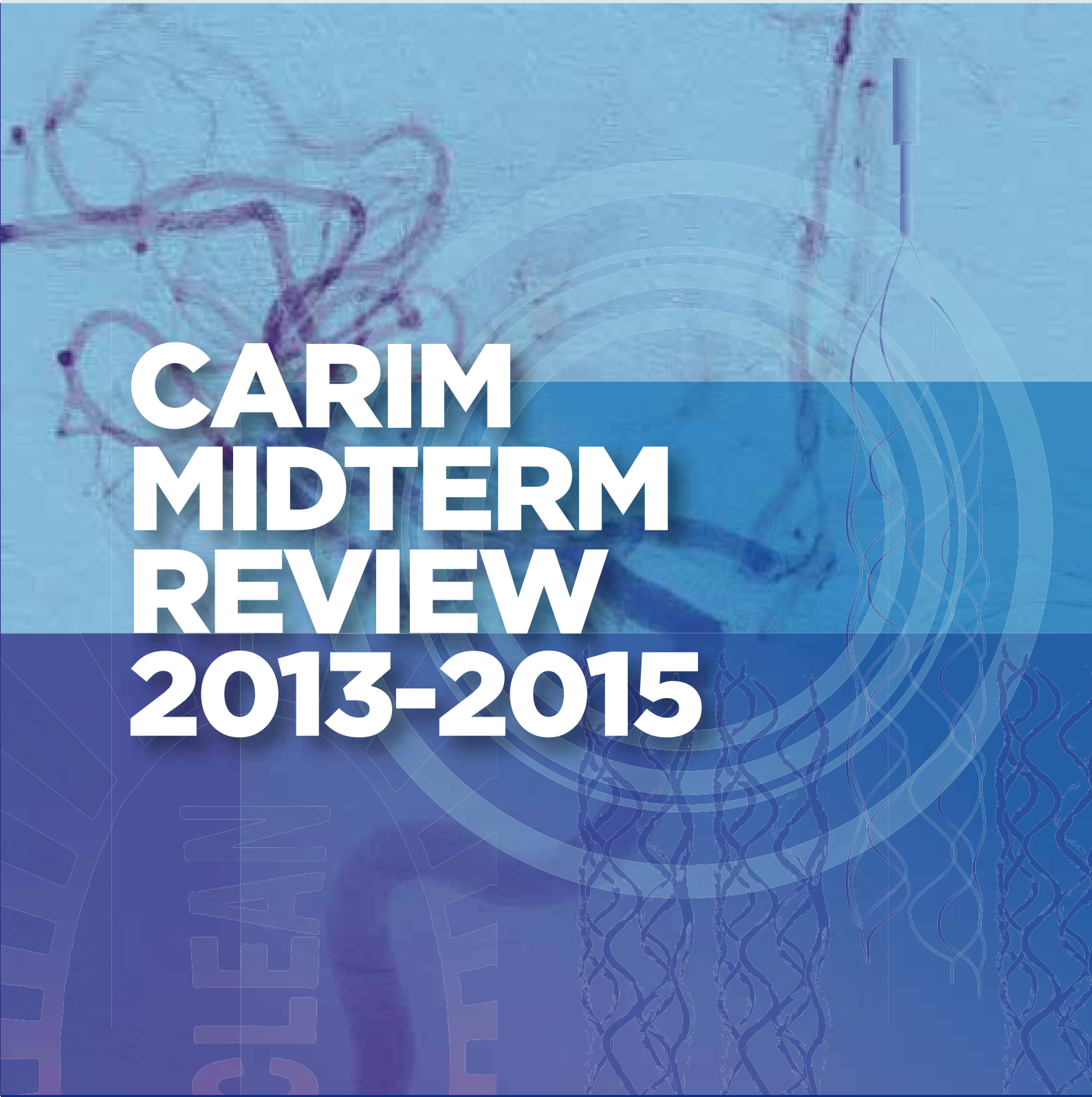

CARIM MIDTERM REVIEW 2013-2015

School for Cardiovascular Diseases

Maastricht UMC+

Maastricht University

1976 2016 40

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ANNEXES

1 EVALUATION OF THE LAST EXTERNAL REVIEW

GENERAL

The ERC acknowledges the detailed description of CARIM's activities and ambitions in the 'CARIM Self Evaluation 2007-2012 report', which provides an overview of the efforts that have been made since the last ERC evaluation in 2007 to sustain and improve quality of CARIM's research and education programmes and strategic decision-making procedure. With respect to the scientific director and theme leaders, the ERC is convinced that they are excellent scientists and managers, particularly to create cohesion between the staff members of CARIM. The growing cooperation between CARIM and the university hospital in the Cardio Vascular Centre (CVC), and the further development of strategic alliances and networks at the regional, national, and international level are important for CARIM's ambition to maintain its status of an international top institute in cardiovascular diseases and may open up new avenues to innovation, staff recruitment and funding. In this part of the Midterm review, an extensive description of the recommendations and the corresponding follow-up is given. See annex 1 for the report of the External Review Committee (ERC) and the reaction to the Executive Board.

FUNDING

Fund raising activities will become even more important for CARIM than they already were. According to the ERC, CARIM should explore further possibilities to improve its grant acquisition. Fund raising has improved since the restructuring (new composition and more structured schedule) of the research council in 2014, esp. personal grants resulted in six NHS Dr. E. Dekker grants in 2015. While the ERC finds several initiatives e.g. for Horizon 2020 promising, CARIM should further improve its visibility and activity within larger networks and in forming strategic alliances. In 2015, 8 out of 53 Horizon 2020 applications from CARIM were granted (some still pending), which is one of the highest scores within Maastricht University. In this context, a Horizon 2020 training by Willem Wolters and the training "How to Write a Competitive Proposal for Horizon 2020" given by Sean McCarthy were organised by the CARIM Strategic Board. In addition, alternative routes to research funding through private donations and international alliances will be pursued.

At the same time, further strategic decisions are needed on how to cope with the expected reduced funding (both from the University and from the third money stream). CARIM has already been working on this issue in recent years and will continue with this process in the future. In order to not only deal with the budget cuts/ reduced funding but to recover a strategic reserve as well, additional measures regarding research formation have been decided upon by CARIM's governance and their implementation has been started. Firstly, in compliance with the Faculty's decision, the first money stream labelling of scientific staff will be reduced to a maximum of 0.5 FTE per person. This measure will be implemented in two phases: 50% of the reduction by July 1, 2016 and the other 50% by July 1, 2017. In total, this implies a reduction of 6.5 FTE, which leads to a financial gain of about k€ 600. Additional individual CARIM allowances for special tasks (e.g. group leaderships) will be incorporated in the strategy, but these have not been assigned yet. Furthermore, Principal Investigators (PIs) and their groups will be allocated based preferentially on defined translational research topics. This measure contains a reduction of the current PI programs by 7 (from 27 to 20), which leads to a gain of k€ 650 (on average a reduction of approximately 1 FTE per group). In total both measures will lead to a cost reduction of about 1.2 m€. While part of this gain is necessary to cope with reduced first money stream, it is anticipated that as from 2018 approximately half of this amount will be invested in (non-structural) strategic developments within CARIM's research groups.

Despite the FTE reduction in scientific staff, the tenure track system is only temporarily on hold and will be reintroduced with a 0.5 FTE perspective in 2018. The tenure track system is a major strategic instrument of CARIM and has proven to be instrumental in securing a new generation of excellent researchers. To decide on the question as to whom to include in CARIM's tenure track program will be one of the top strategic challenges CARIM is facing in the nearest future. Since

the discussion on scientific priorities of CARIM has been intensified during recent years, the contribution of each individual potential tenure tracker to the overall scientific objectives of CARIM will be increasingly important for these decisions. In addition, the transparency in the communication of tenure track procedures will be improved by formulating clear criteria, both for the chosen candidate at entrance of the track as the evaluation of the candidate during the track. A potential drawback of this system is that it may limit capacities in the future and reduce the flexibility of strategic decision making in the present. Thus, next to identifying talent at an early stage within our premises for a tenure track, it is advisable to search for and invest in keep the recruitment of excellent scientific staff from external institutions.

IMPROVE TRANSLATIONAL CONNECTION

One of the leading points in the ERC report is the translational connection and the collaboration of CARIM with the HVC (Heart and Vascular Centre) within the CVC. CARIM and HVC have projected their integration by aligning its research foci within its translational objectives as mentioned in the CVC masterplan of 2013 and elaborated thereafter. These objectives are Thrombosis and Haemostasis; Complex Arrhythmias; Heart Failure; Macrovascular Complications; and Microvascular Complications. Investments have been made in translational researchers (Jordi Heijman, Gudrun Antoons) and PhD students. Furthermore, in the last three years the above mentioned translational CARIM-HVC foci have been incorporated in solid CARIM-HVC infrastructure for research, diagnosis and management of aortic aneurysm, atrial fibrillation, sudden death and cardiogenetics, dilated CMP, vascular and valve calcification. Important examples include facilities for molecular imaging, The Maastricht Study, Thrombosis Expertise Center and Complex Arrhythmia Unit.

These developments have been made possible in the past three years through a joint vision of CARIM and HVC and a common program coordinated through 2-weekly one hour meetings where board members and management (Jacobs, Unger, Hackeng, Schotten, Crijns, Hoogervorst, Olivier - previously van Oosterhout - and Van der Zander) are present. The synchronisation between CARIM and HVC on candidates for the 'Toptalenten Programma' within the aligned objectives topics – considering both clinicians and experimental researchers - is a good example of our common goals. Similarly, translational clinical and preclinical duo formation has strengthened bonds between researchers within CARIM and HVC. Furthermore the representation of both clinician-researchers and preclinical researchers at important meetings like the yearly CARIM day, the regular SWOT analysis meetings of CARIM/HVC as well as social events like *'zomerborrel'* and 'winter meeting' are yet other examples. All of these were extremely helpful in abating previous cultural and management differences.

EFFECT MORE FLEXIBILITY WITHIN THE PI STRUCTURE

One of the critical comments of the ERC was a certain inflexibility of the PI structure. As a result, the PI programme will be more strictly monitored and enforced by taking appropriate measures. In general, the PI ships will be evaluated annually, and only if rigorously defined quality criteria will have been met on a three-year average, be eligible for renewal. Establishing and implementing the above-mentioned quality criteria will be one of CARIM's immediate tasks. This strategy enables a more flexible PI structure allowing, inter alia, CARIM junior staff to become CARIM PIs.

THEME I

The ERC considered Theme I well focused, innovative, and productive with an excellent output and valorisation. While the ERC recognises the improvement of interaction with clinical departments, translational research within Theme I should be further stimulated. Theme I will in the future put more effort in improving the translational connection and will collaborate more with the other themes, especially with the clinical departments.

Currently, Theme I is very active in translational medicine through integration of patient care and basic thrombosis

in the Thrombosis Expertise Center (HVC -Theme I Hugo ten Cate) and by integrating basic research in the clinic by linking coagulation factor activity to atrial fibrillation (Henri Spronk/Uli Schotten/Harry Crijns). The core activity "design and synthesis of molecular contrast agents" (Hackeng) has joined forces with HVC (Michael Jacobs; Hugo ten Cate) and Cardiology (Bas Bekkers) to apply a novel thrombus PET probe in detecting thrombi in venous and arterial thrombosis. In addition, the program on vascular calcification (Leon Schurgers) very successfully joined with Internal Medicine (Bram Kroon) on a clinical trial on calcification regression by Vit-K intake. Furthermore, Theme 1 has an active program on personalized anti-platelet medicine (Judith Cosemans) and has an designated officer for translational medicine (Paola van der Meijden).

Theme I is currently investing in broadening its international network through involvement in Horizon2020 initiatives and bilateral alliances between CARIM and foreign Institutes. Examples of the latter are the Universities of Mainz, Aachen, Munich, Münster, Leeds, Cambridge, Padua and Minneapolis. Visiting professors as well as PIs from these institutes have been appointed within Theme I, who take part in research and education of young scientists within Theme I and CARIM.

THEME II

The ERC is pleased to note that Theme II has become an internationally recognised group renowned for its outstanding research in arrhythmias. In addition, this theme has an established international visibility in dilated cardiomyopathy. This provides an opportunity to combine arrhythmia and heart failure.

In the opinion of the ERC, the interaction between arrhythmias – both atrial fibrillation and ventricular arrhythmias – and heart failure research should be enhanced. A restructuring of Theme II is proposed to improve alignment of basic and clinical research in order to ensure a robust translational research axis with optimal use of basic and clinical research infrastructure. Theme II will focus on complex cardiac arrhythmias and structural heart disease related to hypertrophic and dilated cardiomyopathies ("thick heart HF" and "thin heart HF", respectively). Cross links within the programs will be advanced including imaging and genetics/ multiscale modelling. The following programs are foreseen: 1) complex atrial fibrillation; 2) sudden death and cardiogenetics; 3) electrical heart failure; 4) dilated cardiomyopathy; and 5) diastolic heart failure. The restructuring of Theme II includes a name change from 'Cardiac Function and Failure' to 'Complex Arrhythmias and Structural Heart Disease". Investments will be done mainly to reinforce the connections between complex arrhythmias including Atrial Fibrillation and Ventricular Tachycardia/Ventricular Fibrillation, on one hand, and both types of cardiomyopathy as mentioned above, on the other. Investment in genetics is mandatory.

Three programs within Theme II were mentioned in the report as "not performing as well as the other programs": 'Mitochondrial disease', 'Clinical heart failure' and 'Intermediate cardiac metabolism'. These programs will in the future no longer be part of CARIM, their PI ships will be withdrawn, and scientific staff within the groups will be re-allocated or only kept at minimal formation.

THEME III

The ERC finds the research within Theme III an ambitious endeavour, which requires collaboration with other themes and clinical departments and research schools such as MHeNs, and believes that further re-structuring is necessary in order to maintain and improve quality and productivity. The proposed restructuring is the result of the detailed analysis of Theme III at the time of the ERC preparations and visit, an intensive round of talks with Theme III PIs in the first half year of 2015 and the outcome of the "Vascular Network" and "Microvascular" initiatives. The results of these steps were discussed with the Scientific Director of CARIM and the Daily Board in September 2015.

Basic considerations in proposing a new program for Theme III have been: 1) More focus in Theme III by reducing the number of programs from 11 to 6; 2) Improve alignment between the CARIM Theme III activities and the focus areas of the CVC along with

transformation of Theme III from 'Vascular Biology' to 'Vascular Biology and Medicine'; 3) Less strict compartmentalization between Theme III and the other two CARIM themes, i.e. 'Thrombosis and Haemostasis' and 'Complex Arrhythmias and Structural Heart Disease'.

The implementation of this proposal, which is still in progress, is aimed at the creation of five programs and a technical imaging platform, whereas a sixth program is proposed as a joint investment by Theme I and Theme III. The programs are: 1) Atherosclerosis; 2) Arterial stiffening and hypertension; 3) Diabetic vascular complications; 4) Neurovascular disease; 5) Regenerative and reconstructive vascular medicine; 6) Venular thrombosis and insufficiency. Regarding program 6, the Departments of Vascular Surgery and Biochemistry/ Internal Medicine have considerable expertise in this field of research and have already joined this expertise in the execution of various clinical trials.

The Maastricht Study is a main asset as it is a prospective state-of-the-art deep phenotyping cohort study in ~10,000 individuals without and with type 2 diabetes that will yield unprecedented insights into the causes and consequences (cardiovascular and otherwise) of type 2 diabetes. Recruitment has started in 2011 and ~7000 individuals have been extensively phenotyped (Q1, 2016). In accordance with the ERC's advice, CARIM has, and will further develop, an active strategy to ensure sufficient high-level expertise to take full advantage of the many possibilities that the study is yielding. Attracting an internationally recognised scientist to oversee the Maastricht Study and assist the team leader is one of CARIM's priorities and will be implemented when the targeted strategic financial reserve has been developed. This is expected at the beginning of 2018.

VALORISATION AND INFRASTRUCTURE

Regarding the subject of valorisation and infrastructure, the following recommendations were given in the ERC report, followed by CARIM's implementation:

- The valorisation of research outcomes should be further explored and requires more discussion, especially in Theme II and III. Theme II should be more active in establishing spin-offs (as is Theme I). Several efforts have been and are being performed to increase knowledge utilization and the number of spin off companies (e.g. MyRhythm BV, Mirabilis Therapeutics BV).

- Further development of complex genetics was another point of concern mentioned in the ERC report: Complex genetics needs to be further developed into a solid group for structuring the programme and acquiring funds in competition (e.g. Horizon 2020). Complex Genetics, urgently requested for years by several members of cardiology and other groups, has recently been given a substantial boost by CARIM from ABR funds. Monika Stoll, Professor for Genetics at Münster University, Germany, has been appointed Principal Investigator at CARIM in 2015 (the first female PI after years) together with a visiting professorship which has been advanced to a full (0.2 FTE) professorship for Genetic Epidemiology at Maastricht University with an additional post-doc position. Professor Stoll is now actively involved in many projects finally enabling investigation of major cardiovascular complex genetic objectives within CARIM. This move has already proven to be fruitful in terms of successful grant applications and first high quality publications which are underway. Currently, monogenetic projects are being implemented between the Departments of Cardiology (Heymans cs) and Genetics (Brunner cs).

- Following the suggestion by the ERC, CARIM enforced the activities in the field of systems biology. With the appointment of the professors Ilja Arts and Monika Stoll (see above), two internationally strong scientists with expertise in molecular and genetic epidemiology were attracted. Both professors are officially affiliated with the Maastricht Centre of Systems Biology (MaCSBio) that has been installed in 2015. Further systems biology expertise already present in CARIM (complex genetics, signal analysis, mechanistic models of cardiovascular mechanics and electrophysiology) has been clustered in the 'CARIM Working Group for

Cardiovascular Systems Biology'. This working group is still independent of MaCSBio but the intention is to integrate the activities in this working group into the research program of MaCSBio.

- Replacement of the current animal facility: The decision to build a new facility (BMC, Biomedical Center), has been taken by Maastricht University. This will create new opportunities and solve the problems with the present facility that have been acknowledged by the ERC with a separate letter to the Dean. CARIM is taking a major responsibility in the reorganisation of the new animal facility, among others by involving the so-called Muroidean Facility (MF) in the process. The MF is a newly formed institution at CARIM - supported by the faculty that takes care of the organization and performance of small animal experimentation. It consists of several experienced technicians and is lead in a cooperative way by a cooperative group of young CARIM scientists (Judith Cosemans, Marjo Donners, Koen Reesink, Blanche Schroen and Sander Verheule).

- The (molecular) imaging facility should become a self-sustained central interfaculty unit, with strong involvement of CARIM, and the collaboration with the newly established University Professors should be enforced. During the last few years, Maastricht has gradually developed into one of the largest European centers for biomedical imaging techniques and procedures, providing a huge chance for interdisciplinary research in all thinkable directions. CARIM has a longstanding inter-theme collaboration between design and chemical synthesis of molecular imaging agents (Theme I) and imaging of cardiovascular disease (Theme III). In addition, with the advent of three new University Professors from the MERLN and M4I institutes, each concerned with another aspect of future-oriented analytic technologies, the local expertise has been further enhanced and needs to be implemented in the scientific routine of CARIM's researchers. At present, there is still a process going on of individual exchange between newcomers and resident scientists about scientific questions and possible methodological answers, and first joint projects are now running on enhancing mass spectral ionization yields by chemical modification (Hackeng - Heeren M4I), and topological induction of smooth muscle cell calcification (Schurgers - De Boer (MERLn). The potential of these multiple co-operations can be regarded as very high if not unique, and it needs to be further exploited.

- Encourage the general use of technical (core) facilities. Apart from the animal and imaging facilities, other options are currently being further explored, not only on a School level, but on a faculty level as well.

CHALLENGES AND STRATEGIC ALLIANCES

According to the ERC, local cooperation with several research schools as well as international cooperation like strategic alliances with (EU-)regional institutes is thriving but should be further stimulated, since it offers CARIM access to people, innovation and shared grants. Co-operation with institutions beyond CARIM has been a matter of concern to CARIM's governance. This relates for once to the basic-clinical co-operations taking shape, among others, in the CVC structure or in co-operations with the Radiology Department, but also to more intensive exchange between CARIM and the other research schools at Maastricht University. A start has already been made with MHeNs in 2013/14 with common symposia and scientific interactions on neurovascular topics with Robert van Oostenbrugge, head of the Neurology Department, as a new PI of CARIM. This move will be continued this year with NUTRIM, including a joint PhD program. With the other research-oriented schools, co-operations exist at present on a bottom-up level, and in a next step, one can look into further institutionalisation.

The Aachen-Maastricht link has a long tradition and has now been intensified, among others, from a joint PhD Program (Tilman Hackeng) to an ITN initiative (INTRICARE) within Horizon 2020 (Thomas Unger), the vascular programme on AA (Michael Jacobs/ Thomas Unger) and a professorial exchange between IMCAR in Aachen and CARIM (Joachim Jankowski/ Erik Biessen). Further intensive co-operations exist

with the University of Mainz (Hugo ten Cate, Johan Heemskerk) and with the University of Münster (Monika Stoll). A joint program with the University of Leeds will be initiated (Tilman Hackeng/Rob Ariëns/Paul Stewart) In addition, as should be the case, numerous individual co-operations exist with the other Dutch- and many European and Overseas universities, which cannot all be mentioned here. Especially the new European Horizon 2020 program has given rise to a great number of scientific co-operation networks spanning all over Europe, and CARIM is participating in more than twenty of them with increasing tendency and a relatively high success rate (see above). Finally, a joint PhD program "Research Doctorate in Hypertension, Vascular Biology and Thrombosis" between Maastricht University and the University of Padua (Thomas Unger, Tilman Hackeng, Bram Kroon, Paolo Simioni and Gian Paolo Rossi) is being established.

EDUCATIONAL PROGRAM

The ERC acknowledged the high quality of CARIM's PhD theses/programs and, while this must be maintained, options to reduce the duration of the PhD track should be explored. This matter has been discussed extensively and repeatedly in all CARIM boards during the last year. In the Planning & Control talks of the scientific- and financial director with the individual PIs, the 'PhD question' is consistently raised, and avenues to recruit more excellent young researchers to the PhD program of CARIM are sought in a mutual effort. CARIM is currently working on an internal PhD incentive program, independently of the well-accepted gratification handed out to the individual promotion teams. Further, a shortening of the average trajectory is aimed for to comply with national and European developments and to guarantee exchangeability in joined interuniversity PhD programs. The shortening of the general trajectory will also allow spending financial gains on the excellent 10% of PhD students in their early post-doc period for spending time abroad and other purposes.

