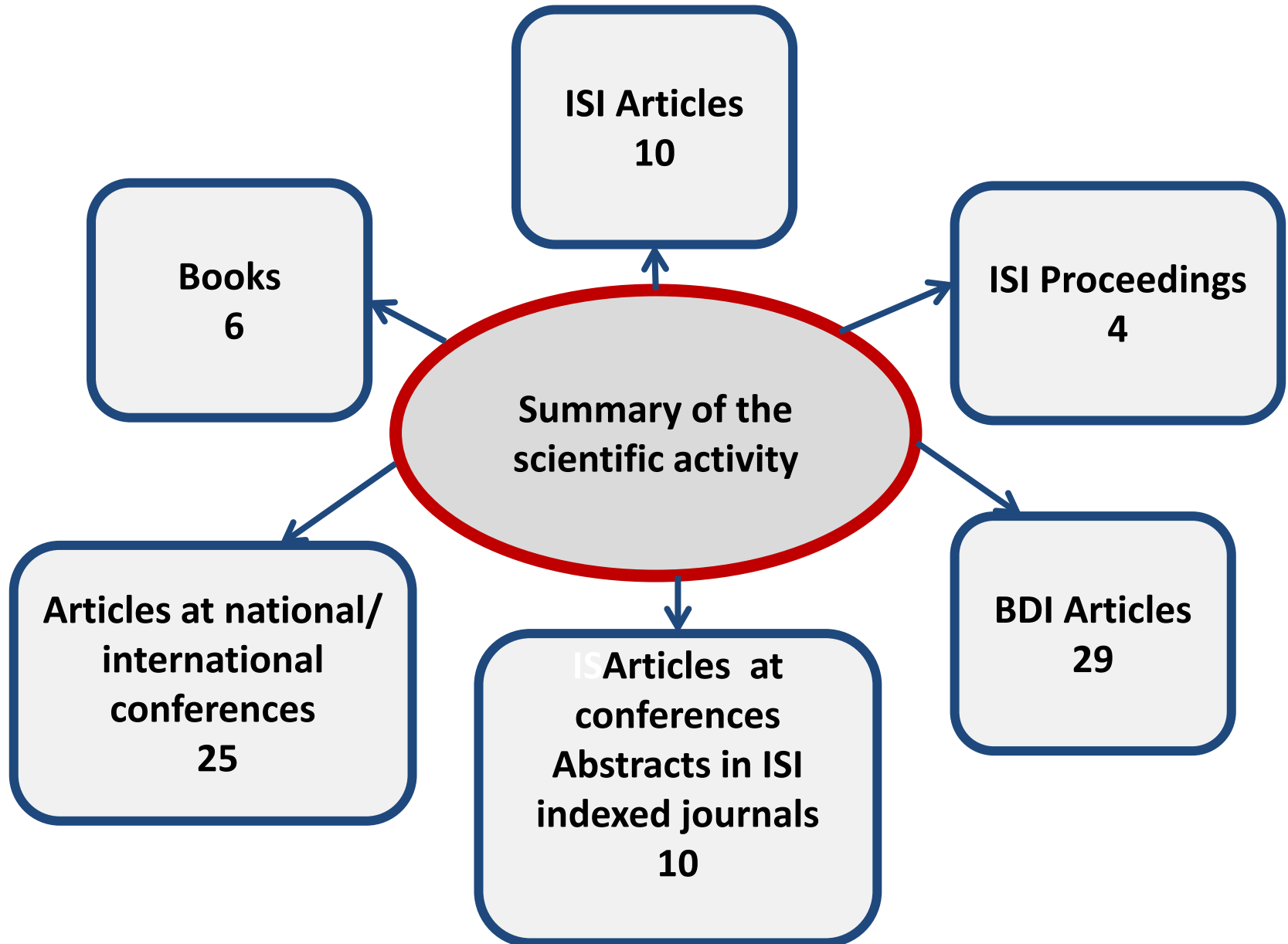
# ACADEMIC ACHIEVEMENTS

# Books

4 books first author/co-author before 2010  
After 2010 – 8 book chapters



# Publications





# Citations

Google Academic

Indexuri pentru citate	Toate	Din 2011
Referințe bibliografice	78	76
<b>h-index</b>	<b>5</b>	<b>5</b>
i10-index	3	3



**Citations**

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The Scopus Author Identifier assigns a unique number to g  
identifier, it is grouped separately. In this case, you may see

Țiņ, Diana

Universitatea Transilvania din Brasov, Faculty of Medicine,  
Brasov,

Author ID: 32267586100

Documents: 15

Citations: 45 total citations by 45 documents

**h-index: 4**

Co-authors: 43

Subject area: Medicine , Materials Science [View More](#)