In 2011, CARIM implemented a new PhD training and education programme, the CARIM Research, Education and Supervision plan (CaRES plan), composed of a Research, Education and Supervision plan. In their report the ERC considered this programme to meet the current criteria for a high quality PhD training programme, as it is flexible, clearly structured, and puts effort into monitoring the research progress and quality of supervision of the PhD students. In April 2015 the CaRES plan was integrated into a faculty-wide, new training and supervision plan, referred to as TRACK.2. This web-based platform allows PhD's to enter relevant information and CARIM to monitor PhD progress more in an easy and structured way. A new CARIM post-doctoral fellowship has been installed to enable top CARIM PhD students to spend time abroad in acquiring international scientific and cultural experience in preparation for NWO personal grant applications.

Currently, CARIM is investing in international recruitment of PhD students from India, China, UK, Portugal and the Middle East, as well as by developing joint/double PhD programs with the aforementioned established European partners.

2 MIDTERM REVIEW

2.1 OBJECTIVES AND RESEARCH DATA

The research institute's main tasks include high-quality scientific research and the training of PhD students within the broad area of cardiovascular disease. The research effort not only aims to contribute to our understanding of the processes underlying cardiovascular disease, but also helps students to become independent researchers. A second aim of CARIM's research is that it should provide a basis for clinical practice (translational aspect). The specific PhD and Master's training programs provide a broad approach within our knowledge domain and aim to introduce the students into aspects of basic and applied science. This aim is reflected in the research institute's course program, which includes courses on new developments in molecular biology and sophisticated physical measuring methods, for example, as well as courses focusing on clinical problems. Most courses are based on the principles of active participation and problem solving. Seminars and Master classes organised by the institute, as well as one-day scientific meetings organised by the various research groups or departments within the school, also address basic and applied aspects of research. To translate research into clinical practice, CARIM, in close collaboration with the Heart and Vascular Centre (HVC) of the Academic Hospital Maastricht, under the name of the Cardiovascular Centre Maastricht (CVC) is aiming to develop into a unique internationally recognised centre of excellence in cardiovascular medicine in research (including translational research and medical care).

To summarise, CARIM's mission is to:

1. Generate new and improve current knowledge about the processes underlying cardiovascular diseases by carrying out pioneering scientific research extending from 'molecule to patient to population', i.e. the etiology, pathophysiology, clinic, therapy and epidemiology of cardiovascular and metabolic diseases;
2. Stimulate and facilitate the collaboration between basic and clinical scientists, as an essential factor in ultimately improving health care;
3. Maintain and strengthen international recognition as a centre of excellence in cardiovascular medicine;
4. Train Master's-, PhD- and MD students to become independent researchers and post-doctoral fellows to become leading scientists, capable of functioning in multidisciplinary research programs at universities or other academic and non-academic institutions;
5. Evaluate new findings, products and techniques for applicability in health care, often in collaboration with private companies;
6. Publish scientific results in highly ranked journals.
7. Communicate scientific findings and their translational benefits within the public domain.

At CARIM, basic mechanisms as well as early diagnosis and individual risk stratification of cardiovascular diseases are studied, allowing faster translation of new research concepts to clinical practice. New findings, products and techniques, which can be applied in healthcare, are evaluated, often in collaboration with private companies, and the results of scientific research are published in high-ranking international journals. Master's students, PhD students and MD students are trained to become independent researchers, and post-docs are trained to become leading scientists in the field of cardiovascular disease. CARIM is built around three broader research themes, each led by a program leader: I) Thrombosis and Haemostasis, II) Complex Arrhythmias and Structural Heart Disease and III) Vascular Biology and Medicine.

The focus of Theme I 'Thrombosis and Haemostasis' (Theme leader: Prof. Tilman Hackeng) is directed at deciphering impairments of proteins, platelets, and the vessel wall in relation to the development of venous and arterial thrombosis. Reflecting on the blueprint of Virchow's triad that defines thrombosis as an imbalance between blood composition, vessel wall and components of flow, Theme I explores the multifactorial cause of thrombosis that has a high societal impact on the population, i.e. venous thrombosis (oral contraceptive use; pregnancy), and worldwide is the major cause of mortality, i.e. arterial thrombosis. Focus areas are structure functional analysis of coagulation proteins, coagulation factors and

platelets as initiators of venous and arterial thrombosis, in silico drug design, development of molecular imaging agents, and pathogenesis of vascular remodeling and calcification, up to levels that allow development of novel diagnostic tools and therapeutic strategies. These areas reach out into the clinic through many translational initiatives firmly supported by Theme I Thrombosis Expertise Center (TEC).

Research within Theme II 'Complex Arrhythmias and Structural Heart Disease' (Theme leader: Prof. Harry Crijns) focusses on complex cardiac arrhythmias and structural heart disease. The former includes atrial fibrillation, ventricular arrhythmias and sudden death, the latter relates to hypertrophic and dilated cardiomyopathies (thick heart failure and thin heart failure). The following programs are in foreseen: 1) Complex atrial fibrillation; 2) Sudden death and cardiogenetics; 3) Electrical heart failure; 4) Dilated cardiomyopathy; 5) Diastolic heart failure. Cross links within the programs are advanced imaging and complex genetics/multiscale modeling to enhance early individualised diagnosis and patient tailored treatment. Each of the programs in Theme II is coordinated by a basic scientist and a clinical researcher.

Research in Theme III "Vascular Biology and Medicine" (Theme leader: Prof. H. Struijker-Boudier) focusses on translational research of micro- and macrovascular dysfunction in the context of specific cardiovascular diseases that are a major burden to an ageing society, namely (1) atherosclerosis; (2) hypertension and chronic kidney disease; (3) diabetes and the metabolic syndrome; (4) stroke and cognitive impairment; (5) aortic aneurysm and (6) venous disease. Theme III integrates the basic expertise of CARIM in the areas of molecular biology, biochemistry, bioengineering and vascular imaging with the clinical expertise in the area of vascular medicine in the CVC. Each of the programs in Theme III is coordinated by a basic scientist and a clinical researcher.

These three themes will comprise after CARIM's restructuring around 21 programs, led by a Principal Investigator (PI) or a team of PIs/senior researchers. However, during the evaluation period CARIM contained 27 programs (annex 2). The PIs are responsible for the scientific progress of their program, for linking activities and seeking collaborations between PIs and themes, for mentoring of PhD students and post-docs and, finally, for the financial basis of the program. All three themes involve basic and clinical programs.

2.2 COMPOSITION

Table 1 gives an overview of the total number of CARIM employees between 2013 and 2015. Per December 31, 2015, CARIM employed 210,4 FTE (full time equivalents) in total, consisting of 46,8 FTE scientific staff (university and hospital staff), 30,3 FTE postdocs, 77,3 FTE (internal) PhD students and 55,9 FTE support staff. The numbers show a reduction of staff members in the past three years, both research staff (176,7 FTE in 2013 to 154,4 FTE in 2015) as support staff (71,3 FTE in 2013 to 51,7 in 2015 FTE). The scientific staff that has been contributed by the azM has increased over the years, in all themes, but especially in Theme II, due to the intensification of existing collaborations and the start of new ones within the ongoing translational programs co-financed by the HVC.

About 50% of CARIM scientific research staff consists of PhD students (internal). On top of that, CARIM had on average 35 additional external PhD students per year, in particular researchers who are officially registered as PhD candidates, but not employed by CARIM (Table 1).

Although the number of postdocs decreased over the past three years from 46,7 FTE to 30,3 FTE CARIM values this category of co-workers. Postdoc positions are offered to talented PhD students preferentially after gaining international experience or in order to prepare them for this, as a next step in their scientific career, and CARIM benefits of the productive output in terms of publications of the candidates after their PhD. Furthermore, the best candidates are coached to prepare personal grants like the NWO Talent Scheme (Veni, Vidi, Vici) and/or Dr E Dekker grants.

TABLE 1 RESEARCH STAFF AT SCHOOLS AND RESEARCH PROGRAMME LEVEL (#/FTE)

	2013		2014		2015	
SCHOOL LEVEL	#	FTE	#	FTE	#	FTE
Scientific staff FHML (1)	80	40,4	78	38,9	76	34,5
Scientific staff azM	34	5,9	32	9,2	29	12,3
Post-docs (2)	59	46,7	43	35,2	38	30,3
Internal PhD students (3)	91	83,8	89	81,1	82	77,3
Total research staff	**264**	**176,7**	**242**	**164,4**	**225**	**154,4**
Support staff (research) (4)	104	71,3	83	57,5	75	51,7
Support staff (managerial) (5)	5	4,2	5	4,2	5	4,2
Total staff incl azM	373	252,2	330	226,1	305	210,4
Total staff excl azM	339	246,3	298	216,9	276	198,1
External PhD students (6)	56		50		60	
Visiting fellows/professors (7)	22		26		20	
THEME I	#	FTE	#	FTE	#	FTE
Scientific staff FHML (1)	13	8,1	14	8,8	12	6,8
Scientific staff azM	6	0,4	6	1,6	5	1,8
Post-docs (2)	15	10,5	9	6,6	8	6,8
Internal PhD students (3)	25	22,0	25	21,5	21	19,5
Total research staff	**59**	**41,0**	**54**	**38,4**	**46**	**34,9**
Support staff (research) (4)	18	13,8	17	9,6	14	7,8
Total staff incl azM	77	54,8	71	48,0	60	42,7
Total staff excl azM	71	54,4	65	46,5	55	40,9
External PhD students (6)	11		10		8	
Visiting fellows/professors (7)	7		6		9	
THEME II	#	FTE	#	FTE	#	FTE
Scientific staff FHML (1)	31	16,8	32	17,4	28	14,2
Scientific staff azM	12	1,0	16	4,2	13	5,3
Post-docs (2)	25	22,1	16	15,0	15	13,4
Internal PhD students (3)	33	31,3	36	33,3	30	29,5
Total research staff	**101**	**71,2**	**100**	**69,9**	**86**	**62,4**
Support staff (research) (4)	27	17,7	20	14,6	21	14,5
Total staff incl azM	128	88,8		84,5	107	76,9
Total staff excl azM	116	87,8		80,3	94	71,6
External PhD students (6)	19		16		30	
Visiting fellows/professors (7)	8		11		7	
THEME III	#	FTE	#	FTE	#	FTE
Scientific staff FHML (1)	36	15,5	32	12,8	36	13,5
Scientific staff azM	16	4,5	10	3,4	11	5,2
Post-docs (2)	19	14,1	18	13,7	15	10,2
Internal PhD students (3)	33	30,5	28	26,3	31	28,3
Total research staff	**104**	**64,6**	**88**	**56,1**	**93**	**57,2**
Support staff (research) (4)	59	39,9	46	33,3	40	29,4
Total staff incl azM	163	104,4	134	89,4	133	86,6
Total staff excl azM	147	99,9	124	86,0	122	81,4
External PhD students (6)	26		24		22	
Visiting fellows/professors (7)	9		8		3	

1) Comparable with WOPI-categories HGL, UHD and UD; tenured and non-tenured staff appointed at FHML
2) Comparable with WOPI-category 'Onderzoeker' (1, 2, 3, 4) with completed PhD, not belonging to scientific staff (with WOPI-categories HGL, UHD and UD)
3) Standard PhD (employed)
4) All support staff working on research (research assistants, lab technicians, and other support staff not working at the management office
5) Support staff working at the School's management including the Scientific Director
6) External PhD (externally or internally funded but not employed)
7) Visiting fellows are researchers/Professors who visit the School for a period of typically one week up to three months to work with School's staff members

Finally, CARIM hosts about 20 visiting international fellows and professors every year. CARIM has a renowned reputation in hosting Marie Curie Early stage researchers as well Marie Curie Post-docs coming from various European countries. Co-financed by St Annadal foundation, the Van der Laar Fund and the Hemker fund, CARIM has been able to attract structurally new expertise through the appointment of visiting professors (see table 2) who worked at the Maastricht site for on average a six month to a year period. Not only the Maastricht cardiovascular research benefits from the expertise, which comes available through visiting professorships, but the renowned candidates also bring in stimulating impulses into CARIM's PhD Education Program.

TABLE 2 VISITING PROFESSORS CARIM

NAME	DEPARTMENT	CHAIR	PROFESSORSHIP/APPOINTMENT
Professor Kevin Mayo	Biochemistry	Hein Wellens visiting professorship	Professor of Biochemistry, Molecular Biology & Biophysics, Lab Medicine & Pathology, University of Minnesota, Minneapolis, MN, USA
Professor Monika Stoll	Cardiology	Hein Wellens visiting professorship	Leibniz-Institute for Arteriosclerosis Research (LIFA) at the University Muenster, Genetic Epidemiology of Vascular Disorders. Muenster, Germany
Professor Antiono Zaza	Cardiology	Hein Wellens visiting professorship	University of Milano, Dept Biotechnology and Bioscience, Milano, Italy
Professor Jan Hoorntje	Cardiology	St. Annadal visiting professorship	Intervention Cardiology
Professor Rob Ariëns	Biochemistry	H.C. Hemker visiting professorship	University of Leeds; Honorary appointment

2.3 FINANCING

Table 3 presents information concerning funding and expenditures of the School. The table shows a slight shift in the overall funding of the School towards more research funds and contract grants (71% in 2015 compared to 66% in 2013) and less direct funding (29% in 2015 compared to 34% in 2013). The total expenditures (includes OBP personnel costs) decreased in the last three years, from € 24.492 in 2013 to € 19.488 in 2015. The largest part of this decrease can be found in the personnel costs, which is explained by a decrease of the number of staff members, both OBP and scientific staff, from 252,2 FTE in 2013 to 210,4 FTE in 2015 (see chapter 2.2). On a programme level, the same trend is visible for each theme. The distribution of Technicians in fixed positions has been changed. Before 2012 every 1.0 FTE Scientific Staff (tenured) was entitled of 0,9 FTE support. As from 2012 this has been changed in 0,7 FTE.

Two major developments influenced CARIM's staff reduction over the years 2013-2015:

- The extensive budget cut the Faculty opposed on CARIM as from 2012 (-10% of the Direct Funding in 2012 and -11% as from 2013).
- Less external funding compared to previous years where Technical Top Institute (TTI) grants were executed and dominated the third party financed research in CARIM substantially. As from 2013 to 2015 the CTMM, TI Pharma and BMM programs, in which CARIM research groups participate, gradually ended. These voluminous programs were not yet compensated fully by new grants from e.g. EU, CVON etc.

2.4 RESEARCH QUALITY

2.4.1 DEMONSTRABLE RESEARCH PRODUCTS FOR PEERS: A DESCRIPTION OF THE RESEARCH OUTPUT

The results of CARIM's scientific output - both at School and Theme level from 2013 until 2015 - are presented in Table 4. The number of publications within CARIM has increased from 635 publications (refereed articles with IF (SCI-SSCI) (WI-1), other refereed articles and letters to the editor) in 2013 to almost 700 publications in 2015, 564 of which appeared in peer-reviewed journals. Within all CARIM themes the number of publications increased in the three-year period. In Theme I, the refereed articles with IF (WI-1), even show an increase of one-third from 93 in 2013 to 124 in 2015. For CARIM, the average number of refereed publications per year FTE academic tenured researcher in the period of 2013-2015 was 13,7. This number is slowly increasing over the years; the last evaluation report shows an average of 12,1 (2007-2012).

TABLE 3 FUNDING AT SCHOOLS AND RESEARCH PROGRAMME LEVEL

INSTITUTIONAL LEVEL	**2013**		**2014**		**2015**	
Funding	FTE	%	FTE	%	FTE	%
Direct funding (1)	**57,86**	**34%**	**52,93**	**34%**	**42,02**	**29%**
Research funds (2)	19,25	11%	21,65	14%	24,85	17%
Contract research (3)	88,06	51%	77,34	49%	70,55	49%
Other (4)	6,61	4%	5,51	3%	6,70	5%
Total funding (excl. azM)	**171,78**	**100%**	**157,43**	**100%**	**144,12**	**100%**
Expenditure	k€	%	k€	%	k€	%
Personnel costs	16.456	67%	15.341	71%	13.865	71%
Other costs	8.036	33%	6.145	29%	5.623	29%
Total expenditure	**24.492**	**100%**	**21.486**	**100%**	**19.488**	**100%**
THEME I*						
Funding	FTE	%	FTE	%	FTE	%
Direct funding (1)	11,06	27%	10,75	29%	8,30	25%
Research funds (2)	4,00	10%	6,00	16%	7,50	23%
Contract research (3)	22,50	55%	17,10	46%	16,10	49%
Other (4)	3,00	7%	3,00	8%	1,20	4%
Total funding	**40,56**	**100%**	**36,85**	**100%**	**33,10**	**100%**
Expenditure	k€	%	k€	%	k€	%
Personnel costs	2.284	58%	2.003	61%	1.731	58%
Other costs	1.638	42%	1.296	39%	1.236	42%
Total expenditure	**3.922**	**100%**	**3.299**	**100%**	**2.967**	**100%**
THEME II*						
Funding	FTE	%	FTE	%	FTE	%
Direct funding (1)	22,80	33%	24,40	37%	16,20	28%
Research funds (2)	12,40	18%	8,30	13%	10,00	17%
Contract research (3)	32,85	47%	31,15	47%	28,05	48%
Other (4)	2,10	3%	2,00	3%	3,80	7%
Total funding	**70,15**	**100%**	**65,85**	**100%**	**58,05**	**100%**
Expenditure	k€	%	k€	%	k€	%
Personnel costs	3.356	58%	3.302	62%	2.753	61%
Other costs	2.480	42%	1.982	38%	1.728	39%
Total expenditure	**5.836**	**100%**	**5.284**	**100%**	**4.481**	**100%**
THEME III*						
Funding	FTE	%	FTE	%	FTE	%
Direct funding (1)	23,00	38%	16,78	31%	16,52	32%
Research funds (2)	2,85	5%	7,35	14%	7,35	14%
Contract research (3)	32,71	54%	29,09	54%	26,40	51%
Other (4)	1,51	3%	0,51	1%	1,70	3%
Total funding	**60,07**	**100%**	**53,73**	**100%**	**51,97**	**100%**
Expenditure	k€	%	k€	%	k€	%
Personnel costs	4.623	55%	3.880	60%	3.037	55%
Other costs	3.773	45%	2.631	40%	2.442	45%
Total expenditure	**8.396**	**100%**	**6.511**	**100%**	**5.478**	**100%***

*The sum of the FTEs of the programmes is less than the total of the School, because some FTEs cannot be allocated to one of the themes.

1) Direct funding by FHML/Maastricht University ('basis financiering'/lump sum budget)
2) Research grants obtained in national scientific competition (e.g. grants from NWO, ZonMw and KNAW)
3) Research contracts for specific research projects obtained from external organisations, such as industry, governmental ministries, European organisations, including ERC, and charity organisations
4) Funds that do not fit the other categories
5) The funding in FTE includes the total research staff but excludes the azM-staff
6) The funding in % in the research programme should be compared to the total within each research programme

TABLE 4 MAIN CATEGORIES OF RESEARCH OUTPUT AT SCHOOLS AND PROGRAMME LEVEL RESEARCH

	2013	2014	2015
SCHOOL LEVEL			
Refereed articles (SSI/SSCI) (1)	518	526	564
Other refereed articles (2)	117	87	132
Total refereed articles (3)	635	613	696
Books	1	1	4
Book chapters	5	9	11
PhD theses	35	33	34
Conference papers (4)	3	1	27
Patents and professional publications (5)	11	11	7
Publications at the general public (6)	n.a.	n.a.	n.a.
Other research output	n.a.	n.a.	3
Total publications	690	668	791
THEME I			
Refereed articles (SSI/SS I) (1)	93	104	124
Other refereed articles (2)	24	15	21
Total refereed articles (3)	117	119	145
Books	1	n.a.	7
Book chapters	1	n.a.	7
PhD theses	7	10	10
onference papers (4)	n.a.	n.a.	n.a.
Patents and professional publications (5)	6	6	2
Publications at the general public (6)	n.a.	n.a.	n.a.
Other research output	n.a.	n.a.	n.a.
Total publications	131	135	169
THEME II			
Refereed articles (SSI/SS I) (1)	209	214	239
Other refereed articles (2)	41	43	53
Total refereed articles (3)	250	257	292
Books	n.a.	1	3
Book chapters	1	5	3
PhD theses	14	8	21
onference papers (4)	3	1	16
Patents and professional publications (5)	6	4	4
Publications at the general public (6)	n.a.	n.a.	n.a.
Other research output	n.a.	n.a.	1
Total publications	274	276	340
THEME III			
Refereed articles (SSI/SS I) (1)	281	280	290
Other refereed articles (2)	68	36	63
Total refereed articles (3)	349	316	353
Books	1	n.a.	1
Book chapters	3	5	4
PhD theses	14	17	12
onference papers (4)	n.a.	n.a.	7
Patents and professional publications (5)	n.a.	2	2
Publications at the general public (6)	n.a.	n.a.	n.a.
Other research output	n.a.	n.a.	2
Total publications	367	340	381

1) Refereed articles published in an international journal, which is mentioned in the (Social) Science Citation Index (SSI or SSCI) of Journal Citation Reports (JCR) (wi-1)
2) Refereed articles published in an international journal, not included in the SSI-SSCI (wi-2), editorial materials, letters to the editor and refereed articles in a national (Dutch) journal (wn)
3) The sum of the refereed articles (SSI/SSCI) and the other refereed articles
4) Congress paper/proceeding papers (non-refereed). A proceeding paper is as such presented on a congress and published in an international (scientific) journal. This category does not include a congress abstract, whether or not published in an (international scientific) journal
5) Patents and publications aimed at professionals in the public and private sector ('professionele publicaties'). The purpose of professional publications is to distribute knowledge among professionals in the field. This category is mostly published in a general oriented journal or a non-specialist journal
6) Also known as 'populariserende artikelen'
7) Other types of research output (if applicable), such as abstracts, editorships, inaugural lectures, designs and prototypes (e.g. engineering) and media appearances

2.4.2 DEMONSTRABLE USE OF RESEARCH PRODUCTS BY PEERS

Scientists at CARIM annually publish a large number of scientific publications in journals both within and outside their own field (table 4). Not only is the number of publications high, but so is their scientific impact. In recent years the average impact factor (IF) of the journals, in which these articles have been published, has shown an average IF of 4.8 in 2013-2015.

Commissioned by the Dutch Federation of University Medical Centres (NFU), the Centre for Science and Technology Studies (CWTS) performs an annual analysis of the bibliometric data from the eight Dutch UMCs. Since this analysis started, CARIM has scored consistently at a level well above the world average. Strikingly, CARIM has shown a very sharp increase in more recent years. There has been an increase from 1.46 in 2007 to 1.97 in 2012, meaning that in the crown indicator MNCS (Mean Normalised Citation Score), CARIM scores very high compared to the world average. In particular, the MNCS of Theme I even had a larger increase, from 1,05 in 2007 to 1,70 in 2012. The MNCS indicates the impact of a research unit's articles compared to the world citation average (being 1.0) in the subfields in which the research unit is active. That means that the publications of CARIM are cited almost twice more frequently than the world average.

Table 5 gives a year-weighted overview of CARIM's bibliometric statistics indicating: P: Number of articles (normal articles, letters, notes and reviews) published in journals processed for the Web of Science (WoS) version of Thomson Scientific's Citation Indexes (CI), MCS: Average number of citations per publication, or citations per publication ratio (self-citations excluded). MNCS: The impact of a research unit's articles, compared to the world citation average in the subfields in which the research unit is active. MNJS: The impact of the journals in which a research unit has published (the research unit's journal selection), compared to the world citation average in the subfield covered by these journals.

TABLE 5 BIBLIOMETRIC STATISTICS CARIM 1997-2012/2013

	P	MCS	MNCS	MNJS
SCHOOL LEVEL				
2004-2007	1490,3	9,5	1,46	1,32
2005-2008	1507,8	11,0	1,56	1,35
2006-2009	1558,5	12,8	1,76	1,41
2007-2010	1673,3	13,5	1,87	1,48
2008-2011	1740,0	13,3	1,91	1,55
2009-2012	1918,0	14,5	1,97	1,54
THEME I				
2004-2007	246,0	7,7	1,05	1,27
2005-2008	248,0	7,7	1,09	1,29
2006-2009	273,8	9,2	1,47	1,47
2007-2010	302,3	10,4	1,51	1,49
2008-2011	318,8	12,1	1,69	1,64
2009-2012	336,3	13,8	1,70	1,58
THEME II				
2004-2007	478,3	9,8	1,50	1,39
2005-2008	460,0	11,5	1,57	1,46
2006-2009	475,8	13,3	1,77	1,50
2007-2010	515,0	13,1	2,00	1,56
2008-2011	554,8	13,4	2,07	1,55
2009-2012	679,8	15,2	2,17	1,49
THEME III				
2004-2007	811,0	9,6	1,55	1,31
2005-2008	872,8	11,3	1,66	1,33
2006-2009	926,0	13,1	1,82	1,37
2007-2010	1004,3	14,0	1,87	1,45
2008-2011	1043,8	13,2	1,83	1,52
2009-2012	1116,5	13,9	1,87	1,55

In terms of the MNCS score, CARIM has the highest score of all schools within FHML (see Figure 1). Articles from the CARIM Department of Cardiology are quoted even more than twice as frequently than the world average in the last years (2,17).

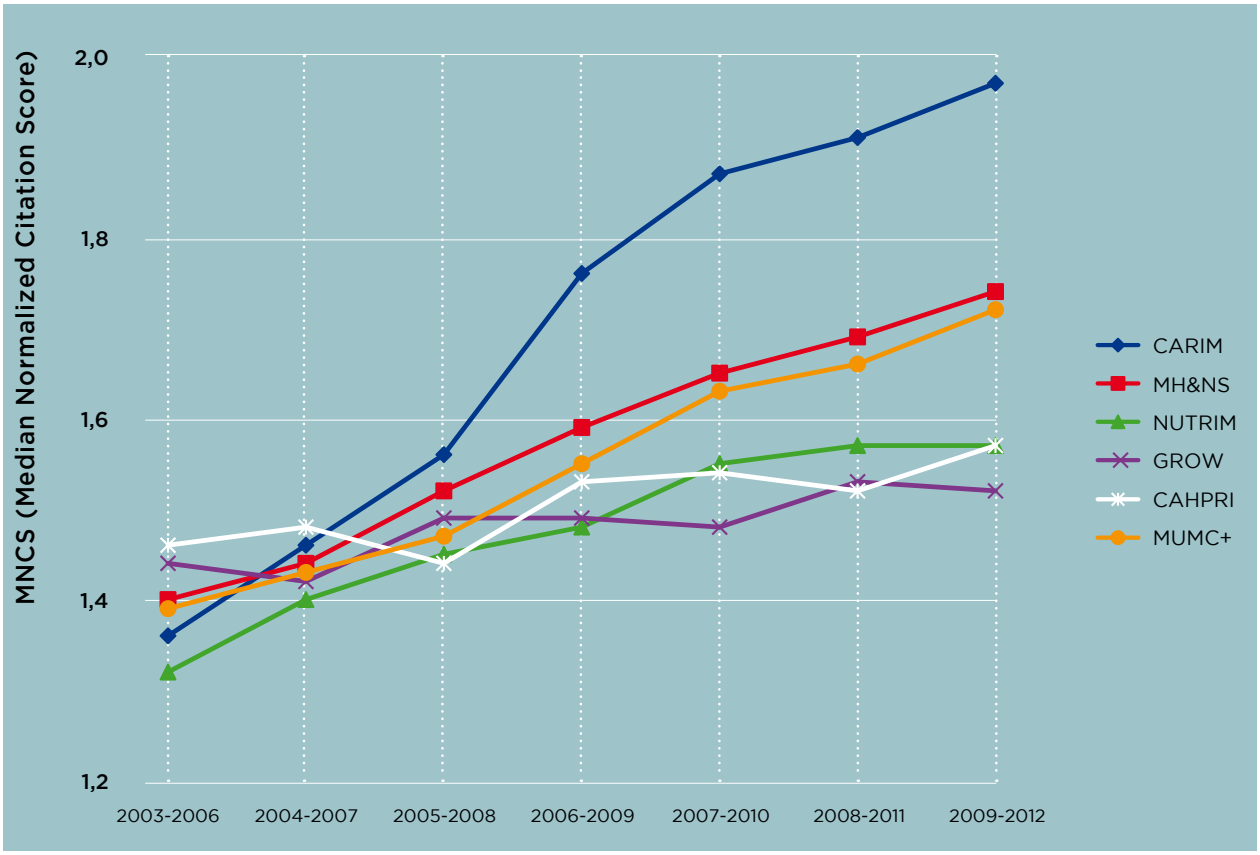

FIGURE 1 MNCS SCORE FHML

Not only in Maastricht, CARIM has a very high citation score, but also nationally CARIM scores the highest compared to the other UMCs in the field of cardiac & cardiovascular systems*: "..the scores vary between 1.96 (Maastricht UMC+) and 1.38 (UMC Groningen)..."*(Van Welie, S.D., Van Leeuwen, T.N. , Bouma, J.C. and Klaassen, A.B.M. Netherlands Heart Journal, 2016.). In addition, the publication states that Maastricht UMC+ has a very high citation score and a strong cardiovascular research field and mentions CARIM as one of the top institutes for translational cardiovascular research in Europe.

When assessing the quality of scientific output, it is also important to look at the number of publications in the top 10% and top 10%-25% ranking journals. In the period from 2012-2015, approximately one-third of CARIM publications ranked in the top 10% journals (Table 6a), i.e. those journals that have been ranked as the top 10% in various subject categories by the Journal Citation Reports of the ISI. In 2014, this percentage was as high as 32,4%. The data of 2015 are not finalised yet. An additional one-third of CARIM's papers have been published in the top 10%-25% ranking journals (Table 6b). The total number of publications over the period 2013-2015 is discussed in paragraph 2.4.1.

TABLE 6A OVERVIEW OF THE NUMBER AND PERCENTAGE OF PUBLICATIONS IN THE TOP 10% RANKING SCIENTIFIC JOURNALS 2013-2015

2013	168	32,4%
2014	169	32,1%
2015	n.a.	n.a.

TABLE 6B OVERVIEW OF THE NUMBER AND PERCENTAGE OF PUBLICATION IN THE TOP 10%-25% RANKING SCIENTIFIC JOURNALS 2013-2015

2013	174	33,5%
2014	172	32,7%
2015	n.a.	n.a.

Finally, the Hirsch-index (Hirsch J., Proc Natl Acad Sci USA 2005;102: 16569) is a strong indicator of the academic reputation of individual scientists. Table 7 shows an overview of the Hirsch-index for all CARIM PIs and the Scientific Director. Only the researcher's articles and reviews were included in the calculation; letters to the editor and other publications were not taken into account. As an additional parameter, the m-index (h-index divided by the number of years starting with the year of the first publication used to calculate the h-index) is also presented to compare scientists of differing seniority.

TABLE 7 HIRSCH-INDEX AND M-INDEX OF CARIM'S SCIENTIFIC DIRECTOR AND PRINCIPAL INVESTIGATORS (AS PER MARCH 2016, SOURCE: ISI WEB OF SCIENCE, *= GOOGLE SCHOLAR (TO ACCOMMODATE PUBLICATIONS BEFORE 1989)

NAME	DEPARTMENT	H-INDEX	YEARS OF PUBLICATION	M-INDEX
Erik Biessen	Pathology	42	25	1,7
Matthijs Blankesteijn	Toxicology & Pharmacology	26	27	0,96
Hans Peter Brunner-La Rocca	Cardiology	37	21	1,8
Harry Crijns	Cardiology	78	28	2,8
Hugo ten Cate	Biochemistry	42	27	1,5
Tammo Delhaas	Biomedical Engineering	27	23	1,2
Tilman Hackeng	Biochemistry	40	25	1,6
Johan Heemskerk	Biochemistry	45	28	1,61
Stephane Heymans	Cardiology	35	15	2,3
Jan Glatz	Genetics & Cell Biology	65	27	2,42
Bram Kroon	Internal Medicine	41	25	1,64
Jos Maessen	Cardiothoracic Surgery	30	29	1,0
Robert van Oostenbrugge	Neurology	26	14	1,8
Mark Post	Physiology	43	24	1,8
Frits Prinzen	Physiology	44	34	1,29
Chris Reutelingsperger	Biochemistry	52	30	1,7
Harald Schmidt	Toxicology & Pharmacology	75	29	2,6
Uli Schotten	Physiology	37	19	1,95
Bert Smeets	Genetics & Cell Biology	41	27	1,5
Coen Stehouwer	Internal Medicine	94	30	3,1
Monika Stoll	Biochemistry	36	20	1,8
Harry Struijker Boudier	Toxicology & Pharmacology	44	27	1,6
Thomas Unger	Scientific Director	90*	35	2,6
Hans Vink	Physiology	36	25	1,44
Paul Volders	Cardiology	30	23	1,3
Christian Weber	Biochemistry	81	24	3,4
Joachim Wildberger	Radiology	38	21	1,8
Leon de Windt	Cardiology	45	17	2,7

2.4.3 DEMONSTRABLE MARKS OF RECOGNITION FROM PEERS

The academic reputation of the CARIM research staff is illustrated by important signs of recognition. These for example include personal grants (annex 3), invitations to present at major national and international meetings and congresses (annex 4), memberships of editorial boards (annex 5), as well as memberships of national and international scientific boards (annex 6).

Furthermore, CARIM researchers have been very active in EU networking activities and forming (inter)national alliances. Fifty-three "Horizon 2020" grant applications with CARIM researchers involved were submitted in 2014 and 2015, of which 8 have been granted (some still pending). In this matter, CARIM has one of the highest success rates of Maastricht University. Strategic alliances that are in place are (among others) with the University Medicine Johannes Gutenberg-University of Mainz, University of Münster, RWTH University Clinic Aachen, the University of Bordeaux, Medtronic Bakken Research Center BV, Bayer Health Care and Siemens AG.

Finally, CARIM researchers collaborate, at several degrees of intensity, with researchers all over the world (see annex 7).

2.5 RELEVANCE TO SOCIETY

Cardiovascular diseases are still the number one cause of death worldwide. While in most industrialized countries death from stroke and acute myocardial infarction has been decreasing over the last decades, heart failure becomes more and more important as a dominant cause of morbidity and mortality. Cardiovascular diseases cannot be avoided, but their clinical onset can be delayed and their progression can be slowed down. In many cases, acute cardiovascular events such as stroke or myocardial infarction can even be prevented by adequate therapeutic management. By doing excellent research, CARIM will help to improve the quality of life, medical research, progress in medicine and treatment of patients with cardiovascular diseases. Furthermore, about 50% of CARIM's PhD students continue their career in the health care sector, e.g. as a staff member in the hospital or following an education to become specialists, being involved in patient care directly.

In the following paragraphs, diverse examples of CARIM's relevance, impact and added value to society is explained. One example, research on electro-mechanics of the heart of Professor Frits Prinzen (Dept. of Physiology), is further explained in a narrative, an in-depth explanation of the relevance of the research unit's work to society and how various indicators are visible in one project (see annex 8).

2.5.1 DEMONSTRABLE RESEARCH PRODUCTS FOR SOCIETAL TARGET GROUPS

Good examples of the societal impact of CARIM researchers can be found in the results of the many clinical trials conducted by CARIM's clinical scientists:

- Data obtained in the Maastricht Study (Prof. Coen Stehouwer) can and will be used to inform and shape primary, secondary and tertiary prevention of diabetes, cardiovascular disease and associated comorbidities. For example, in-depth analysis of quantitative data on sedentary behaviour has shown that risk of type 2 diabetes can be reduced by ~20% by replacing 30 minutes of sitting (average, 9 h/day) by 30 min of walking, independent of other types of physical activity such as engaging in sports.
- Another study which attracted significant media attention was the MR CLEAN Study in which Prof. Robert van Oostenbrugge and Dr Wim Zwam (Dept. of Neurology) are participating. MR CLEAN, a multicentre randomized clinical trial of endovascular treatment for acute ischemic stroke in The Netherlands, was the first study that showed an important benefit of the treatment for patients with acute ischemic stroke due to intracranial large vessel occlusion. The trial results have been published in The New England Journal of Medicine of January 1, 2015. The impact of this trial on the treatment of acute ischemic stroke was huge, as it brought up a total new treatment option for acute ischemic stroke. Furthermore, it revolutionized the delivery of stroke services as the demand for interventional services escalated exponentially. Only in The Netherlands at least 2000 people might be eligible for this treatment. It also gives hope for patients with a devastating type of stroke as this treatment will result in a favourable outcome (independency) in one out of seven treated persons.
- In the Worm Study, PI teams (headed by Prof. Paul Volders and Prof. Monika Stoll) at CARIM investigate a large Dutch-German founder population with excess SCD over multiple generations, segregating the SCN5A deletion mutation c.4850_4852delTCT, p.Phe1617del. SCN5A encodes for the main subunit of the cardiac sodium channel. Genealogical research has identified two ancestral couples (currently considered potential founders), who lived in the 16th century near the river Worm, at the south-eastern border of The Netherlands with Germany. Hence the name "Worm Study". Sudden cardiac death (SCD) claims almost a million deaths annually in Western Europe and the USA, accounting for 15-20% of all natural deaths, and up to 50% of all cardiovascular deaths. Ventricular fibrillation (VF) is the most common underlying arrhythmia. Previous research has demonstrated a strong heritable component contributing to the risk for SCD, yet the underlying genetic mechanisms remain largely unclear. The unraveling of genetic contributors to arrhythmia is important for diagnostic purposes, risk stratification, elucidation of molecular pathways, and the identification of potential therapeutic targets. The Worm Study reached the front page of local newspapers on June 15, 2013 (Dagblad de Limburger) and October 3, 2015 (Limburgs Dagblad), and appeared in various inside articles of national newspapers. Radio, TV and www coverage followed thereafter. Besides, there have been patient information meetings in the last years. E.g. one for mutation carriers and family members of the Worm population (Heerlen, April 26, 2015), and another as the National Day Inherited Heart Diseases (Maastricht, October 3, 2015), with attendance of a broader audience interested in inherited heart disease.

Examples of societal relevance can be found in the basic research programmes as well. Structural bioinformatics and drug design efforts of the Department of Biochemistry (Theme I) has contributed to the second release of the online database of small molecule modulators of protein-protein interactions (http://www.ippidb.cdithem.fr). One series of such modulators was discovered and optimised (Gerry Nicolaes) in collaboration with researchers from Amsterdam and Nijmegen, is targeted against the interaction between the proteins TRAF6 and CD40. These modulators have been shown to represent a series of drug like molecules that now serve as lead compounds for the development of a completely novel method for anti-atherosclerotic drugs, an application for which a patent has been granted. Such drugs hold great promise for the general public, since our compounds appear to be able to reduce atherosclerotic plaque size, as well do

they induce a more stable plaque phenotype. Study of the anti-inflammatory properties of activated protein C, has resulted in the unexpected identification of a novel form of low-anticoagulant heparin which has strong cytoprotective properties Gerry Nicolaes, Chris Reutelingsperger/Coen Hemker). This heparin is able to protect animals from death in an in vivo model of sepsis. A patent was obtained for the use of the heparin in sepsis and a spin-off company was established by the UM, in collaboration with the Basic Pharma group (Geleen, the Netherlands). The spin-off, called Matisse Pharmaceuticals, aims at introducing the new heparin to the market, for use in systemic inflammatory disease, like sepsis. Currently there is no pharmacotherapy in sepsis available, despite the facts that there are an estimated 19 million cases of sepis a year, with associated mortality rates for sepsis patients being 20-30%, a number which even exceeds this in septic shock patients.

The CARIM research project that appeared most in the media in the last few years is the cultured beef project of Professor Mark Post. Tissue engineering or Regenerative Medicine in general has focused on replacing damaged or dysfunctional organs and tissue by healthy tissues, which are grown de novo and ex vivo from biomaterials and autologous cells. It has been fantasized for almost 80 years that this technology could be used to grow food, in particular, meat. We have been culturing bovine myoblasts and engineering bovine skeletal muscle to make the world's first cultured hamburger that we presented in August 2013. This essentially provided the proof of concept that meat can be made through tissue engineering. If this process can be made resource and cost efficient, the societal impact of the technology would be tremendous. Project resulted in recent years in 3 spin-off companies (Qorium B.V., MosaMeat B.V., Cell2Tissue B.V.), 2 m€ in private funding in 2013-2015, 9 scientific papers in 2013-2015, 2 book chapters, 2 webinars, 50-70 invited lectures per year, internationally, lecture Universiteit van Nederland in 2015, World Technology Award by World Technology Summit (Time magazine & AAAS, 2013), featuring in 2 documentaries, shortlisted for the IDFA Amsterdam, featuring in many TV items internationally, countless newspaper and popular journal articles, 185.000 hits on Google search, 5 TEDx presentations and 4250 videos on YouTube.
Furthermore, several CARIM researchers took efforts in transferring their research results to societal target groups, by being involved in primary or secondary educative projects, give lectures to a general audience or contribute to policy reports. Mark Post, Tilman Hackeng and Bert Smeets have for example been involved with the project Kidzcollege/Teenzcollege, an initiative from Maastricht University that offer lectures for children and teenagers in the region to bring them in contact with science in an accessible and understandable way.

2.5.2 DEMONSTRABLE USE OF PRODUCTS

CARIM researchers put a lot of effort in translating their research knowledge to products. This valorisation is achieved in diverse ways, for example by companies that have been established and patents have been requested as a result of research outcomes (Mirabilis Therapeutics, 2015; Mattisse Pharmaceuticals BV, 2014; Qorium BV, 2015; MyRhythm BV, 2015) or collaborating with already existing companies.

Another means of valorisation is the use of research products by societal groups. Within CARIM, research within the Department of BME (Joost Lumens, Tammo Delhaas, Koen Reesink, Theo Arts and Willem Dassen) has for example resulted in the clinical application 'CircA-adapt', a mathematical model of the human heart and circulation, which is developed with the aim to facilitate research and education in cardiovascular (patho-)physiology and can be downloaded free of charge. It enables real-time simulation of cardiovascular system dynamics in a wide variety of physiological and pathophysiological situations. The entire cardiovascular system is modelled as a concatenation of modules representing cardiac chambers, valves, blood vessels, and peripheral vascular beds. Currently, simulations appear so realistic. Presently, the CircAdapt Simulator is successfully integrated in the first, second and third year of the Medical curriculum at Maastricht University. The simulator is also used in teaching courses for residents in Cardiology and Pediatrics, as well as on several conferences for Pediatricians. The great potential of the CircAdapt simulator as an educational

tool led to implementation of this tool in Medical Curricula in other Dutch Universities (Radboud University Medical Center, Utrecht University, and (as of 2016) University of Amsterdam), as well as in South Africa (Stellenbosch University) and the USA (university of Utah). Currently, e-courses for the European Society of Cardiology are being developed. The potential of the CircAdapt model as educational and fundamental research tool has been brought to footlight in various publications, ranging from editorials in the European Heart Journal to publications in newspapers. The press release by Maastricht University Medical Center (17 Feb 2014) entitled "Computermodel voor het simuleren van hartafwijkingen" has led to several online publications. Besides these activities related to CircAdapt, our research group also: gave lectures at various high schools (HAVO5 / VWO5) in Den Bosch, Helmond and Asten; participated in the MUMC+ open days in 2013, 2014 and 2015 and organised the FIMH2015 conference in Maastricht (Functional Imaging and Modeling of the Heart).

Another example of a product which was designed for a societal target group is the application 'mijnhartfalencoach', designed by the Department of Cardiology (Hans Peter Brunner-La Rocca) in collaboration with e-Health specialist Sananet (Sittard, NL) (grant European INTERREG IVb- program). The goal of the app is to improve the guidance of chronic heart failure patients. After discharge from the hospital, the patient can monitor his health status continuously via the app, which leads to a lower number of people being hospitalized and increases the knowledge of patients on heart failure leading to an improvement of quality of life.

2.5.3 DEMONSTRABLE MARKS OF RECOGNITION BY SOCIETAL GROUPS

CARIM has recently engaged in three new CTMM (Center for Translational Molecular Medicine) projects, which focus on applying the translational aspects of molecular medicine so that scientific results as quickly as possible in actual patient care: MICRO-BAT 2014 (PI Prof. Johan Heemskerk), ECAF (PI Prof. Uli Schotten) and deAGEpyr (PI Prof. Casper Schalkwijk). Furthermore CARIM was involved in 2013-2015 involved in two TI Pharma projects: "Renin-angiotensin system blockade beyound angiotensin II" (PIs Harry Struijker Boudier/Jo De Mey) and "Exploitation of toll-like receptors in drug discovery" (PI Stephane Heymans) and two BMM projects: "IDiDAS" and "iVALVE (PI Mark Post).