THOMSON REUTERS

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- h-index [?]: 4**

# Projects

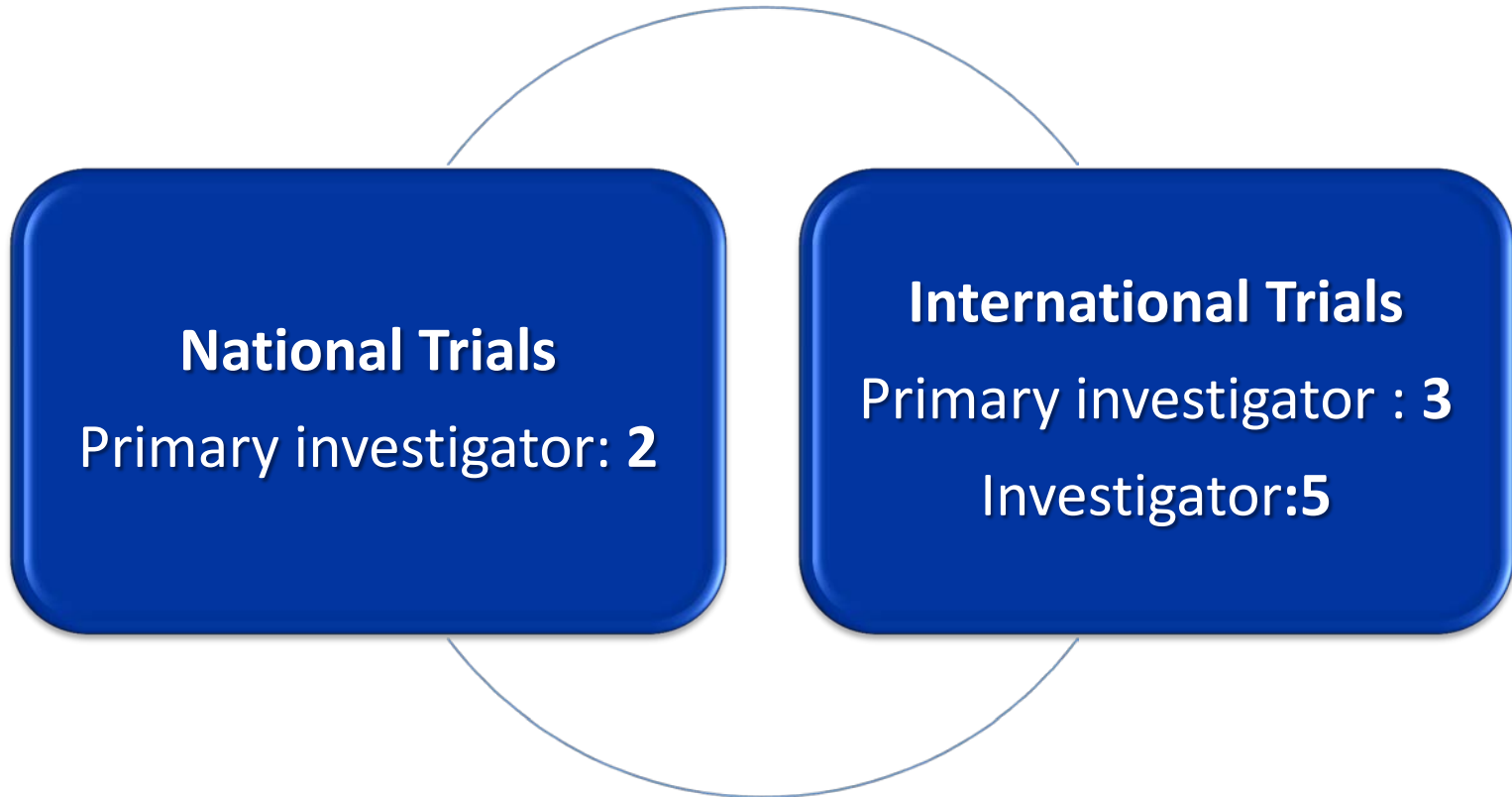
## National grants

- Director of 2 projects
- Member of 7 projects

## International grants

- Director of 1 project
- Scientific expert of 1 project
- Member of 1 project

# Projects



# Membership of scientific and professional organizations – national level

**Romanian Society of Cardiology**



**Board Member since 2014**

**President of the Acute Cardiac  
Care Working Group since 2014**



**Romanian Society of Internal  
Medicine**

# Membership of scientific and professional organizations – international level

**European Society of Cardiology**



**EUROPEAN  
SOCIETY OF  
CARDIOLOGY®**

**ESC Fellow since 2010**



**Electrophysiologist  
International Community  
Alliance EPIC Alliance**



**EPIC Alliance**

# Membership in the Scientific Committee at scientific events

**Conferința Națională  
a Grupurilor de  
Lucru**

**2015**

**2016**

**Sibiu**

**Conferința  
Națională de  
Cardiologie**

**2015**

**2016**

**Sinaia**

**New Trends on  
Sensing-  
Monitoring  
telediagnosis for  
Life Science**

**2014**

**2015**

**Brașov**

# Membership in Journal's Review board

## **Publicații românești**

Bulletin of the Transilvania University of Brașov.