Several marks of recognition can already be found in the previous paragraphs. CARIM research frequently appear in national, regional and popular magazines and television and radio programmes e.g. De Limburger, de Telegraaf, Elsevier, BNR radio, EenVandaag, Trouw, Chapeau, L1 radio and television, NPO, DWDD. Furthermore, CARIM researchers have received several prizes, mostly scientific, but also public ones, e.g. the World Technology Award on societal aspects of world food supply (Mark Post) and the Edmond Hustinx Prize 2014 on replacement, reduction and refinement of animal experimenting (Judith Cosemans).

2.6 PHD DURATION AND SUCCESS RATE

In 2015, the number of (internal) PhD students at CARIM equaled approximately 77 FTE/82 students (see chapter 2.2). Table 8 shows an overview of the number of regular PhD candidates who started between 2005 and 2011. The primary aim of those PhD students with an employee status at CARIM is to conduct research and they have an obligation to graduate. The enrolment of new PhD students in 2009, 2010 and 2011 was significantly higher than in other years. The most important reason for this increase is the Maastricht Study which started in 2009. During the whole evaluation period, the ratio male/female PhD students was about 50/50. In total 62% of the PhD students who enrolled in 2005-2011 have finished their PhD track. However, the average duration of the promotions is substantially longer than the four years originally set for a PhD student. One of the reasons for this longer duration is the integration of the PhD period into the clinical education track. Another reason is the wish to obtain extra experimental data in order to publish in higher ranked journals.
As already mentioned in chapter 1 of this midterm report, both CARIM and the Faculty Board have taken measures to reduce the average promotion time.

TABLE 8 STANDARD PHD-CANDIDATES (1)

ENROLMENT				SUCCESS RATES						
Starting year	Enrolment (male/female) M	F	Total M+F	Graduated in year 4 or earlier	Graduated in year 5	Graduated in year 6	Graduated in year 7 or later	Total graduated	Not yet finished	Dis-continued
2005	15	10	25	0/0%	5/20%	4/16%	10/40%	19/76%	0/0%	6/24%
2006	6	12	18	3/17%	5/28%	5/28%	0/0%	13/72%	0/0%	5/28%
2007	15	9	24	3/13%	9/38%	2/8%	5/21%	19/79%	2/8%	3/13%
2008	10	10	20	0/0%	5/25%	5/25%	4/20%	14/70%	2/10%	4/20%
2009	18	16	34	2/6%	8/24%	9/26%	3/9%	22/65%	6/18%	6/18%
2010	12	19	31	1/3%	11/35%	6/19%	n.a.	18/58%	11/35%	2/6%
2011	20	18	38	2/5%	9/24%	1/3%	n.a.	12/32%	25/66%	1/3%
Total	96	94	190	11/6%	-	-	-	117/62%	45/24%	27/14%

1) Standard PhD-candidate with employee status and conducting research with primary aim/obligation to graduate; (AiO, promovendus)

TRACK.2 demands that each PhD and each supervisor reflect on the progress of the PhD trajectory on a regular base. Moreover, each PhD also reflects on the quality of supervision. In case of substantial delay or insufficient scores the CARIM PhD-coordinator is notified automatically and can take action. Furthermore, in 2015 FHML issued a number of measures that may reduce overall time for thesis completion, via a combination of incentives (completion of thesis within 4 years) and discouragements (PI remains financially responsible for PhD student's salary until thesis approval).

2.7 RESEARCH INTEGRITY

CARIM's scientists and PhD students are obliged to follow the national guidelines for Research Integrity (VSNU; Association of Universities in the Netherlands).

At the level of the Maastricht UMC+ a special research code has been developed, which is published on the website (http://crispmaastricht.nl/en/?page_id=401). The Research Code Maastricht UMC+ provides those involved in research with a clear description of the rules for ethical and socially responsible conduct in scientific research, as it is very important for the Maastricht UMC+ Board that all its researchers work according to existing legal and regulatory requirements. Therefore, every new researcher (including PhD-students) who will receive their contract from the HR-department is informed about the existence of the Maastricht UMC+ Research Code.

At the UM level a special "Regulation for Scientific Integrity" was developed, which clearly describes the UM policy in this area. The Executive Board has appointed a counsellor on scientific integrity, who is the contact person for questions or complaints concerning scientific integrity. The counsellor will try to mediate in the complaint or otherwise to reach an amicable resolution. If this is not possible, he will guide the complainant to file the complaint to the Committee for Scientific Integrity UM, who will then take it further and will advise the Executive Board. Furthermore, at University level, special 'Days on Research Ethics' were organised in 2014, aimed at PhD students and postdocs.

Regarding the way raw and processed data are stored, CARIM informed his researchers on the documents "Gedragscode Wetenschappelijke Integriteit UM" and "The Netherlands Code of Conduct for Academic Practice 2004". Decided is that this subject becomes part of the annual Planning & Control talks with the PIs, to monitor this more closely. PhD students are able to follow courses on correct handling and storage of data, organized by the University Library. Importantly, soon after the start of their appointment PhD students are asked to get familiar with the general guidelines for proper scientific conduct and have to indicate that they will adhere to these guidelines.

One important future aspect in this respect is the protection of storage and proper handling of research data. For that purpose an innovative and comprehensive ICT data infrastructure must be set up within the Maastricht UMC+.

In April 2015 the CaRES plan was integrated into a faculty-wide, new training and supervision plan, referred to as TRACK.2. This web-based platform allows PhD's to enter relevant information and CARIM to monitor PhD progress more in an easy and structured way. Each PhD student has to be mentored by 2 to 3 supervisors, of which at least one is responsible for daily supervision. The supervision team meets on a regular basis with the PhD student to discuss research progress, possible bottlenecks and planning. In addition, TRACK.2 automatically sends out instructions to each PhD and each supervisor to reflect on the progress of the PhD trajectory twice a year. Moreover, each PhD also reflects on the quality of supervision. In case of substantial delay or insufficient scores the CARIM PhD-coordinator is notified automatically enabling him to respond timely.

Finally, Professor Harry Struijker-Boudier is a member of the University's Committee on Scientific Integrity.

2.8 SWOT ANALYSIS

In February 2016, a SWOT analysis was performed for which all scientific CARIM staff was asked for input. Approximately two-third of the invited researchers filled in the Excel file, which was completely open for every remark. The results are presented in Table 9.

TABLE 9 RESULT OF THE SWOT ANALYSIS PERFORMED IN FEBRUARY 2016

STRENGTHS	WEAKNESSES
- Fruitful collaborations between departments and groups within CARIM - High quality research and excellent research projects - Strong research groups - Group of young talented staff - Excellent research facilities; imaging, biobanking, MF, computational biology - National and international position and status as excellent cardiovascular centre - Translational potential - Wide variety of topics covered within the cardiovascular research domain	- Insufficient animal facility - Insufficient level of core facilities (e.g. cell culture, imaging, MS) - Financial situation which leads to a reduction in staff members, increase of workload and difficulties in keeping staff or recruiting new people - Current PI structure, PI too central, role not well defined - CARIM is underrepresented in national and European subsidy committees
OPPORTUNITIES	**THREATS**
- Cooperation with University Professors and newly established institutes (M4I, MERLN, MaCSBio) - External collaborations - Collaboration other Schools (MHeNS, NUTRIM, GROW) - Increase (EU) funding and explore alternative funding options - Strong regional network - Further integration of CARIM and the HVC - Involvement of CARIM in development of a new animal facility - Involvement of CARIM in design and development of faculty core facilities (NMR; imaging; Muroidean Facility; MS)	- Loss of competitiveness, both internally within CARIM, but also in the (inter)national cardiovascular field - Disbalance between research time and education/ other activities (partly due to downlabeling research formation to max. 0.5 FTE) - Further budgetary restrictions - Decreasing interest of national and international funding organisations in cardiovascular diseases - Data handling, ICT structure inefficient

Based on this analysis, already ongoing actions and possibilities within CARIM's reach, the following topics have been defined:

a Role of the PI in CARIM: Role description, responsibilities, good practice, PI criteria, PI duos as standard approach?
b Translational research: Opportunities and challenges of translational research, CARIM-HVC relation, how to improve the CARIM/HVC corporate identity;
c EU and other funding opportunities: EU participation/funding, alternative fund raising strategies, crowd funding, Health Foundation Limburg;
d Vision and innovation: What drives science and CARIM's research in 10 years from now? What expertise is missing?

2.9 STRATEGIC PLANS

A recent investigation into cardiovascular research at Dutch university medical centres published in the Netherlands Heart Journal came to the following conclusion:

…"In Maastricht cardiovascular research is clustered in the School for Cardiovascular Diseases (CARIM), one of the top institutes for translational cardiovascular research in Europe…" [1]

As much as this appraisal confirms the strategic decisions of CARIM in the past with their influence on the present performance, it represents also an obligation to maintain and improve research quality in order to meet the challenges of the future.

Strategic decisions can be helped by forces from outside and inside the institution. The ERC review in 2014 with its numerous detailed suggestions for improvement as well as SWOT analyses in 2014 and 2016 performed by CARIM investigators were quite supportive in shaping the present strategic plans.

CARIM boasts of a substantial number of excellent researchers, both basic and clinical. As this report reveals, their innovative projects have been acknowledged nationally and internationally by the acquisition of collaborative and individual grants, publications in high-ranking journals as well as invited lectures around the world and several prestigious awards. The three research foci of CARIM, namely 'Thrombosis and Hemostasis', 'Cardiac Function and Failure', and 'Vascular Biology' have survived many attempts of modification and turned out to be solid, sustainable columns of research which can harbour multiple distinct research topics as an umbrella.

However, slight changes will always have to be made in order to adapt to current and future needs, in this case mainly to make the translational aspects of CARIM's research more visible. Thus, in the future, Theme II will change to 'Complex Arrhythmias and Structural Heart Disease', and Theme III to 'Vascular Biology and Medicine'.

INCREASE FUNDING

The decrease of internal and external funding, experienced in recent years and expected in those to come, is considered a real threat by CARIM investigators. Therefore, a major strategic effort now and in the future will be to improve the funding situation. For direct funding, the School depends on the so-called FHML 'performance-funding system', which was readjusted in such a way, that the number of PhD graduations per year determines the amount of funding per School. This means that CARIM has to increase the number of PhD defenses per FTE to cope with the present requirements of university funding and to lign up with the other research schools. Major efforts will therefore be required from CARIM researchers to recruit and supervise a greater number of internal and external PhD students.

With respect to external funding, grant acquisition from national and international resources will have to be further enforced, and the presence and visibility of CARIM investigators in national and international gremia of grant-giving agencies has to be enhanced. A focus will be participation in mutual grant applications both nationally (e.g. CVON in the Netherlands) and internationally (e.g. the European Horizon 2020 and following programmes). Leadership in consortia of these programmes by CARIM investigators will be strongly encouraged. Additional grant opportunities outside the traditional academic ones and collaborations with industry will be actively sought for. Furthermore, CARIM researchers will be stimulated to participate in national committees and European working groups.

GO TRANSLATIONAL

One of the main points, not only in the most recent ERC report, but also in the previous one is the translational connection and the collaboration with the HVC in the CVC. While the translational connection is already in place with numerous collaborations between basic

1 The joint cardiovascular research profile of the university medical centres in the Netherlands. Van Welie SD, van Leeuwen TN, Bouma CJ, Klaassen AB. Neth Heart J. 2016 Apr 4. [Epub ahead of print]

and clinical researchers, its potential is not yet fully developed (see SWOT analysis).

CARIM will improve this connection within its strategic plans by aligning its research foci along the translational objectives as mentioned in the CVC masterplan of 2013, for example 'Thrombosis and Haemostasis', 'Complex Arrhythmias', 'Heart Failure', 'Macrovascular Complications (incl. Athero, Aortic Aneurysms, Vascular Stiffness)' and Microvascular Complications (incl. Vascular Dementia, Diabetes). To put this strategy in practice, translational pairs have to be formed for subtopics within the themes, each consisting of a basic- and clinical researcher, in order to moderate the respective inter-thematic group.

However, despite a strong focus on translational research aspects, CARIM will remain a "playground" for curiosity-driven, original basic research, which is an essential prerequisite for seminal scientific innovations that may or may not have a translational potential in the future.

ADAPT THE PI STRUCTURE

One of the weaknesses of CARIM's research structure was felt to be a rather inflexible PI system. In line with the ERC recommendations and to regain financial maneuverability, CARIM has already substantially reduced the number of its PI-ships. The interplay between faculty, Schools, departments and PI-ships as executed at Maastricht University and academic hospital can be considered as quite complex and gives often rise to some uncertainty about financial and other responsibilities. Several younger CARIM scientists would like to be given more recognition and financial freedom concerning the handling of their individual grants. CARIM has started a discussion process on this topic to think about new structures of governance that may serve future requirements of research flexibility, while at the same time conserving those structures that have proven to be valuable in the past.

VALORISATION AND INFRASTRUCTURE

Valorisation will stay one of the important goals of CARM in the future. In this respect, Theme I has been leading the field in the recent past but the other themes will gradually line up with the foundations of new start-up companies. Generally speaking, CARIM is doing quite well in the valorisation field and will do in the future while not forsaking its academic demands and qualities, a balance which has to be defined continuously.

Concerning infrastructure, a major drawback was unanimously felt to be the condition and governance of the animal facility which has led to an exodus of animal research from Maastricht to other extramural institutions in recent years. In the future, this problem will be at least partly solved by the construction of a new research building to house the animal facility and by new structures of governance therein including the recently created Muroidean Facility (MF) of CARIM which will be part of the animal facility's advisory board. Along these lines, other badly needed multi-user units are currently being established conjointly by the faculty and the research schools (microscopy, MRT), and other units (e.g. cell culture) will have to follow.

In conclusion, future strategies of CARIM will build on the scientific quality already reached, will be striving for further innovation, will focus on carefully selected themes, will strengthen all kinds of collaboration and of translational aspects, while always encouraging individual scientific curiosity and excellence and fostering young researchers' talents.

EDUCATION

Both CARIM and the Faculty have taken measures to reduce the average time it takes to complete a PhD thesis. For instance, TRACK.2 demands that each PhD and each supervisor reflect on the progress of the PhD trajectory on a regular base. Moreover, each PhD also reflects on the quality of supervision. In case of substantial delay or insufficient scores the CARIM PhD-coordinator is notified automatically and can take action. Furthermore, in 2015 FHML issued a number of measures that may reduce overall time for thesis completion, via a combination of incentives (completion of thesis within 4 years) and discouragements (PI remains financially responsible for PhD student's salary until thesis

approval). At the same time, within CARIM the discussion is reopened about the thesis criteria. This discussion is still ongoing. Collectively, it is anticipated that these measures will help to reduce the average duration of the PhD trajectory.

2.10 VIABILITY

Cardiovascular disease will remain one of the main causes of death in the Netherlands and in the entire world and research to understand the underlying mechanisms and to develop new innovative therapies in this area will therefore remain important for the decades to come. This is a motivation for CARIM to find solutions to problems and collaborate with stakeholders to ensure societal impact.

FINANCIAL PROSPECT

By the end of 2017, the restructuring of CARIM will be finalized and a strategic reserve will have been created. The tenure track system will become active again, and young talents will have an opportunity to get a permanent position. Additionally excellent scientific staff will be recruited from outside CARIM.

For direct funding, the School depends on the so-called FHML 'performance-funding system', which was readjusted in such a way, that the number of PhD graduations per year is a critical parameter to determine the amount of funding per School. CARIM is currently lagging behind compared to the other schools and will have to increase the number of PhDs, for example by recruiting external PhD students (see page 8), without forsaking the traditionally high quality of its PhD defenses. Since quality of the output in terms of publications in high-ranking journals has been always CARIM's priority. That means that besides emphasis on recruitment of PhD's, post-docs and junior researchers will also be appointed to achieve high quality output in the long run, in order to maintain CARIM's international scientific reputation.

More than 50% of CARIM's funding comes from third parties. In the future CARIM will have to open up new avenues to attract external funding to achieve its goals. The unique collaboration between the HVC and CARIM will open up new grant possibilities in so-called Value Based Health Care programs in order to secure a continuous money stream. Regarding research grants and projects, by incorporating the strategies as described in the previous paragraph, funding will be improved in the upcoming years. After a dip in concluding new contracts and grants in the years 2013 and 2014, CARIM's portfolio has grown substantially in 2015 (see table 10). For the near future we foresee a further growth in new projects and personal grants that will secure the financial continuity of the School.

TABLE 10 NEW CONTRACTS AND GRANTS CONCLUDED WITHIN CARIM; THIRD PARTY PORTFOLIO

	2011	**2012**	**2013**
2014	**2015**		
2nd money stream	1.255	1.999	610
2.329	1.992		
3rd money stream	16.625	7.029	8.041
2.473	7.741		
Total	13.880	9.028	8.651
5.103	9.733		

RESEARCH QUALITY

CARIM is one of the top institutes in the field of curiosity-driven as well as translational cardiovascular research. To keep this status, further alignment with the HVC, investments in excellent researchers and innovative research projects are necessary. This will be achieved with the funds from CARIM's strategic reserve.

INNOVATION

Scientific innovation has always been and will always be a major stronghold of CARIM's research programmes. In this respect, prospects are promising. A substantial number of personal grants has been acquired recently and many CARIM researchers are actively involved in networking and programme consortia. By improving its visibility in national and European committees, CARIM's prospects will further improve. In addition, the number

of spin-off companies, based on knowhow/IP developed in CARIM's (basic) research programs, is rising. To facilitate this development, close collaborations with the Maastricht Valorisation Centre (MVC) and the Health Campus are on-going.

NEXT GENERATION

Part of CARIM's policy is to recognise, stimulate and support talented students and staff and retain them by offering suitable career opportunities. The process starts at the level of the Master's students and does not stop until the level of established researchers. The tenure track system is an essential element in this regard. Furthermore, CARIM connects to the Dean's central policy in the recruitment of young talents on faculty level. Eight CARIM researchers are participating in the "Top Talent Program" of the Faculty from 2014 and 2016. A final instrument CARIM offers to researchers is the help of the Research Council in coaching the application for personal grants.

Maastricht University

Faculty of Health, Medicine and Life Sciences

To: Executive Board
Mbb4-6

Your reference	*Our reference*	*Direct line*	*Maastricht*
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Subject: **short reaction on the evaluation report of the External Review Committee of the School CARIM**

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Dear professor Paul,

In 2014 an External Review Committee (ERC) has conducted the assessment of the research carried out within the School for Cardiovascular Diseases (CARIM) in the period 2007-2012. In the evaluation report (October 2015), the ERC has formulated some useful recommendations.

The faculty Board and the School CARIM are addressing these recommendations and follow-up actions on these ERC recommendations are already being elaborated. In the coming period these recommendations will be further taken into account. An extensive reaction concerning the follow-up of these recommendations will be sent to the Executive Board in September 2016, together with the midterm evaluation of the School CARIM which will take place in 2016 over the period 2013-2015.

As requested in your letter of December 18, 2015 (with reference 2015.10.2301-LM-DT), we will publish this letter (as a short reaction on the ERC recommendations), together with the final ERC report, on the UM and CARIM website.

Yours sincerely,

Prof. Dr A.J.J.A. Scherpbier
Dean FHML

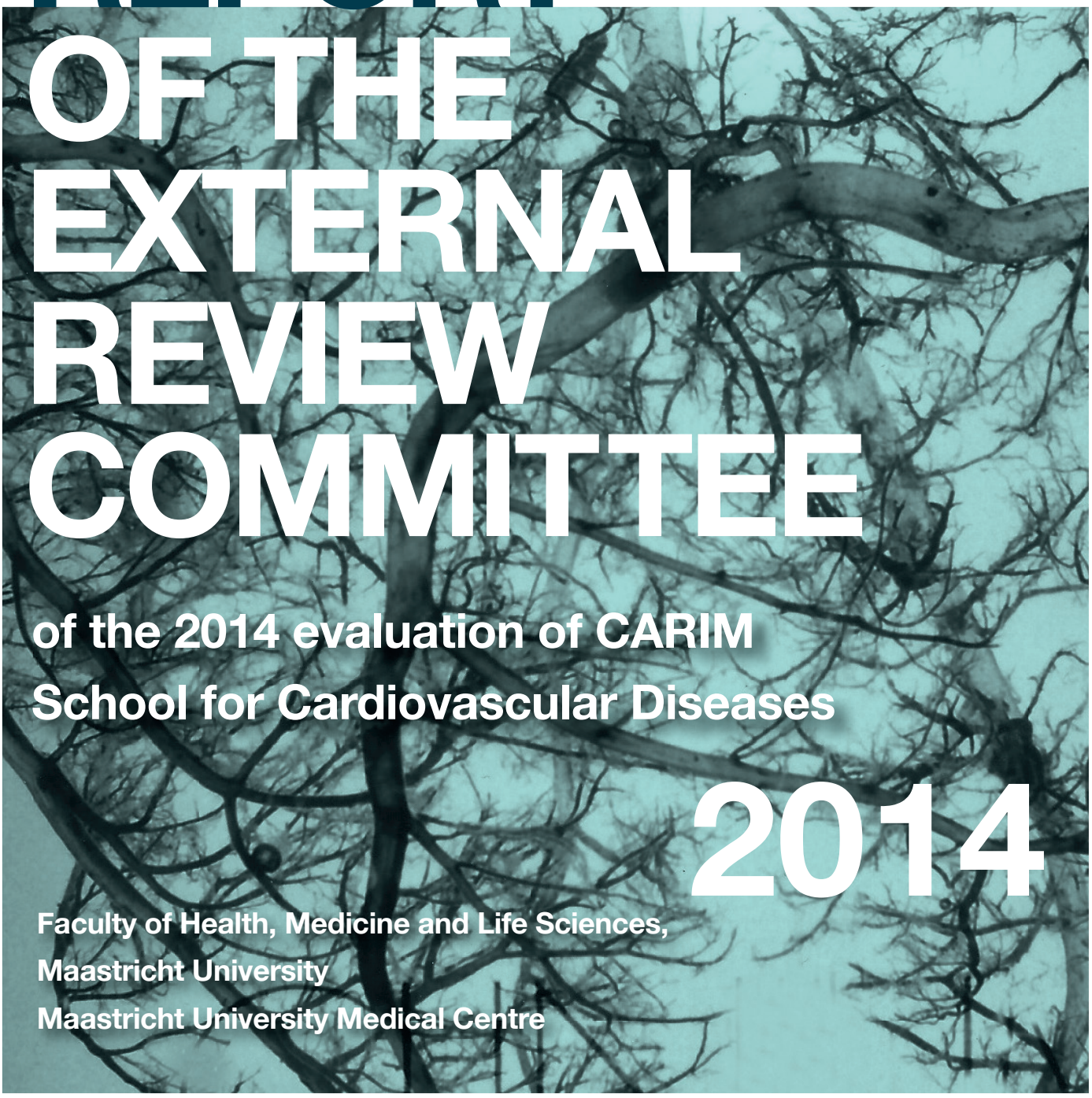
Maastricht UMC+

academisch ziekenhuis Maastricht

Maastricht University

School for Cardiovascular Diseases

REPORT OF THE EXTERNAL REVIEW COMMITTEE



of the 2014 evaluation of CARIM School for Cardiovascular Diseases

2014

Faculty of Health, Medicine and Life Sciences,
Maastricht University
Maastricht University Medical Centre

School for Cardiovascular Diseases

REPORT OF THE EXTERNAL REVIEW COMMITTEE

of the 2014 evaluation of CARIM School for Cardiovascular Diseases

Faculty of Health, Medicine and Life Sciences,
Maastricht University
Maastricht University Medical Centre

INTRODUCTION

Scope and context of this review

This assessment covers the research, the Research Master programme and the PhD training programme as carried out in, or in collaboration with and under responsibility of the Cardiovascular Research Institute Maastricht (CARIM), School for Cardiovascular Diseases. For several decades already, CARIM has a strong position in the international cardiovascular research and aspires to be one of the top institutes for translational cardiovascular research in Europe.

The assessment is executed by an External Review Committee (ERC) at the request of the management of CARIM and of the Dean of the Faculty of Health, Medicine and Life Sciences (FHML) following approval by the Executive Board of Maastricht University. The assessment of the institute is carried out in accordance with the rules of the Standard Evaluation Protocol (SEP) 2009-2015, the protocol for periodic research assessment in the Netherlands (updated June, 2010). This protocol has been drawn up by the Association of Universities in the Netherlands (VSNU), the Netherlands Organisation for Scientific Research (NWO) and the Royal Netherlands Academy for Arts and Sciences (KNAW). The main criteria in SEP evaluations are quality, productivity, societal relevance and vitality and feasibility.

The terms of reference

In accordance with the SEP, the terms of reference of the ERC are defined as a major tool to advise the Board and Management of CARIM to sustain and improve quality of their research and education programmes and to give foundation to strategic decision-making procedures. The focus of the assessment should be on the educational programmes and on the scientific research programme, which should include judgment of CARIM's scientific productivity, the relevance of the research and the institute's viability. The Dean of the FHML has asked the ERC to pay special attention to the relation between the strategic choices of CARIM and the further development of the Cardiovascular Center Maastricht (CVC), and to CARIM's ability to respond adequately to new developments in the field, based on its strategy. In addition, the Dean appreciates the ERC's opinion whether the CARIM's PhD training programme sufficiently reflects the broad area of research, CARIM is engaged in, and the quality of the programme. Finally, the ERC has been asked to pay attention to the duration of the average PhD trajectory within CARIM.

The mission of CARIM

As described in the self-evaluation report 2007-2012 the mission of CARIM is to:

- Improve current knowledge of the processes underlying cardiovascular diseases by carrying out pioneering and excellent scientific research extending from 'molecule to patient to population', i.e. the epidemiology of cardiovascular and metabolic diseases;
- Stimulate and facilitate the collaboration between basic and clinical scientists, as an essential factor in ultimately improving health care;
- Develop into an internationally recognised centre of excellence in cardiovascular medicine;
- Train Master's students, PhD students and MD students to become independent researchers and post-docs to become leading scientists who are capable of functioning in multidisciplinary research programmes at universities or companies;
- Evaluate new findings, products and techniques for applicability in health care, often in collaboration with private companies;
- Publish scientific results in highly ranked journals.

The strategic goals

Based on a SWOT analysis and its follow-up strategic meeting, the strategy for the coming years has been divided into the following areas: research, collaboration, infrastructure, funding, CVC (translation to the clinic), education and publication strategy. A regular series of strategic meetings specifically addressing the question of how CARIM has to respond to the changes in the scientific landscape will be installed.

The future research strategy of CARIM is to:

- Keep the strength of the current Theme I (Thrombosis and Haemostasis) and II (Cardiac Function and Failure) intact and explore that these can be even further strengthened by a cardio metabolic programme, taking into account the links with the new Cardiovascular Center Maastricht (CVC) within Maastricht UMC+;
- Redefine the Vascular Biology theme (Theme III) following discussions about combining macro- and microvascular research;
- Develop, in collaboration with the Heart and Vascular Center (HVC) of the Academic Hospital Maastricht, into an internationally recognised centre of excellence in cardiovascular medicine;
- Intensify projects with other schools of Maastricht University such as NUTRIM, CAPHRI and MHeNS;
- Extend strategic alliances and collaborative programmes with other programmes within the Netherlands (such as Chemelot) and outside (such as the Helmholtz-Institute in Aachen and the RWTH Aachen University Clinic);
- Enhance integration into international collaborative projects, particularly in view of the opportunities of the EU Framework Program for Research and Innovation (Horizon 2020);
- Establish an excellent PhD programme and train Master's students in cardiovascular research.

CARIM has the ambition to be one of the leading research institutes in translational cardiovascular research in Europe, and to be a top ten player in the period leading up to 2020. It wants to be considered as a world leader in the fields of atherosclerosis research, atrial fibrillation and heart failure. It also wants to continue to provide important international contributions in the field of molecular imaging. As during the past years, cardiovascular scientists from around the world are encouraged to join CARIM, because CARIM values open communication, close cooperation, high ambitions, good facilities and a critical learning environment.

EVALUATION

The External Review Committee and the mode of operation

The External Review Committee (ERC) consists of six internationally recognised leading scientists, well acquainted with the current research practice of relevant disciplines and who cover the various other areas of CARIM's (managerial) activities (see annex 1). They have all signed a declaration of independence to avoid future discussions about potential conflicts of interest (see annex 4). The ERC was supported by the managerial staff of CARIM, including the secretary. Several weeks in advance of the site visit, the members of the ERC received the self-evaluation report regarding the self-assessment of the research activities and educational programme of CARIM, and the terms of reference for the evaluation and the visiting programme. On a secluded website of CARIM a complete set of these data and other relevant documentation was made available to the committee, like the evaluation protocol (SEP), recent annual reports of CARIM, the evaluation report for the 2007 evaluation of CARIM, the latest CARIM midterm and the 2012 document Cardiovascular Center Maastricht (CVC), the joint and integrated further development of the Heart and Vascular Center (HVC) and CARIM into one international center of excellence.

The programme of the site visit, which took place from 4 to 6 June, 2014, in Maastricht (see annex 2), included presentations on CARIM and its various research themes, poster presentations and demonstrations by staff members and PhD students, and presentations of the Master and PhD programmes. The ERC had discussions with (PhD) students regarding the training programme, and with tenure trackers, Top Talents and post docs regarding their training programme and career prospects. The ERC also met - before and at the end of the audit - with the Dean of the FHML, the Scientific Director and the Board of CARIM, and the Director of the HVC.

Overall impression

The ERC acknowledges the detailed description of CARIM's activities and ambitions in the "CARIM Self Evaluation 2007-2012" report, which provides a good overview of the efforts that have been made since the last ERC evaluation in 2007 to sustain and improve quality of CARIM's research and education programmes and strategic decision-making procedures. Since 2007, CARIM has been involved in several transitions that are critical for further and successful development of CARIM into an international top institute: an ongoing process of extensive renewal at both the institutional level (change of scientific director, two new theme leaders, refocusing of the research programme) and the university level (merging of two faculties and the academic hospital into Maastricht UMC+, novel alliances at the national and (EU-) regional level), and a rejuvenation of leadership in research projects. Some of these transitions are still going on.

With respect to the scientific director and theme leaders, the ERC is convinced that they are excellent scientists and managers, particularly to create cohesion between the staff members of CARIM. As the scientific director will retire in 2017, it is advised to look for a successor in time, to guarantee a gradual transition of leadership. With respect to the merging of the two faculties and the university hospital, there is a risk that due to differences in culture, management control and legal entity between the university (including CARIM) and the hospital, further development of translational medicine may slow down. However, the ERC is confident that CARIM is of high quality and can become an international top institute in translational cardiovascular research. The growing cooperation between CARIM and the hospital in the CVC, and the further development of strategic alliances and networks at the national and (EU-)regional level are important for this ambition and may open up new roads to innovation, staff recruitment and funding (especially Horizon 2020). The latter may also compensate for the expected reduced funding (notably when in 2014/2015 the large public-private subsidies for technological top institutes, TTI's, like the Center for Translational Molecular Medicine, CTMM, will cease) and annual budget cuts (8-10% by the FHML from 2011 onwards).

Evaluation of the research themes

According to the SEP, each research group or programme (i.e. theme) should be assessed according to the four criteria. The committee may use qualitative and quantitative indicators (on a five-point scale) and indications.

Theme I: Thrombosis and Haemostasis

The focus of Theme I (with four programmes) is directed at deciphering impairments of (coagulation) proteins, platelets, and the vessel wall in relation to the development of venous as well as athero-thrombosis. Theme I explores the multifactorial cause of thrombosis. The ERC considers this relatively small theme very well focused, innovative, and productive with an excellent output and valorisation. The programmes within Theme I are strong and coherent and score similar on each criterion. For all 4 programmes, junior staff members are in place and are coached by Theme I, CARIM and the FHML to become future PIs within Theme I.

The **quality** is ranked as 5 (excellent) based on:
The high output and relevance of the scientific results
- The leadership of the group as demonstrated by the recruitment of talented investigators, the research management, successful funding from outside and the creation of international collaboration with groups in Germany, the UK, France and the USA
- The high international academic reputation in the field of thrombosis and haemostasis
- The coherence of the programme including athero-thrombosis, venous and arterial thrombosis

The **productivity** is ranked as 4-5 (very good to excellent) based on:
- The large number of publications in high-ranking journals (Impact Factor above 10)
- The number and quality of completed PhD theses
- The contributions to translational medicine, e.g. the 'Thrombosis Expertise Centre'
- Use of research facilities (protein engineering and molecular imaging agent development) by third parties
- The development of intellectual property (more than in the other themes)

The **societal relevance** is ranked as 5 (excellent) based on:
- The interaction (and recognition by) with stakeholders, such as the Dutch Heart Foundation and the Dutch Thrombosis Foundation and industry, shows the societal quality of the work
- The role of one of the PIs from Theme I as chairman of the Scientific Advisory Board of the Dutch Thrombosis Foundation
- The role of one of the PIs from Theme I as president of the Netherlands Society on Thrombosis and Hemostasis
- This theme stands out in the relatively large number of spin-offs most of which realised within the scope of CTMM programmes
- The Vitamin K cookbook for patients with thrombosis to provide more knowledge on the level of vitamin K in the diet

The **vitality and feasibility** is ranked as 4 (very good) based on:
- The process of changing the research themes to include athero-thrombosis (in conjunction with Theme III)
- State of the art research facilities on protein structure analysis, thrombin generation and platelet aggregation microscopy under flow conditions

In line with the 2007 ERC recommendations, there is now more interaction with clinical departments, especially in the CVC and with the Maastricht study on diabetes mellitus and cardiovascular disease. This translational research should be further stimulated, for instance with diagnostic trials and better use of large and complex data. As the patient population of the Maastricht hospital is rather small to study relevant clinical applications (bleeding and thrombotic disorders, thromboembolism, personalized medicine), the theme will profit from a larger (local, national and (EU-)regional) network to perform this, preferably with combined use of common research and expertise of other themes. An example is the collaboration with Theme II to study the thrombosis risk in patients with atrial fibrillation. The Thrombosis Expertise Centre (TEC), as part of Theme I in collaboration with the CVC, is another very good local initiative with potency for regional extension.

The group is internationally renowned for its expertise in protein engineering of (variant) coagulation proteins which are used for structure function analysis. Mass spectrometry

Evaluation of the research themes

and 700 MHz protein NMR have been acquired for protein structure determination and both protein/protein and protein/drug interaction. The role of coagulation proteases in the onset and progression of atherosclerosis and thrombosis is studied in a large cohort of individuals at risk of coronary vascular disease. Translational lines with many clinical departments are in place on the design and synthesis of molecular imaging agents for PET, SPECT and MRI. Flow assays for thrombus formation and novel procedures for platelet function are used to determine the contribution of platelets to disease.

Theme I stimulates the general use of technical (core) facilities, for instance in programme 2 (Vascular aspects of thrombosis and haemostasis); this also should be further encouraged.

The expected reduced funding (by the University, but also externally) poses a real threat for this theme. The ERC recommends further strategic discussions how to cope with this threat.

Theme II: Cardiac Function and Failure

Research within Theme II (with 12 programmes) focuses on heart failure, ventricular arrhythmias and atrial fibrillation. The main aims are to gain insights into the basic biology of heart failure and arrhythmias and to develop early diagnostic and therapeutic strategies based on concepts developed in the laboratory and in clinical practice. Within this theme there is a wide variance between the programmes in the assessment based on the criteria. Three of the twelve programmes are not performing as well as the others: 'Mitochondrial disease', 'Clinical heart failure' and 'Intermediate cardiac metabolism'.

The **quality** is ranked from 3 (good) to 5 (excellent) based on:
- The high output and the relevance of the scientific outcomes of most of the programmes
- The high international academic reputation in the field of clinical and experimental cardiology of most of the programmes
- The leadership of (primary) individuals such as in cardiomyopathy, gene regulation, atrial fibrillation and electro mechanics
- The decision to create a common experimental cardiology laboratory which comprises PIs from both clinical and preclinical programmes
- The strategy to strengthen complex genetics

The **productivity** is ranked as varying from 3 (good) to 5 (excellent) based on:
- The number of publications about clinical and experimental cardiology in high ranking journals by most of the PIs
- The contributions to translational medicine, e.g. the 'Complex Arrhythmia Unit' and the 'Heart Failure Unit'
- The number of completed PhD theses of which several *cum laude* defenses

The **societal relevance** is ranked from 3 (good) to 5 (excellent) based on:
- Societal impact: the continuing increase of life expectancy of the (Dutch) population is associated with a higher incidence of cardiac arrhythmias and cardiac failure which are the research topics of this theme
- The role of one of the PIs from this theme as chairman of the Scientific Advisory Board of the Dutch Heart Foundation
- The start-up of several spin-off initiatives

The **vitality and feasibility** is ranked from 2 (satisfactory) to 5 (excellent) based on:
- The strengthening complex genetics by instituting a chair in genetic epidemiology and statistical genetics
- The creation of a theme transcending (I and II) experimental cardiology laboratory for PIs in clinical and experimental programmes

Heart failure and arrhythmia research has been strengthened through the creation of a common experimental cardiology laboratory ('Greater Cardiology Lab'), which comprises several PIs (clinical and pre-clinical) within Cardiology. The clinical heart failure programme is particularly focused on the management of non-ischemic, non-valvular cardiomyopathies.

The ERC is pleased to note that Theme II has become an internationally recognised group renowned for its outstanding research in arrhythmias. Regarding atrial fibrillation, the research group is member of a number of

Evaluation of the research themes

national and transatlantic high-profile scientific networks. The coherence in this programme has been improved by the start of invasive and non-invasive characterisation of atrial electrophysiological complexity in patients. As part of the integration of clinical/preclinical research programmes, patient cohorts (including a biobank) and epidemiologic studies have been instituted.

To the opinion of the ERC, the interaction between arrhythmias - both atrial fibrillation and ventricular arrhythmias – and heart failure research should be enhanced. Electrical management of heart failure appears a successful topic. Theme II has the unique opportunity to expand on sharing complimentary expertise in experimental and clinical mechanisms e.g. electrical heart failure due to atrial fibrillation and ventricular ectopy, sudden arrhythmogenic death in diastolic heart failure, genetics of arrhythmias and heart failure. Complex genetics can set the stage for such integration. Additionally, molecular biophysics, including computational modelling to integrate clinical and preclinical data, should be considered in this respect. In this way the 'Greater Cardiology Lab' is just one of many facilities capable to implement this integration.

The implementation of complex genetics with a recently founded chair has been quite an important development for Theme II, from which in particular the programmes of sudden arrhythmogenic death, atrial fibrillation, electrical management of heart failure and cardiomyopathies will profit and integration within these programmes should be promoted. This discipline which makes use of large data sets, will need to be further developed to a solid group (or even core facility in the framework of the CVC), for structuring the programme and acquiring funds in competition (Horizon 2020). The ERC welcomed the developments of complex genetics in this theme, which has been greatly stimulated and structured by the recently founded part-time chair. Because of its relevance to the research lines of a number of PIs in Theme II but also in Theme I and Theme III (many of them dealing with complex multifactorial diseases with some heritable factors), complex genetics expertise should be further reinforced in CARIM. Fruitful cooperation with the existing large department of genetics needs to be given high priority.

The experiments within Theme II require access to experimental animal facilities (notably with large animals like dogs). As the existing (central) facility is no longer up-to-date and cannot further be improved to fulfill all current requirements of researchers and (Dutch and EU) legislation, the ERC strongly recommends replacement by a new facility in the very near future.

Theme II has a few spin-offs. It should be more active in this respect as is Theme I, and needs more support of a central valorisation office (i.e., the technological transfer office "Biomedical Booster"). Several initiatives for external funding (Horizon 2020) are promising.

The reduction in first money funds – mainly assimilated by appointing less support staff and PhD students - especially puts pressure on PIs to attract researchers (this is not only applicable for Theme II but basically for all themes; see also under Funding).

Theme III: Vascular Biology

Following the leave of Prof. Daemen and several of his co-workers in 2012, a number of changes in programmes and leadership of this theme have taken place. The programme "Plaque Instability" had to be modified and is now being rebuilt under new PI leadership in the Department of Pathology with a strong emphasis on molecular and imaging techniques. The research in Theme III (with 11 programmes) is now centred around microvascular dysfunction; athero-thrombosis; arterial stiffening; vascular smooth muscle cell plasticity; endothelial dysfunction; vascular calcification; advanced glycation, and inflammation. These processes are studied in the context of specific cardiovascular diseases that are major burdens to an ageing society (with chronic diseases), namely diabetes and the metabolic syndrome, hypertension and chronic kidney disease, stroke and cognitive impairment, acute coronary syndrome and heart failure, aortic aneurysm and venous disease. This is an ambitious interdisciplinary endeavor which requires collaboration with other themes and clinical departments and research schools such as MH&NS. It is expected that it will create opportunities for successful grants from Horizon 2020 and KIC's in the field of health.

Evaluation of the research themes

The programmes within Theme III are coherent and score similar on each criterion.

The **quality** is ranked as 4 (very good) – 5 (excellent) based on:
- Large number of publications about clinical and preclinical aspects of vascular biology and medicine in high impact scientific international journals
- Leadership had undergone a change following the leave of Professor Daemen. The group has managed to keep its high level of performance with new members entering
- The Maastricht study is nationally and internationally a unique large cohort study on the metabolic syndrome
- The high international academic reputation

The **productivity** is ranked as 4 (very good) – 5 (excellent) based on:
- The large number of publications in high ranking scientific journals
- The number and quality of PhD theses
- State of the art imaging facilities (the Hybrid PET MRI scanner is the only one in the Netherlands and one of the few in the world)

The **societal relevance** is ranked as 5 (excellent):
- High societal impact; the key processes which constitute the research programme are studied in the context of cardiovascular diseases that are major burdens to an ageing society

The **vitality and feasibility** is ranked as 4 (very good) based on:
- Intensive cooperation with the other CARIM themes and research schools within the FHML
- A Vascular Network Group has been created to optimise the interaction between basic and clinical scientists

An imaging platform will be added for use by all themes.

The Maastricht Study is an epidemiological study in 10,000 individuals that focuses on the causes and consequences of the metabolic syndrome, type 2 diabetes and cardiovascular disease, and uses extensive phenotyping of the microcirculation, the macrocirculation and the heart. It is a unique, very large and important cohort study on diabetes and glucose metabolism. The study can significantly contribute to the scientific knowledge of type 2 diabetes. The first round of this study concerns mainly phenotyping, mostly performed by a substantial number of studies of PhD students. The involvement of an internationally recognised scientist to oversee the study and assist the theme leader (who carries several other responsibilities) should be discussed. The ERC considers the long-term funding of this study a serious challenge.

The ERC believes that further re-organisation of Theme III - by sharing focus, concepts, facilities and platforms - can improve quality and productivity.

Most programmes of Theme III make use of animal facilities. Thus, also for this theme a new up-to-date centralized animal facility is urgently needed. This also holds for the other themes, especially Theme II. In this respect, another centralized (general or core) facility which also is important for CARIM's research, has been recently funded, the Maastricht Centre for Systems Biology (MaCSBio).

The vascular biology theme is currently being re-structured, and the outcome of this determines to a large extent the vitality of this theme. The ERC is interested to know the consequences for the management of Theme III, on which aspects the programme will be focused and how the funding will be organised.

Funding

In the past years, CARIM has been very successful in collecting funds from both the university (direct funding) as well as from external sources (grants and contract funds) like NWO/ZonMw, CTMC, Dutch Heart Foundation, Netherlands Thrombosis Foundation and EU- funds. More than 50% of the funding of CARIM was derived from such th.ird parties. Lately, the economic crisis has led to budget restrictions by the government which also affects universities. In addition, more competition among research groups and changes regarding the funding policies of the external organisations create a challenge for research institutes to be successful in the future.

The annual budget of CARIM in 2012 (approximately M€ 25) was 15 % higher than in 2007, mainly due to an increase of contract research grants (in 2011). Overall direct funding was more or less stable. The volume of research grants obtained in national and international competition varied over time. Funding by grants and contract funds increased for all themes. With 262.8 FTE (full-time equivalent) staff, 98.4 FTE PhD students, and a budget of approximately M€ 25 in 2012, CARIM is one of the largest cardiovascular research institutes in Europe, producing more than 500 refereed scientific (WI-1) articles in high impact journals and an average of about 30 PhD dissertations per year.

In the highly competitive field of cardiovascular medicine in which CARIM operates, together with the increasing restrictive financial conditions like the termination of the TTI-grants and the expected reduction in annual faculty budget, it will be - even more than indicated in the 2007 evaluation - a challenge to maintain and improve these high levels of in- and output.

Continuous networking and combining forces, i.e. promoting and intensifying functional collaboration with other local and (EU-)regional institutes are needed to recruit excellent researchers and to compete successfully for (EU- and NWO-)grants in the field of translational cardiovascular research. Good initiatives are the regional Thrombosis Expertise Centre (TEC) and the Complex Arrhythmia Unit, both are also crystallisation points of the CVC. SENECA, the Theme I initiative for an Initial Training Network (a Marie Curie action within Horizon 2020) between CARIM, RWTH Aachen, the Karolinska Institute Stockholm and King's College London, aimed at joint/double doctorates between these institutions, is another promising example. Individual financial incentives as well as an increase of the strategic budget are needed, and their policy should be reconsidered.