Jurnal Medical Brașovean

## **Publicații internaționale**

Case Reports in Internal Medicine

Vascular Health and Risk Management

Medical Devices: Evidence and Research

Research reports in Clinical Cardiology

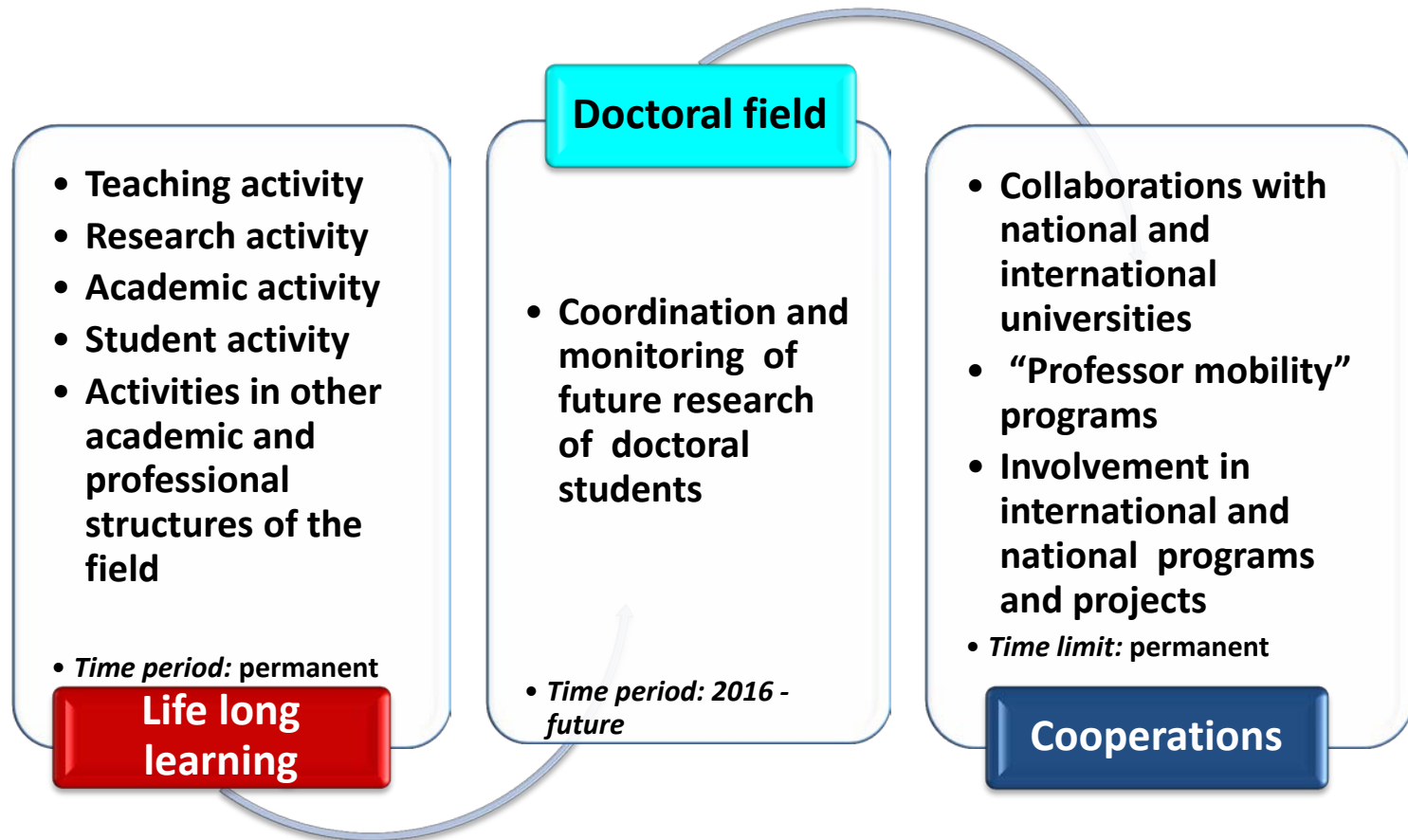
Open Access Emergency Medicine

International Journal of General Medicine

**SCIENTIFIC, PROFESSIONAL  
AND ACADEMIC FURTHER  
DEVELOPEMENT PLANS**



# Development directions for the professional career



# Improve the professional visibility

In the scientific  
comitee of national  
and international  
conferences

In the professional  
structures

Editorial and  
scientific  
boards of indexed  
speciality journals

As keynote speaker  
and moderator

International scientific  
structures



# Development directions for the scientific activity

## Research

- Participation in national and international grants
- Participation in national and international conferences, networking
- Continuing the ongoing researches and developing new ones

## Publishing

- Books, book chapters
- Articles in journals indexed in ISI Thomson Reuters DB and BDI with high index of visibility
- Articles published in conference proceedings

# Development directions for teaching activity

- Modern and attractive teaching classes
- Keeping up-to-date
- Encouraging research activity among students
- Teaching in English - for foreign students and students visiting our University through ERASMUS or other types of mobilities
- Implementing a new course concerning the implantable devices in cardiovascular pathology and I will be the course coordinator - in cooperation with Department of Materials Science and Engineering
- Organizing and participating to post-graduate training programs dedicated to physicians and to medical personnel