Challenges and strategic alliances

Since the last review, significant progress has been made in the development of the Cardiovascular Centre Maastricht (CVC), the unique vehicle for the translation of new fundamental insights of CARIM's research into clinical innovation in the HVC of the hospital. The foundation of CVC to provide excellence in cardiovascular patient care, research and education looks promising with the start of two crystallization points (TEC and Complex Arrhythmias Unit), combined with the allocation of an annual budget of approximately 1 M€ from the hospital. The ERC already mentioned differences in culture, management control (HRM strategies) and legal entity (governance structure and IP regulations) between CARIM as part of the university (basic research and innovations which may lead to patient care in the future) and the HVC as part of the hospital (operational excellence in patient care) and which may slow down further development. Referring to the increasing restrictive financial conditions, this threat deserves special attention.

The implementation of complex genetics by instituting a chair for a well-known scientist is a very appropriate decision and requires further discussion about the interaction with the department of genetics and how other themes (I and III) may profit from this expertise.

The local cooperation with several research schools (like CAPHRI, GROW, NUTRIM and MH&NS), especially in the Maastricht Study and the CVC, is still limited and should be further encouraged.The international cooperation like strategic alliances with (EU-)regional institutes - also thanks to CARIM's location nearby the border - is going well and should be further stimulated. It offers CARIM access to people, innovation and shared (EU-)grants.

Regarding perceived poorly performing programmes, CARIM needs to find a way to cut these programmes, and in this progress may also deliberate a modification of the currently rather inflexible organisational PI-structure.

Tenure track

The elegant Tenure Track Programme of CARIM and the Top Talent Programme of the FHML/university allow talented young scientists to obtain a permanent employment contract. In 2012 the first 'tenure tracker' obtained a permanent position at CARIM; she may also serve as a role model for female scientists. In this respect, the ERC appreciates that, instead of focussing exclusively on expertise, a balanced (50/50) pool of male/female 'tenure trackers' has been created.

The PI-system is becoming rather inflexible because PIs belong to the tenured or permanent staff and are relatively young. It is a great challenge for CARIM to make this system of (programme) leaders more flexible and also open for talented females; at present only one of the recently appointed PIs is female.

Although the formal procedures for programmes like Tenure Track and Top Talent seem clear, young researchers still experience some lack of transparency in the communication, especially with respect to these procedures, future perspectives and the way (PI-)vacancies are filled. The ERC is concerned about this, and believes that – besides more transparency - a mentor is particularly crucial in coaching advanced PhD students and postdocs.

Valorisation and infrastructure

Valorisation is overall good to excellent, particularly in Theme I with a number of spin-offs. Many recent valorisations have been within the scope of CTMM programmes. As the funding of CTMM will soon end, there should be renewed attention for valorisation with Theme I as an example.

The animal facilities of the faculty are no longer up-to-date, they cannot longer be improved to fulfill all current requirements of researchers and (Dutch and EU) legislation and thus require replacement in the very near future. As there is a strong emphasis on translational research in CARIM, the ERC considers a new animal facility essential for CARIM's competitiveness in scientific quality and grant acquisition. It will offer opportunities for combining experiments, e.g. by using multiple organs and tissues from single animals by different schools and research groups, thereby responding to the societal ambitions for Replacement, Reduction and Refinement (three R's, or 3V-alternatives) of animal experiments. A state-of-the-art animal research facility is absolutely necessary, at least for a medical school, to compete with leading institutes in a particular field, to do excellent research in a proper way, to speed translational research, to acquire grants and projects, and to attract industrial partners.

The ERC noticed that a large budget (> M€ 20) is available for a new animal facility (called VivariUM) and that progress has been made towards final decision-making. Hopefully, the new animal facility, complying with Dutch and EU legislation regarding animal housing and research, but closely linked to the research schools of Maastricht UMC+, can be opened within the next two or three years. To address the current unsatisfactory situation which lasts already for some years, the ERC has written a separate letter to the Dean and the Executive Board of the university (see annex 3).

Three recent initiatives should be mentioned in particular. In view of the importance of cardiovascular genetics for CARIM's research programme, in particular for the programme on heart failure and cardiac hypertrophy, it was important to establish a new chair of complex genetics/ genetic epidemiology. The international network of this new chair, together with the expertise of the department of genetics which is centred around monogenetics, may lead to a genomics-based cardiovascular research platform working at the highest level in the newly launched CVC. Systems biology (MaCSBio) is a good initiative; it is an opportunity to relate this as a general tool or core facility more closely to genetics. At present, systems biology is not yet explicitly visible within CARIM and separated over the programmes. The Vascular Network Group of Theme III is a promising facility with many interactions between basic researchers of several schools and clinicians, for example in the field of inflammation. Although several scientists of the network have basic knowledge of immunology, novel innovative expertise is needed, from outside and at chair level.

The educational programme

The ERC judges the PhD programme very positively. It is broad, flexible and clearly structured; it is up to date and meets the current criteria for a high quality PhD training programme. The programme offers excellent training of a new generation of creative researchers. The number of PhD students is relatively large, but almost all of them get a job after finishing the thesis. The advice to put more effort into monitoring the quality of supervision of PhD students has been successfully implemented in the CARIM Research, Education and Supervision (CARES) plan. This plan provides more transparency for all stakeholders, a better monitoring of the progress during the PhD trajectory, improvement of the quality of the PhD thesis, preparing the PhD student (for example with so-called transferable skills) for the job market, also outside the university, and a strict schedule to finish the PhD (training) trajectory in time. The web-based PhD monitoring programme which has recently been developed by all research schools in collaboration with an IT company, TRACK.2, offers a useful supplement.

Currently the PhD duration is 62.9 months (more than 5 years). Although this seems long, the ERC acknowledges some rather inevitable causes for this delay, not mentioned above. Firstly, the competitive Dutch system requires to comply with increasing standards of PhD theses, in the health sciences sometimes even leading to about four refereed publications in the thesis (only submission is not enough). Secondly, as a consequence - the time it takes to publish the paper. Thirdly the subsequent thesis administration, and finally - if applicable - the integration of the PhD period into the clinical education track.

Nevertheless, the PhD-duration needs to be reduced, particularly from a financial point of view and career perspectives (e.g., to prevent loss of career potential). One way is to replace the number of mostly low impact publications (the majority has an impact factor below 3-4 IF) by a few ones with higher impact factor.

The ERC is hopeful that the implementation of the CARES plan and the new TRACK.2 plan also reduces the average time it takes to obtain a PhD.

CONCLUSIONS

Taking all the previous mentioned arguments into account, the outcome for the evaluation for the School overall is the following:

Quality:	very good to excellent (4-5)
Productivity:	very good to excellent (4-5)
Societal relevance:	excellent (5) The relevance is very high, since cardiovascular diseases remain one of the leading causes of death in the Netherlands (currently 27%, and about 33% 10 years ago) and the Western world. So, there is a continuous need for dedicated translational research on prevention, diagnosis and treatment of cardiovascular diseases.
Vitality and feasibility:	very good (4) Once the animal facilities have been improved (see annex 3) this may be very good to excellent (4-5).
Overall:	very good to excellent (4-5)

Summary of the recommendations

Fund raising will be even more important for CARIM than in the past period. EU- funding programmes like Horizon and EU-regional programmes offer a long-term support, and CARIM should explore the possibilities to improve its grant acquisition. The ERC recommends to stimulate networking and collaboration (locally, nationally and internationally) in order to compete successfully for grants in the field of translational cardiovascular research. Further strategic discussions are needed on how to cope with the expected reduced funding (from the university as well as externally).

Translational research is strong but should be further stimulated and CARIM should keep working on enforcing and intensifying the collaboration of HVC-CARIM in CVC.

The animal facility urgently needs to become up-to-date as has already been recommended in a letter of the ERC to the dean. ERC recommends a new animal facility which is essential not only for CARIM, but the whole faculty's competitiveness in scientific quality and grant acquisition.

Systems biology should be enforced. It is recommended to further discuss the need of this area for CARIM, the FHML and other faculties in Maastricht, and an interfaculty centre should be created.

Regarding perceived poorly performing programmes, CARIM needs to find a way to cut these programmes, in spite of the rather inflexible organizational PI structure. At the level of the three CARIM themes, the further reorganisation of Theme III, and partialy Theme II, is necessary in order to improve quality and productivity.
Valorisation of research outcomes in Themes II and III should be further explored and requires more discussion.
The funding and initiation of the Maastricht Study is a major recent accomplishment of Theme III.
Complex genetics needs to be further developed into a solid group for structuring the programme and acquiring funds in competition (Horizon 2020). Fruitful cooperation with the existing large department of genetics needs to be given high priority.

While the high quality of the PhD theses/programme must be maintained, options to reduce the duration of the PhD track should be explored.

The imaging facility should become a self-sustained interfaculty unit, independent from CARIM, and collaboration with the newly established University Professors should be enforced.

The transparency in the communication of Tenure Track procedures should be improved.

ANNEX 1

Members of the External Review Committee CARIM, June 2014

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ANNEX 2

Program ERC CARIM 2014

Date: Wednesday June 4 – Friday June 6, 2014

Wednesday June 4

Morning	Arrival ERC members in Maastricht, NH Hotel Maastricht, Forum 110, 6229 ER Maastricht Bestuurszaal, Bestuurstoren University Hospital, MUMC+
13.00-14.00	Lunch ERC members and Board Members School
14.00-15.30	Installation of the External Review Committee (ERC) by Prof. A. Scherpbier, Dean FHML - Introduction Research School by Prof. Th. Unger - Overview Dutch research funding system by Prof. T. Hackeng - Overview program ERC - Discussion
15.30-16.00	Closed meeting ERC members Bonte zaal, UNS 50 H.1331
16.00-16.15	Introduction CARIM program by Prof. Th. Unger, Scientific Director CARIM
16.15-16.45	Presentation Theme I 'Thrombosis and Haemostasis' by Prof. T. Hackeng
16.45-17.45	Discussion
17.45-18.00	Closed meeting ERC members Chateau Neercanne, Cannerweg 800, 6213 ND Maastricht
18.30	Drinks and dinner ERC with Dean FHML, Director and Board Members School

Thursday June 5

Bonte zaal, UNS 50 H.1331

9.00-9.30	Presentation Theme II 'Cardiac Function and Failure' by Prof. H. Crijns
9.30-10.30	Discussion
10.30-10.45	Closed meeting ERC members
10.45-11.00	Coffee break
11.00-11.30	Presentation Theme III 'Vascular Biology' by Prof. C. Stehouwer
11.30-12.30	Discussion Oxfordlaan 70
12.30-12.50	Meeting with Dean FHML concerning animal facilities
12.50-13.30	Lunch and closed meeting ERC 4th floor 'Terras', University Hospital, MUMC+
13.30-16.00:	Viewing CARIM posters including guided tour CARIM facilities UNS50 4.324A (Theme I), MUMC 5 H2.046 (Theme II), UNS 50 1.351A (Theme III)
16.00-18.00	Meeting with Tenure Trackers, Top Talents and post docs; per Theme De Groote Societeit, Vrijthof 36, 6211 LE Maastricht
18.30	Informal (buffet) dinner with CARIM scientific staff, technical staff and PhD students

Friday June 6

UNS 50 1.351A
Presentations on The Cardiovascular Center (CvC)

8.30-8.50	CvC, by Prof. M. Jacobs, director Heart Vessel Centre
8.50-9.05	The Maastricht Study, by Ronald Henry
9.05-9.20	Thrombosis Expertise Center, by Hugo ten Cate
9.20-9.35	Arrythmia Unit, by Harry Crijns Rode Zaal (Coen Hemkerzaal), UNS 50 k 0.480
9.40-10.10	Presentation PhD training program by M. van Bilsen Several locations
10.10-11.10	Time slot for CARIM Course Week Rode Zaal (Coen Hemkerzaal), UNS 50 k 0.480 Presentations on new developments (Moderator: Prof. Th. Unger)
11.10-11.20	The vascular contribution to cognitive impairment, by Robert van Oostenbrugge
11.20-11.30	Vascular Network Group, by Koen Reesink
11.30-11.40	Hypercoagulability causes atrial fibrosis and promotes atrial fibrillation, by Uli Schotten
11.40-11.50	Novel RNA targets in heart failure, by Stephane Heymans
11.50-12.00	Regulation alternative splicing, by Elisabetta Castoldi
12.00-12.10	Marie Curie ITN, by Tilman Hackeng Bestuurszaal, Bestuurstoren University Hospital, MUMC+
12.30-13.00	Lunch
13.00-14.30	Closed meeting ERC
14.30-15.30	Feedback to Board, Director Research School and Dean FHML
15.30-17.00	Closed meeting ERC, including site visits upon individual requests members ERC (several locations)
17.00	End

ANNEX 3

Letter to the Dean FHML concerning animal facilities

To Prof.Dr. A.J.J.A. Scherpbier
Dean of the Faculty of Health, Medicine and Life Sciences
Maastricht University
P.O. Box 616
NL - 6200 MD Maastricht

Amstelveen, June 24, 2014

Dear Professor Scherpbier,
On behalf of the External Review Committee (ERC) of CARIM, once again I would like to draw your attention to the animal facilities of your institution, which seem to be no longer up-to-date and therefore require replacement in the very near future. On various occasions in the CARIM self evaluation 2007-2012 references are made to the construction of the VivariUM, a new animal facility, where laboratories and equipment are shared by multiple users. This should replace the present Central Animal Facilities (CPV), which cannot longer be improved to fulfil all current requirements of researchers and (Dutch and EU) legislation. At the moment, much of the animal research of CARIM and other schools takes place in peripheral laboratories which are allocated within the departments. Besides, the SWOT analysis states that animal experiments are increasingly performed extra muros; clearly, this is not efficient and costly.
This situation has been noticed already several years ago, also by some members of the ERC. About one third of the animal research projects approved by the animal experiments committee (DEC) are performed within CARIM. So, it is obvious that in the SWOT analysis of CARIM the non-competitive state of the present animal facilities and the apparently capricious pace of development of the new VivariUM are seen as real threats. The discussions during our visit on June 4-6, 2014, with principle investigators of CARIM and others confirm this.
In our view, an up-to-date animal facility is a multi-user facility for all faculty schools, within the university and the academic hospital. Its service should also be offered to other partners in the region. This core facility combines the expertise of several researchers on animal research and makes more efficient use of the existing staff and equipment. It also allows the staff to better facilitate temporary research support required for projects in collaboration with industry. As there is a strong emphasis on translational research in CARIM, the ERC considers the new VivariUM absolutely essential for CARIM's competitiveness in grant acquisition. It offers opportunities for combining experiments, e.g. by using multiple organs and tissues from single animals by different research groups, thereby responding to the societal ambitions for Replacement, Reduction and Refinement (three R's, or 3V-alternatives) of animal experiments. The facility is absolutely necessary, at least for a medical school, to compete with leading institutes in a particular field, to do excellent research in a proper way, to speed research, to acquire grants and projects, and to attract industrial partners.
In our closed meeting with you, on June 5, 2014, we were pleased to hear that a large budget (> M€ 20) is available for the VivariUM and that progress has been made to final decision-making. We hope that the new animal facility, complying with Dutch and EU legislation regarding animal housing and research, but closely linked to the schools, can be opened within the next two or three years.
Replacement, reduction and refinement of animal experiments are of paramount importance, for society and for researchers, also within CARIM. In this respect, we note that the two-yearly Willy van Heumen award for alternatives on experimental

ANNEX 3

animal use has been given to Prof.Dr. J. van Heemskerk on the occasion of the 8th Work Congress on alternatives and animal use in life sciences (Montreal, Canada, August 25, 2011). Everyone agrees that the use of animals for scientific purposes should be minimalised as far as possible. However, within the strategic choices of the research profile of CARIM, it is inevitable that animals are used, including large animals like goats, pigs and dogs (e.g., within theme II). For several reasons, we would like to stress the necessity of facilities for dog experiments. First of all, important aspects of arrhythmias or conduction diseases can only studied in dogs because of the specific properties of the conduction system and the anatomy of the atria as compared to other experimental animals. Secondly, these aspects of electrical cardiac disorders are traditionally a very strong part of the UM's and CARIM's research portfolio. Third, there are only two academic institutions with capabilities to perform dog experiments in the Netherlands so that excluding dogs from the plans for a VivariUM would weaken the competitiveness of Dutch academic cardiovascular research significantly.
Some of the societal topics mentioned above are listed in the (draft) leaflets* enclosed. These folders with general information regarding animal research have been established with the cooperation of one the members of the ERC and of the Dutch society for the prevention of cruelty to animals ("Dierbescherming").

Sincerely yours,
On behalf of the external review committee of CARIM,

Prof.Dr. W.G. van Aken, Chairman

Copy to Prof.Dr. M. Paul, Chairman of the Executive Board of Maastricht University

*see http://www.informatiedierproeven.nl/files/Brochure%20SID/ZoDoende%20Brochure_2012-Digi.pdf

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Competence and independence of peer review committee members

1. A member of the peer review committee bases his/her assessment primarily on:
   · the Standard Evaluation Protocol 2009-2015; Protocol for Research Assessment in the Netherlands
   · if applicable: additional instructions of the Board of Maastricht University and/or of the Dean of the Faculty of Health, Medicine and Life Sciences

2. In giving a judgement on the quality of research, a member of the peer review committee grounds his/her assessment on the following information:
   · the self evaluation report and accompanying documentation
   · if applicable: additional information provided on request of the peer review committee
   · interviews, lectures and talks carried out within the framework of the assessment

3. A member of the peer review committee meets the generally known quality demands within scientific research, including:
   · competence and professionality
   · independence and objectivity
   · care and consistency
   · transparancy and impartiality

4. A member of the peer review committee experiences no personal, scientific, financial or any other potential conflicts of interest in participating in the research assessment of the School for Cardiovascular Diseases (CARIM) of the Maastricht University Medical Centre+ and is therefore both qualified and competent to carry out his/her task as an independent assessor.

5. A member of the peer review committee reports any potential conflicts of interest in advance to the chairman of the review committee.

I declare that I have read the above-mentioned and that I will follow these to the best of my ability.

Place and date: Maastricht, 4th June 2014

Signature:……

Name: ……..

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Abbreviations

CAPHRI	School for Public Health and Primary Care
CARES plan	CARIM Research Education and Supervision plan
CARIM	School for Cardiovascular Diseases
CTMM	Center for Translational Molecular Medicine
CVC Maastricht	Cardiovascular Center Maastricht
ECOS	Research School Accreditation Committee
ERC	External Review Committee
EU	European Union
FHML	Faculty of Health, Medicine and Life Sciences
GROW	School for Oncology & Developmental Biology
Horizon 2020	the EU Framework Programme for Research and Innovation
HVC	Heart and Vascular Center
IF	Impact Factor
KIC	Knowledge and Innovation Community (within Horizon 2020)
KNAW	Royal Netherlands Academy of Arts and Sciences
Maastricht UMC+	Maastricht University Medical Centre+ (MUMC+)
MacsBio	Maastricht Centre for Systems Biology
MHeNS	School for Mental Health and Neuroscience
NUTRIM	School for Nutrition, Toxicology and Metabolism
NWO	Dutch Foundation for Scientific Research
PI	Principle Investigator
SEP	Standard Evaluation Protocol
SWOT analysis	Strengths, Weaknesses, Opportunities and Threats analysis
TEC	Trombosis Expertise Centre
TRACK.2	web-based PhD monitoring program developed in collaboration with an IT company
TTI	Technological Top Institute
VSNU	Association of universities in the Netherlands

School for Cardiovascular Diseases

Maastricht UMC+

academisch ziekenhuis Maastricht

azM

Maastricht University

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2

CARIM PROGRAMMES AND PIS

	PROGRAMME	PI
THEME I **LEADER TILMAN HACKENG**	Blood proteins & engineering	Tilman Hackeng
	Vascular aspects of thrombosis and haemostasis	Chris Reutelingsperger
	Cell biochemistry of thrombosis and haemostasis	Johan Heemskerk
	Clinical thrombosis and haemostasis	Hugo ten Cate
	Structure-function analysis of the chemokine interactome for therapeutic targeting and imaging in atherosclerosis	Christian Weber
	t.b.d.	Monika Stoll
THEME II **LEADER HARRY CRIJNS**	Clinical atrial fibrillation	Harry Crijns
	Cardiomyopathy	Stephane Heymans
	ECM + Wnt signalling	Matthijs Blankesteijn
	Arrhytmogenesis and cardiogenetics	Paul Volders
	Clinical heart failure	Hans Peter Brunner-La Rocca
	Intermediate cardiac metabolism	Jan Glatz
	Gene regulation	Leon de Windt
	Electro mechanics	Frits Prinzen
	Cardiovascular system dynamics	Tammo Delhaas
	Mitochondrial disease	Bert Smeets
	Experimental atrial fibrillation	Uli Schotten
	Surgical intervention	Jos Maessen
THEME III **LEADERS COEN STEHOUWER/ HARRY STRUIJKER-BOUDIER**	Vascular complications of diabetes and the metabolic syndrome	Coen Stehouwer
	Hypertension and target organs damage	Bram Kroon
	Cerebral small vessel disease	Robert van Oostenbrugge
	Microvascular dysfunction and glycocalyx	Hans Vink
	Vascular remodelling in cardiovascular disease	Harry Struijker Boudier
	The vulnerable plaque: makers and markers	Erik Biessen
	Regenerative and reconstructive medicine	Mark Post
	Utilising network pharmacology and common mechanisms for cardiovascular target validation and drug discovery	Harald Schmidt
	Imaging	Joachim Wildberger

ANNEX
3

RESEARCH GRANTS AWARDED TO INDIVIDUALS

NAME	DEPARTMENT	ORGANISATION	AWARD	YEAR
Eline Kooi	Radiology	NWO	Aspasia	2013
Marjo Donners	Pathology	NHS	Dr E. Dekker Senior Postdoc	2013
Kristiaan Wouters	Internal Medicine	NHS	Dr E. Dekker Senior Postdoc	2013
Ellen Dirkx	Cardiology	MUMC+	Kootstra Talent Fellowship	2013
Ellen Dirkx	Cardiology	EU	Marie Curie Talents up	2013
Ellen Dirkx	Cardiology	EMBO	Long Term Fellowship	2013
Ingrid Dijkgraaf	Biochemistry	NWO	Vidi	2014
Blanche Schroen	Cardiology	NWO	Vidi	2014
Ellen Dirkx	Cardiology	NWO	Veni	2014
Blanche Schroen	Cardiology	NHS	Dr E. Dekker Senior Postdoc	2014
Martijn Smulders	Cardiology	NHS	Dr E. Dekker Arts vóór aanvang specialisatie	2014
Susanne de Witt	Biochemistry	MUMC+	Kootstra Talent Fellowship	2014
Jelle Posthuma	Biochemistry	MUMC+	Kootstra Talent Fellowship	2014
Maarten Heusinkveld	Biomedical Engineering	MUMC+	Kootstra Talent Fellowship	2014
Miranda Nabben	Genetics & Cell Biology	NWO	Veni	2015
Jordi Heijman	Cardiology	NWO	Veni	2015
Leon de Windt	Cardiology	NWO	Vici	2015
Marc Strik	Physiology	NHS	Dr E. Dekker Arts vóór aanvang specialisatie	2015
Martijn Brouwers	Internal Medicine	NHS	Dr E. Dekker Junior Staflid	2015
Joost Lumens	Biomedical Engineering	NHS	Dr E. Dekker Senior Postdoc	2015
Judith Cosemans	Biochemistry	NHS	Dr E. Dekker Senior Postdoc	2015
Anna Papageorgiou	Cardiology	NHS	Dr E. Dekker Senior Postdoc	2015
Paula da Costa Martins	Cardiology	NHS	Dr E. Dekker Established Investigator	2015
Andrea Raso	Cardiology	MUMC+	Kootstra Talent Fellowship	2015
Job Verdonschot	Cardiology	MUMC+	Kootstra Talent Fellowship	2015
Martina Calore	Cardiology	EU	Marie Curie Fellowship	2015
Blanche Schroen	Cardiology	NWO	Aspasia	2015
Ingrid Dijkgraaf	Biochemistry	NWO	Aspasia	2015

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Leon de Windt	Cardiology	NWO	Vici	2015
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Joost Lumens	Biomedical Engineering	NHS	Dr E. Dekker Senior Postdoc	2015
Judith Cosemans	Biochemistry	NHS	Dr E. Dekker Senior Postdoc	2015
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Blanche Schroen	Cardiology	NWO	Aspasia	2015
Ingrid Dijkgraaf	Biochemistry	NWO	Aspasia	2015

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MOST IMPORTANT INVITED LECTURES (PIS)

NAME PI	TITLE	OCCASION	YEAR
Bert Smeets	Preventing the Transmission of mitochondrial DNA Disorders: Selecting the good Guys or kicking out the bad Guys	COGI, Vienna, Austria	2013
Bert Smeets	PGD in mitochondrial DNA disorders	ESHRE, München, Germany	2014
Bert Smeets	Preventing the transmission of mitochondrial DNA disorders: selecting the good guys or kicking out the bad guys	ASMRM, Taipei, Taiwan	2014
Bert Smeets	Preventing the transmission of mitochondrial DNA diseases: a tale of man and zebrafish	ESHRE, Lisboa, Spain	2015
Bert Smeets	Selecting Mutation-free Cells in Mitochondrial DNA disease to Prevent Transmission and Develop New Treatment Options	PSRM, Seoul, South Korea	2015
Christian Weber	Chemokines and miRNAs and atherosclerosis	IVBM 2014, Kyoto, Japan	2014
Christian Weber	miRNAs and regional susceptibility to atherosclerosis	FCVB 2014, Barcelona, Spain	2014
Christian Weber	Chemokines in atherosclerosis	GTH Congress 2015, Düsseldorf, Germany	2015
Christian Weber	Regulation of microRNA trafficking in atherosclerosis	Gordon Research Conference on Atherosclerosis 2015, Newry, Maine, USA	2015
Coen Stehouwer	Perivascular fat and the metabolic syndrome	12th Genoa Meeting on Hypertension, Diabetes and Renal Diseases, Genoa, Italy	2013
Coen Stehouwer	Endothelial function and early detection of cardiovascular disease	European Association for Cardiovascular Prevention and Rehabilitation, Annual Meeting, Amsterdam, NL	2014
Coen Stehouwer	Pathogenesis of vascular disease in diabetes	Danish Academy of Science Winter School on Diabetes, Malaga, Spain	2015
Coen Stehouwer	What is vascular ageing?	International Society of Atherosclerosis, Amsterdam, NL	2015
Coen Stehouwer	Role of microcirculatory dysfunction in the pathogenesis of diabetes	Eur Soc Microcirculation, Pisa, Italy	2015
Erik Biessen	Dendritic Cells in Atherosclerosis: Bystanders or Actors?	Dutch German Joint Meeting of Molecular Cardiology	2015
Frits Prinzen	Myocardial dyssynchrony or discoordination?	Am. Coll. Cardiology, San Francisco, USA	2013
Frits Prinzen	Assessment of left ventricular dyssynchrony: Multiscale computer simulations	EHRA Congress, Athens, Greece	2013
Frits Prinzen	Patients with CRT Indications and a RBBB	Heart Rhythm congress, Boston, USA	2015
Frits Prinzen	Endocardial LV pacing	Symposium: Future of Heart Failure Management, Amsterdam, the Netherlands	2015
Hans Vink	Visualising the Glycocalyx	Visit to Children's Hospital of Philadelphia (CHOP) USA	2014
Hans Vink	Visualising the Glycocalyx	Visit to Mayo Clinic, Rochester, USA	2014
Hans Vink	Clinical Assessment of Glycocalyx	World Conference Biomechanics in Seoul, Korea	2015
Hans Vink	Clinical Assessment of Glycocalyx	World Conference Microcirculation in Kyoto, Japan	2015
Hans Vink	Clinical Assessment and Therapy of Glycocalyx	Training for Stanford University, USA	2015
Harald Schmidt	Title unknown	AHA Conference	2014

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MOST IMPORTANT INVITED LECTURES (PIS)

NAME PI	TITLE	OCCASION	YEAR
Harald Schmidt	Title unknown	Conference Am. Kidney Foundation	2015
Harry Crijns	Wenckebach lecture: Back to the future	Netherlands Society of Cardiology	2015
Harry Crijns	Future directions for research in atrial fibrillation	European Society of Cardiology, Amsterdam	2015
Harry Crijns	Persistent AF: electrophysiologist and surgeon lost in isolation	European Cardiothoracic Society Amsterdam, NL	2015
Harry Crijns	Rhythm-AF: what is current practice of cardioversion in Europe	European Society of Cardiology, Barcelona	2014
Harry Crijns	AF progression, a naturally predefined course?	Hamburg Heart Days, Germany	2014
Harry Struijker-Boudier	New drugs for hypertension: what is in the pipeline?	25th European Meeting on Hypertension, Milan, Italy	2015
HP Brunner-La Rocca	Highlights on imaging and biomarkers	European Heart Failure Association	2013
HP Brunner-La Rocca	Pathophysiological Approach to heart failure	EuroPD	2013
HP Brunner-La Rocca	Personalised medicine in heart failure	European Heart Failure Association	2014
HP Brunner-La Rocca	Biomarker guided therapy in chronic heart failure	European Heart Failure Association	2014
HP Brunner-La Rocca	Clinical Examination in heart failure	European Heart Failure Association	2015
Hugo ten Cate	Inflammation and coagulation	Educational lecture SSC, UK	2014
Hugo ten Cate	The future of anticoagulation	ETRO	2014
Hugo ten Cate	Coagulation proteases and cardiovascular disease	CTH Mainz, Germany	2014
Hugo ten Cate	The Robert Muller lecture: coagulation and vascular disease	Mainz, Germany	2015
Hugo ten Cate	Factor XI and cardiovascular disease	50th Angiology symposium, Kitzbuhel, Austria	2015
Jan Glatz	Novel signaling pathways regulating substrate switching in the heart	Keystone Symposium on Mitochondria, metabolism and myocardial functions, Aspen CO, USA	2013
Jan Glatz	CD36 and cardiac lipid metabolism in health and type 2 diabetes	7th International Conference on Lipid Binding Proteins, La Plata, Argentina	2013
Jan Glatz	Cardiac metabolism in diabetes	British Cardiovascular Society Annual Conference, Manchester, UK	2014
Jan Glatz	Ultra-rapid whole-blood point-of-care test: application for early evaluation of patients presenting with chest pain in primary care	3rd Annual Biomarkers in Diagnostics & Therapeutics (BDT2014), Singapore	2014
Jan Glatz	What nourishes me destroys me: Lipids in the heart	11th SHVM conference on “Lipids in Cardiac Health and Disease: From Toxicity to Protection”, Cambridge MD, USA	2015
Joachim Wildberger	Contrast media delivery: Current status. Breast Imaging - current concepts. Dual energy CT applications in clinical routine. CT-guided interventions, clinical cases - FNAB, Core biopsies and RFA.	STAR Program, Specialize Training in Advances in Radiology, Hanoi, Vietnam	2014

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MOST IMPORTANT INVITED LECTURES (PIS)

NAME PI	TITLE	OCCASION	YEAR
Joachim Wildberger	Acute Thorax - Non traumatic thoracic emergencies	Annual Meeting European Society of Emergency Radiology (ESER), Vienna, Austria	2014
Joachim Wildberger	Pulmonary embolism: CTA, perfusion and beyond. Contrast Media Delivery: Standardize and individualize. Prevention of CIN: Overshooting the mark? Dual Energy CT: Brain hemorrhage vs. Contrast after mechanical recanalization. Pulmonary CT perfusion: Are my protocols up to date?	16th Annual International Symposium on Multidetector-Row CT. International Society of Computed Tomography (ISCT). San Francisco, USA	2014
Joachim Wildberger	Chest. Acute pain. Your friend and enemy in emergency radiology. Great Vessels. Innovative choices in cardiovascular imaging.	27th European Congress of Radiology (ECR), Vienna, Austria	2015
Joachim Wildberger	When and why to visit the one-stop-shop. Controversies in cardiac imaging: Triple rule out.	Annual Meeting of the European Society of Cardiac Radiology (ESCR), Vienna, Austria	2015
Johan Heemskerk	Platelet procoagulant activity	Platelet ADP Meeting: Platelet Receptors: From Basic Science to Clinical Practice, Nice/Callian, France	2013
Johan Heemskerk	Mechanisms involved in the platelet procoagulant activity	23rd Biannual International Congress on Thrombosis, Valencia, Spain	2014
Johan Heemskerk	Experimental thrombosis: understanding platelet function (keynote)	EUPLAN Meeting Basic and Clinical Aspects of Platelet Research Including Megakaryocytes, Le Bischenberg, France	2014
Johan Heemskerk	Scrambling the membrane: a regulatory mechanism of platelet function	25th Congress of the ISTH, Toronto, Canada	2015
Johan Heemskerk	Regulation of platelet procoagulant activity (Invited scientific symposium)	57th ASH Annual Meeting, Orlando FL, USA	2015
Leon de Windt	Keynote Speaker, “Defining Academic excellence”	Dies Natalis 2013, Maastricht University	2013
Leon de Windt	Plenary Speaker, “A transcriptional/microRNA circuitry driving cardiac dilation”	Basic Cardiovascular Sciences Scientific Sessions, American Heart Association (AHA) Scientific Sessions 2013, Las Vegas, USA	2013
Leon de Windt	Plenary Speaker, “a microRNA cluster deciding between myocyte hypertrophy and proliferation”	Bi-annual Villa Vigoni congress 2015, “Cells, Genes and Molecules for Cardiac and Vascular Repair”, Villa Vigoni, German-Italian Centre for European Excellence, Menaggio, Italy	
Mark Post	Medical Technology to produce Food	New York Academy of Science, USA	2013
Mark Post	Tissue Engineering for Medical and Food applications	JST_ERATO Tokyo, Japan	2014
Mark Post	Tissue Engineering of vascular grafts	ESC Barcelona, Spain	2014
Mark Post	Lab-grown meat	Harvard Business School Executive course	2015
Mark Post	Future of Meat	World Economic Forum, Summer meeting	2015
Matthijs Blankesteijn	Inflammation as an orchestrator in heart failure	Experimental Biology, Boston, USA	2013

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MOST IMPORTANT INVITED LECTURES (PIS)

NAME PI	TITLE	OCCASION	YEAR
Matthijs Blankesteijn	Circulating inflammatory biomarkers improve the discrimination and reclassification of subjects with subclinical and advanced LV dysfunction	METARDIS project meeting, Leuven, Belgium	2014
Matthijs Blankesteijn	The role of myofibroblasts in infarct healing	Dept. of Cardiology and Angiology, Univ. of Hannover Medical School	2014
Monika Stoll	Extracting biomarkers through bioinformatics	5th AFNET/EHRA consensus conference	2015
Paul Volders	Mitigating and Managing Clinical Cardiovascular Risks: Preserving Effective Medicines	49th Congress of the European Societies of Toxicology (EUROTOX), Interlaken, Switzerland	2013
Paul Volders	Sudden Cardiac Death: Genetics, Mechanisms and Perspectives	Avances y Perspectivas en Biomedicina Cardiovascular, Madrid, Spain	2014
Paul Volders	The End of the Welfare State: Basic Research	Spring Summit of the ESC Heart Rhythm Association, Sophia Antipolis, France	2014
Paul Volders	Genetic Insights for Risk Stratification	Annual Congress of the Belgian Society of Cardiology, Brussels, Belgium	2015
Paul Volders	Arrhythmogenic Mechanisms: Novel Insights	37th Annual Congress of the European Society of Cardiology, London, UK	2015
Robert van Oostenbrugge	MR CLEAN; ingredients to run a successful trial	European Stroke Organisation Conference	2015
Robert van Oostenbrugge	MR CLEAN; first results	Netherlands Heart Days	2015
Stephane Heymans	Myocarditis - State of the art lecture	European Society of Cardiology, London, UK	2015
Stephane Heymans	MicroRNA-146a rewires cardiac metabolism and causes cardiac dysfunction in hypertensive heart disease	Keystone Meeting on non-cardiomyocyte involvement in cardiac diseases, Colorado, USA	2015
Stephane Heymans	Non-coding RNAs: central regulators of cardiac inflammation and disease. European Heart Failure Association (HFA) of the European Society of Cardiology	European Heart Failure Association (HFA) of the European Society of Cardiology, Athens, Greece	2014
Stephane Heymans	Myocardits: future challenges	HFA meeting of the European Society of Cardiology, Athens, Greece	2014
Stephane Heymans	Clinical and Biomarker Predictors of Progression to Heart Failure. 9th Annual Meeting: Transatlantic Heart Failure Biomarker. Cannes. (2014).	9th Annual Meeting: Transatlantic Heart Failure Biomarker, Cannes, France	2014
Tammo Delhaas	Cardiovascular modelling as an adjunct to teaching and research	6th World Congress of Pediatric Cardiology and Cardiac Surgery, Cape Town, South Africa	2013
Tammo Delhaas	CircAdapt: a model to imag(in)e cardiovasculary (patho)physiology	47th AEPC Conference, London, UK	2013
Tammo Delhaas	Computational Study on the Potts Shunt in Pulmonary Hypertension	7th International Conference on Neonatal and Childhood Pulmonary Vascular Disease, San Francisco, USA	2014
Tammo Delhaas	Computational Study on the Cardiovascular System: ventricular-ventricular interaction and right ventricular failure in pulmonary hypertension	3rd Toronto RV symposium, Toronto, Canada	2014

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MOST IMPORTANT INVITED LECTURES (PIS)

NAME PI	TITLE	OCCASION	YEAR
Tammo Delhaas	Determinants of Cardiac Function in a Biventricular Finite Element Model: Geometry vs Myofiber Orientation	Cardiac Physiome 2015, Auckland, NZ	2015
Thomas Unger	Blocking the RAS – the cornerstone in antihypertensive therapy	Second CV Forum, Boston, USA	2013
Thomas Unger	NO generation, blood pressure and vascular stiffness: Lessons from the angiotensin AT2 receptor	Artery 2014, Maastricht, NL	2014
Thomas Unger	BHC Lecturer tour (lecturer of the year)	Belgium, several cities	2015
Thomas Unger	The protective arm of the renin-angiotensin system: from enigma to therapeutic target	ESC Milan, Spain	2015
Thomas Unger	Role of Protective Arm of Renin-Angiotensin System in Cardiovascular Protection Part II	38th Annual Scientific Meeting of the Japanese Society for Hypertension, Japan	2015
Tilman Hackeng	Modular requirements of TFPI function	FASEB Science Research Conferences Proteases in Hemostasis and Vascular Biology, Nassau, The Bahamas	2013
Tilman Hackeng	Tissue factor pathway inhibitor and protein S	The International Society on Trombosis & Haemostasis XXIVth Congress	2013
Tilman Hackeng	Peptide/Protein Based Molecular Targeted imaging of Cardiovascular disease	Haematology Society of Australia and New Zealand, the Australian & New Zealand Society of Blood Transfusion and the Australasian Society of Thrombosis and Haemostasis Interantional Conference. Perth, Australia	2014
Tilman Hackeng	The role of tissue factor pathway inhibitor in atherothrombosis	58th International GTH Meeting, Vienna, Austria	2014
Tilman Hackeng	Remming van de stollingsinitiatie	Opening lecture 20th Amstol Symposium AMC Amsterdam, NL	2014
Uli Schotten	European Network for Translational Research on Atrial Fibrillation	Formal official speech on the 10th anniversary of the Network of Competence for Atrial Fibrillation	2013
Uli Schotten	How do novel insights into the pathophysiology of atrial fibrillation influence our treatment strategies?	Grand Round Seminar Catholic University Leuven, Belgium	2013
Uli Schotten	Atrial Fibrillation: A Maze of Mechanisms	Key note lecture, International Symposium for Modeling of Cardiac Function, London, UK	2014
Uli Schotten	Personalized approaches to guide rhythm control therapies in atrial fibrillation	Debate lecture, 5th consensus conference of the European Heart Rhythm Association, Nice, France	2015
Uli Schotten	Role of atrial fibrosis and fatty infiltration in atrial fibrillation	Gordon Research Conference on Arrhythmia mechanisms, Italy	2015

ANNEX
5

MEMBERSHIPS EDITORIAL BOARDS

NAME	CHARACTER OF MEMBERSHIP (EDITOR, MEMBER OR GUEST EDITOR)	INTERNATIONAL JOURNAL	PERIOD
Aaron Isaacs	Editor	Frontiers in Cardiovascular Medicine	2014 - present
Ben Janssen	Member	Am. J. Physiol - regulatory, integrative and comarative physiology	2008 - present
Bert Smeets	Editor	Clinical and Translational Medicine	2013 - 2015
Casper Schalkwijk	Editor	(co-editor) Diabetologia	2011 - 2015
Casper Schalkwijk	Member	(advisory board) Diabetologia	2015 - present
Casper Schalkwijk	Member	(Editorial Advisory Panel for) Clinical Science	2009 - present
Chris Reutelingsperger	Member	JACC Cardiovascular Imaging	2014 - 2015
Chris Reutelingsperger	Member	J Immunol Methods	2014 - 2105
Christian Knackstedt	Member	Journal of Biomedical Graphics and Computing	2010 - present
Christian Knackstedt	Member	Journal of Cardiology and Therapy	2010 - present
Christian Weber	Editor	Thrombosis Haemostasis	2010 - present
Christian Weber	Editor	Arterioscler Thromb Vasc Biol	2012 - present
Christian Weber	Editor	Molecular Mechanism	2012 - present
Christian Weber	Guest editor	Circulation Research	2010 - present
Christian Weber	Member	Eur Heart Journal	2009 - present
Christian Weber	Member	Basic Res Cardiol	2009 - present
Christian Weber	Member	EMBO Mol Med	2011 - present
Christian Weber	Member	Cardiovasc Res	2012 - present
Coen Stehouwer	Editor	Hypertension	2004 - present
Coen Stehouwer	Editor	Netherlands Journal of Medicine	2005 - present
Coen Stehouwer	Editor	Journal of Diabetes and its Complications	2012 - present
Coen Stehouwer	Editor	Lancet Diabetes Endocrinology	2015 - present
Frits Prinzen	Member	J. Translational Cardiovasc. Research	2013 - present
Frits Prinzen	Member	EUROPACE	2013 - present
Gerry Nicolaes	Editor	World Journal of Haematology	2012 - present
Gudrun Antoons	Editor	Frontiers of Cardiac Electrophysiology	2010 - present
H.P. Brunner-La Rocca	Member	European Heart Journal	2010 - present
H.P. Brunner-La Rocca	Member	EPMA Journal	2015 - present
Harald Schmidt	Editor	PLoS One	ongoing
Harald Schmidt	Member	ESC Cardiovascular Pharmacothery	2015 - present
Harry Crijns	Member	Cardiovascular drugs and therapy	2003 - present
Harry Crijns	Member	European Heart Journal	2010 - present
Harry Crijns	Member	Acta Cardiologica	2014 - present
Harry Crijns	Member	JAFIB	2007 - present
Harry Crijns	Member	Hellenic Journal of Cardiology	2004 - present
Hugo ten Cate	Editor	Thrombosis and Haemostasis	2012 - 2017
Hugo ten Cate	Editor	PlosOne	2012 - present
Hugo ten Cate	Editor	ScienceOpen	2014 - present

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MEMBERSHIPS EDITORIAL BOARDS

NAME	CHARACTER OF MEMBERSHIP (EDITOR, MEMBER OR GUEST EDITOR)	INTERNATIONAL JOURNAL	PERIOD
Jan Glatz	Member	American Journal of Physiology - Heart and Circulatory Physiology	2013 - 2014
Jan Glatz	Member	Journal of Lipid Research	2013 - 2014
Jan Glatz	Member	Prostaglandines, Leukotrienes and Essential Fatty Acids	2013 - 2015
Jan Glatz	Editor	Frontiers in Fatty Acid and Lipid Physiology	2013
Jan Glatz	Guest editor	Prostaglandines, Leukotrienes and Essential Fatty Acids	2015
Joachim Wildberger	Member	RöFo	2006 - present
Joachim Wildberger	Member	Investigative Radiology	2008 - present
Joachim Wildberger	Member	Insights to Imaging	2012 - 2014
Joachim Wildberger	Member	European Radiology	2013 - 2015
Joachim Wildberger	Chair	European Radiology - Section Computed Tomography	2014 - present
Johan Heemskerk	Associate editor	J Thrombosis Haemostasis	2010 - present
Johan Heemskerk	Member	Cardiovasc. Hematol. Agents in Medic. Chem.	2009 - 2013
Judith Sluimer	Member	Molecular Cardiology, Frontiers in Cardiovascular Medicine	2015 - present
Laurent Pison	Guest editor	BioMed Research International	2015
Leon de Windt	Member	Cardiovascular Research	2006 - present
Leon de Windt	Member	Journal of Molecular and Cellular Cardiology	2009 - present
Leon de Windt	Member	European Journal of Heart Failure	2008 - present
Leon de Windt	Member	International Journal of Cardiology - Heart & Vasculature	2014 - present
Leon de Windt	Editor	International Journal of Cardiology	2008 - 2013
Leon de Windt	Member	Circulation Research	2009 - 2015
Leon de Windt	Editor	PLoS ONE	2010 - 2013
Leon Schurgers	Member	Member of the International Society for Thrombosis and Haemostasis	2013 - 2015
Leon Schurgers	Member	Member of the Nederlandse Vereniging voor Thrombose en Hemostase	2013 - 2015
Marc van Bilsen	Member	Acta Physiologica	2013 - 2015
Marc van Zandvoort	Editor	PlosOne	2011 - present
Mark Post	Member	Cardiovascular Research	2008 - present
Matthijs Blankesteijn	Member	Fibrogenesis and Tissue repair	2012 - present
Monika Stoll	Editor	PLoS ONE	2011 - 2014
Monika Stoll	Editor	Frontiers in Cardiovascular Mediicine	2014 - present
Paula da Costa Martins	Editor	PLoS ONE	2012 - present
Paula da Costa Martins	Member	American Journal of Physiology-Heart & Circ	2014 - present
Rory Koenen	Associate editor of Molecular Cardiology	Frontiers in Cardiovascular Medicine	2015
Rory Koenen	Scientific editor	American Journal of Pharmacology and Toxicology	2014

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MEMBERSHIPS EDITORIAL BOARDS

NAME	CHARACTER OF MEMBERSHIP (EDITOR, MEMBER OR GUEST EDITOR)	INTERNATIONAL JOURNAL	PERIOD
Rory Koenen	Scientific editor	American Journal of Blood Research	2013
Sander Verheule	Editor	Frontiers of Cardiac Electrophysiology	2010 - present
Tammo Delhaas	Member	Pediatric Cardiology	2012 - present
Thomas Unger	Member	Cardiovascular Drugs and Therapy	
Thomas Unger	Associate editor	Hypertension Research	
Thomas Unger	Member	Nature Reviews Cardiology	
Thomas Unger	Member	Regulatory Peptides	
Tilman Hackeng	Section editor	Thrombosis and Haemostasis	2015
Tilman Hackeng	Associate editor	Thrombosis Journal	2013 - 2015
Uli Schotten	Member	EuroPace	2007 - present

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MEMBERSHIPS (INTER)NATIONAL SCIENTIFIC BOARDS

NAME	CHARACTER OF MEMBERSHIP	SCIENTIFIC BOARD	PERIOD
Casper Schalkwijk	Member	Member of the Scientific Board of the Dutch Diabetes Research Foundation	2015 - present
Casper Schalkwijk	Member	Council member EASD	2015 - present
Chris Reutelingsperger	Chair	Matisse Pharmaceuticals	2015
Chris Reutelingsperger	Member	Annexin Pharmaceuticals	2014 - 2015
Christian Weber	Chair	ESC Working group on Aterhosclerosis and Vascular Biology	2012 - 2014
Christian Weber	Member	PARCC Scientific Advisory Board	2010 - present
Coen Stehouwer	Member	Artery Society Council	2008 - 2014
Coen Stehouwer	Member	Faculty of 1000	2009 - present
Coen Stehouwer	Member	Zon-Mw-TOP-subsidiecommissie	2011 - present
Coen Stehouwer	Member	NHS-selectiecommissie dr E Dekker programma Clinical Established Investigator	2012 - 2015
Elisabetta Castoldi	Co-chair	ISTH subcommittee on Plasma Coagulation Inhibitors	2010 - 2014
Erik Biessen	Member	Committee Cardiovascular Research Netherlands - Netherlands Heart Foundation	2014 - 2015
Erik Biessen	Member	Dutch Atherosclerosis Society	2014 - 2015
Erik Biessen	Member	NWO-Top grant	2014 - 2015
Erik Biessen	Member	I.W.T. doctorate collegium	2014 - 2015
Erik Biessen	Member	FWO Belgium	2015
Frits Prinzen	Member	EHRA Board (Eur. Heart Rhythm Association)	2014 - present
Frits Prinzen	Chair	EHRA Innovation Committee	2014 - present
Gudrun Antoons	Member	Nucleus ESC working group on cellular cardiac electrophysiology	2014 - present
Gerry Nicolaes	Member	Veni selection committee - NWO MW	2012 - 2015
Harry Crijns	Chair	Netherlands Heart Foundation	2014 - present
Harry Crijns	Member	Netherlands Heart Institute	2001 - present
Harry Struijker-Boudier	Member	Foundation for Circulatory Health, Imperial College, London	2013 - present
Harry Struijker-Boudier	Member	Centre de Recherches des Cordeliers, Paris	2013 - present
Harry Struijker-Boudier	Member	Leibniz Institute for Arteriosclerosis Research, Muenster	2013
Hugo ten Cate	Member	International Society of Thrombosis and Haemostasis	2011 - 2015
Hugo ten Cate	Chair	International Society of Thrombosis and Haemostasis	2012 - 2015
Jan Glatz	Chair	Society for Heart and Vascular Metabolism	2013 - 2015
Jan Glatz	Member	International Society for the Study of Fatty Acids and Lipids	2013
Joachim Wildberger	Chair	Industry Relations Committee European Society of Thoracic Imaging (ESTI)	2011 - present
Joachim Wildberger	Member	Executive Committee European Society of Cardiac Imaging (ESCR)	2014 - present

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MEMBERSHIPS (INTER)NATIONAL SCIENTIFIC BOARDS

NAME	CHARACTER OF MEMBERSHIP	SCIENTIFIC BOARD	PERIOD
Johan Heemskerk	Member	CTH, Center for Thrombosis and Haemostasis, Johannes Gutenburg University Mainz (Gemany)	2009 - 2014
Johan Heemskerk	Member	Landsteiner Foundation for Transfusion Research	2011 - present
Johan Heemskerk	Member	Netherlands Thrombosis Foundation	2010 - present
Johan Heemskerk	Member	European Platelet Network EUPLAN	2011 - present
Johan Heemskerk	Member	International Board of Congresses of the ISTH	2011 - present
Joost Lumens	Member	ESC working group on eCardiology	2015 - present
Joost Lumens	Member	Task Force member of the 5th World Symposium on Pulmonary Hypertension (WSPH), February 2013 Nice (France).	2013
Judith Sluimer	Member	Dutch Endothelial cell Biology Society (DEBS)	2013
Laurent Pison	Member	EHRA Scientific Initiative Committee	2013 - 2015
Leon de Windt	Chair	Evaluation Committee Netherlands Foundation of Scientific Research (NW0) Mozaik PhD stipends	2011
Leon de Windt	Member	Selection Committee member Netherlands Heart Foundation Dr. Dekker stipend “Medical Doctor in training to specialist”	2012 - present
Leon de Windt	Member	ZonMW Committee Translationeel Adult Stamcelonderzoek (TAS)	2013 - present
Leon Schurgers	Member	Scientific advisory board Dutch Kidney Foundation	2013 - 2015
Leon Schurgers	Member	Scientific advisory board NWO Life Sciences and Health	2014 - 2015
Leon Schurgers	Member	Treasurer Dutch Thrombosis Society (NvTH)	2013 - 2015
Marc van Bilsen	Member	ZonMw VENI Committee	2013 - 2015
Marc van Zandvoort	Member	FWO Expert Panel Molecular and Cellular Biology	2015 - present
Marc van Zandvoort	Member	Advisory Board Horizon2020 NMPB	2015 - present
Marc van Zandvoort	Member	Board Dutch Society for Microscopy (NVvM)	2014 - present
Marc van Zandvoort	Member	Board NL-BioImaging-AM	2011 - present
Marc van Zandvoort	Chair	Two-photon Core Facility Aachen Uniklinikum	2009 - present
Marco Das	Member	Educational Committee European Society of Thoracic Radiology (ESTI)	2015 - present
Marco Das	Member	Scientific Program Committee Cardiovascular and Interventional Society of Radiology (CIRSE)	2014 - present
Mark Post	Chair	FIVES	2015 - present
Mark Post	Chair	Nederlandse Vereniging voor Fysiologie	2011 - present
Mark Post	Member	Nederlandse Lymfangiomatose stichting	2015 - present
Mark Post	Member	New Harvest	2013 - present
Matthijs Blankesteijn	Member	Bestuur Nederlandse Vereniging voor Farmacologie	2015 - present
Paul Volders	Member	Executive Board, EHRA, European Heart Rhythm Association, Nice, FR	2011 - present
Paul Volders	Chair	EWGCCE, ESC Working Group on Cardiac Cellular Electrophysiology, Nice, FR	2012 - 2014
Paul Volders	Member	Nucleus, EWGCCE, ESC Working Group on Cardiac Cellular Electrophysiology, Nice, FR	2014 - present
Paul Volders	Member	Board, Hein Wellens Foundation, Maastricht, NL	2014 - present

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MEMBERSHIPS (INTER)NATIONAL SCIENTIFIC BOARDS

NAME	CHARACTER OF MEMBERSHIP	SCIENTIFIC BOARD	PERIOD
Paula da Costa Martins	Member	NWO ALW grant Committee	2014 - present
Paula da Costa Martins	Member	Young ICIN	2014 - present
Paula da Costa Martins	Member	NWO Rubicon grant Committee	2015 - present
Robert van Oostenbrugge	Member	Dutch Brain Foundation	2015 - present
Rory Koenen	Member	Scientific Faculty of the 5th Munich Vascular Conference (MVC),	2015
Stephane Heymans	Fellow	European Heart Failure Association	2015
Stephane Heymans	Fellow	European Society of Cardiology	2015
Stephane Heymans	Nucleus member	Committee of Diastolic Heart Failure, European Heart Failure Association	2010 - 2014
Stephane Heymans	Member	American Heart Association, European Society of Cardiology, European Society of Heart Failure, European Council on Cardiovascular Research	
Stephane Heymans	Member	VIDI selection commission	
Tammo Delhaas	Member	Scientific Advisory Committee STW-project Dr. Ir. R. Vullings	2014 - present
Thomas Unger	Member	Deutsche Liga zur Bekämpfung des hohen Blutdruckes / German Hypertension Society	1990 - present
Thomas Unger	Fellow	Hypertension Council of the American Heart Association (AHA)	
Thomas Unger	Member	European Council on Blood Pressure and Cardiovascular Research (ECCR)	2000 - present
Thomas Unger	Member	German Cardiological Society	
Thomas Unger	Member	European Society of Cardiology (ESC)	
Tilman Hackeng	Member	Scientific Advisory Board Trombosestichting	2014
Tilman Hackeng	Chair	Scientific Advisory Board Trombosestichting	2015
Uli Schotten	Member	Executive Board of the German Network of Competence Atrial Fibrillation (AFNET), AFNET acts as sponsor for translational and clinical trials, annual financial turnover is >10Mio€.	2014 - present
Uli Schotten	Member	European taskforce for the development of guidelines of management of atrial fibrillation	2014 - present
Uli Schotten	Member	Scientific Documents Committee of the European Heart Rhythm Association	2010 - 2013
Uli Schotten	Member	Steering committe of the German Network of Competence Atrial Fibrillation (AFNET)	2011 - present
Uli Schotten	Member	Nucleus of the Working Group for Cellular Electrophysiology of the German Society of Cardiology	2008 - present
Uli Schotten	Chair	Nucleus of the Working Group for Cellular Electrophysiology of the German Society of Cardiology	2010 - 2014
Werner Mess	Member	Neurosonology Research Group of the World Federation of Neurology	2013 - present

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INTERNATIONAL COLLABORATIONS

CONTACT PERSON MAASTRICHT	NAME OF INTERNATIONAL INSTITUTE/ ORGANISATION (CITY)	COUNTRY	TOPIC	NAME OF NETWORK (IF APPLICABLE)	CONTACT PERSON ABROAD	PERIOD
Aaron Isaacs	CHARGE Consortium (Various)		wide range of cardiovascular phenotypes (specifically ECG in my case)	CHARGE Consortium		
Arina ten Cate-Hoek	Padua	Italy	Studies on post-thrombotic syndrome	Within Doelmatigheids-onderzoek	Paola Prandoni	2011 - present
Bas Bekkers	Duke University Medical Center	USA	Cardiac Magnetic Resonance Imaging		Prof. R.J. Kim	2006 - present
Ben Janssen	Univ. Of Bristol	UK	Telemetry measurements of oxygen in the kidney of Cyp1a1-Ren2 rats		M. Koeners	2014 - 2015
Casper Schalkwijk	NYU School of Medicine	USA			Ed Fisher	2015 - present
Chris Reutelingsperger	University Antwerp, Catholic University Leuven	Belgium	Targeted drug delivery and electrical stimulation	Interreg IVA - ELECTRON	Prof. J. Bogers	2014 - 2015
Chris Reutelingsperger	Queen Mary University London	UK	Postdoc exchange and Annexin A1 research	COFUND	Prof. Mauro Perretti	2014 - 2015
Chris Reutelingsperger	Emory University	US	Annexin A1 research		Prof. Asma Nusrat	2014 - 2015
Chris Reutelingsperger	RWTH Aachen	Germany	Annexin A5		Prof. Niko Marx	2014 - 2015
Chris Reutelingsperger	Mount Sinai New York	USA	Annexin A5		Prof. Jagat Narula	
Coen Stehouwer	University of Athens	Greece			Athanase Protogerou	2013 - 2015
Coen Stehouwer	Université Avignon	France			Agnès Vignet	2013 - 2015
Coen Stehouwer	University Washington	United States			Lenore Launer	2013 - 2015
Coen Stehouwer	University Melbourne	Australia			Mark Cooper	2013 - 2015
Eline Kooi	Servier	France	Pharmacological interventions to reduce plaque vulnerability		Dr Benoît Tyl	2013 - present
Eline Kooi	King's College London	UK	Vascular (PET)-MRI		Prof. René Botnar	2005 - present
Eline Kooi	University of Washington	USA	Vascular MRI		Prof. Chun Yuan, Prof. Hatsukami	2010 - present
Elisabetta Castoldi	University of Padua Medical School (Padua)	Italy	Genetics of factor V in bleeding and thrombosis		Paolo Simioni	2005 - present
Elisabetta Castoldi	International Centre for Genetic Engineering and Biotechnology (Trieste)	Italy	Splicing		Francisco E. Baralle / Marco Baralle	2011 - present
Elisabetta Castoldi	University Clinic (Bonn)	Germany	Factor V gene mutations associated with bleeding or thrombosis		Anna Pavlova	2013 - present
Elisabetta Castoldi	University of Milan (Milan)	Italy	Factor V deficiency		Stefano Duga	2014 - 2015

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Elisabetta Castoldi	University of North Carolina at Chapel Hill (Chapel Hill, NC)	USA	Factor V deficiency		Nigel Key	2013 - 2015
Elisabetta Castoldi	University of Leeds (Leeds)	UK	Fibrinogen [illegible]'		Robert Ariëns	2011 - present
Elisabetta Castoldi	University of Lyon I (Lyon)	France	Unexplained inherited bleeding disorder		yesim Dargaud	2014 - 2015
Erik Biessen	LMU Munich	Germany	Inflammation, atherosclerosis	GRK1508	Prof. C. Weber, Prof. O. Soehnlein	2014 - 2015
Erik Biessen	Rikshospitalet, Oslo	Norway	Patient cohorts, biomarkers	Metinflammation, Norwegian Research Council	Prof. P. Aukrust, B. Halvorsen	2014 - 2015
Erik Biessen	University Hospital, Arhus	Denmark	AAV, models		Dr J Bentzon	2014 - 2015
Erik Biessen	RWTH Aachen	Germany	Chemokines		Prof. F. Tacke	2014 - 2015
Erik Biessen	Cincinnati Children's Hospital	USA	Immunology		Dr E Janssen	2014
Erik Biessen	Addenbrook's Hospital, Cambridge University	UK	Immunology		Prof. Z. Mallat, M. Bennett	2014 - 2015
Erik Biessen	CERN Medical Physics Strategies	Switzer-land	Informatics		Dr M Manca	2014 - 2015
Erik Biessen	INSERM, Toulouse	France	Src kinases		Dr Marridoneaux	2014 - 2015
Frits Prinzen	Center for Computational Medicine in Cardiology (Lugano)	Switzer-land	Patient studies and computer simulations in Cardiac Resynchronization		Auricchio, Krause	2013 - 2015
Frits Prinzen	Rovigo General Hospital	Italy	Data analysis Cardiac Resynchronization Therapy		Zanon	2013 - 2015
Frits Prinzen	King's College London	UK	Data analysis patient studies in Cardiac Resynchronization		Rinaldi	2013 - 2015
Frits Prinzen	Karolinska Hospital	Sweden	Clinical studies on Cardiac Resynchronisation		Wecke	2013 - 2014
Frits Prinzen	Massachussetts General Hospital	Boston	Clinical studies on Cardiac Resynchronisation		Singh	2014 - present
Frits Prinzen, Joost Lumens	University Pittsburgh Medical Center	USA	Coupling of patiënt data and computer modeling		Gorcsan	2013 - 2015
Frits Prinzen, Joost Lumens	University of Bordeaux	France	Patient studies and computer simulations in Cardiac Resynchronization		Bordachar, Ploux, Ritter	2013 - 2015
Gudrun Antoons	University of Szeged	Hungary	Pharmacology sodium calcium exchanger	Joint grant	Andras Toth	present
Hans Vink	Beth Isreal Deaconess Medical Ct, Harvard Univ.	US	Glycocalyx Research in ICU		Nate Shapiro	2014 - 2015
Hans Vink	Univ. of Oxford	UK	Glycocalyx Research in Infectious Diseases		Sophie Yacoub	2014 - 2015
Hans Vink	Children's Hospital of Philadelphia	US	Glycocalyx Research in Pediatrics & Anesthesiology		Frank McGowan	2013 - 2015
Hans Vink	Mayo Clinic, Rochester	US	Glycocalyx Research in Pre-eclampsia		Tracey Weissgerber	2014

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Hans Vink	Univ. Pittsburgh Medical Center	US	Glycocalyx Research in Cardiology		John Pacella	2013 - 2015
Hans Vink	Moscow Center for Preventative Medicine	Russia	Glycocalyx Research in Cardiology		Alexander Gorshkov	2014 - 2015
Harald Schmidt	Baker IDI	Australia	Pre-clinical diabetes research		Karin Jandeleit	2010 - present
Harald Schmidt	Uni Würzburg	Germany	Pre-clinical stroke research		Christoph Kleinschnitz	2010 - present
Harald Schmidt	Boehringer-Ingelheim	Germany	eNOS modulation		Martin Michel	2013 - present
Harald Schmidt	Università di Padova, Italy	Italy	ROS targets and co-chaor COST action	COST (EU-ROS)	Fabio Di Lisa	2013 - present
Harald Schmidt	Universidad Autónoma, Madrid	Spain	Alzheimer's disease, ROS biomarkers and targets	COST (EU-ROS)	Antonio Cuadrado	2013 - present
Harald Schmidt	Universidad Autónoma, Madrid	Spain	Pre-clinical stroke research	COST (EU-ROS)	Manuela Garcia	2013 - present
Harald Schmidt	Karolinska Institutet (Stockholm)	Sweden	NOX inhibitors	EUROSTAR	Per Wikström	2014 - present
Harald Schmidt	William Harvey Research Institute, Heart Centre, London	UK	cGMP modulation		Adrian J. Hobbs	2015 - present
Harald Schmidt	Brighton & Sussex Medical School	UK	ROS biomarkers	COST (EU-ROS)	Pietro Ghezzi	2015 - present
Harry Crijns	Birmingham	UK	Atrial fibrillation	CATCH ME	Prof. Paulus Kirchhof	2014 - present
Harry Crijns	Muenster and Birmingham	DE, UK	Atrial fibrillation	AF-NET, EAST	Prof. Paulus Kirchhof	2009 - present
Harry Crijns	Birmingham	UK	Atrial fibrillation		Prof. Greg Lip	2013
Harry Struijker-Boudier	Hopital Lariboisiere, Paris	France	Microcirculation and hypertension		Prof. B. Levy	2013 - present
Harry Struijker-Boudier	KU Leuven Department of Cardiovascular Sciences	Belgium	Hypertension		Prof. J. Staessen	2013 - present
Harry Struijker-Boudier	Various groups in Belgium, Ireland, UK, Germany	EU	Measuring device for arterial stiffness	CARDIS	Prof. P. Segers	2014 - present
Henri Spronk	Hamburg	Germany	Contact activation and disease		Thomas Renne	2012 - present
Henri Spronk	Aachen	Germany	Prohemostatic interventions in major bleeding	Boehringer-Aachen-CARIM	Oliver Grottke	2010 - 2015
Hugo ten Cate	CTH Mainz	Germany	Mechanisms of thrombosis and atherosclerosis	Collaboration CARIM-CTH	Wolfram Ruf	2014 - present
Hugo ten Cate	Bergamo Hospital	Italy	Mechanisms of cancer related thrombosis		Anna Falanga	2008 - present
Hugo ten Cate	Leeds University	UK	Fibrin clot forming and lytic properties		Robert Ariens	2012 - present
Jan Glatz	University of Manchester (Manchester)	UK	Application of plasma FABP as early marker for acute myocardial infarction		R. Body	2013 - 2015
Jan Glatz	Dokuz Eylül University (Izmir)	Turkey	Cardiac lipid metabolism in health and disease		G. Güner	2013 - 2015

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CONTACT PERSON MAASTRICHT	NAME OF INTERNATIONAL INSTITUTE/ ORGANISATION (CITY)	COUNTRY	TOPIC	NAME OF NETWORK (IF APPLICABLE)	CONTACT PERSON ABROAD	PERIOD
Jan Glatz	Hong Kong University of Science and Technology (Hong Kong)	Hong Kong (China)	Application of plasma FABP as early marker for acute myocardial infarction		R. Renneberg	2013 - 2015
Jan Glatz	University of Texas Medical School (Houston)	USA	Metabolic modulation as therapy for cardiac disease		H. Taegtmeyer	2013 - 2015
Jan Glatz	University of Alabama (Birmingham)	USA	Metabolic modulation as therapy for cardiac disease		M.E. Young	2013 - 2015
Jan Glatz	University of Iowa Diabetes Center (Iowa City)	USA	Metabolic modulation as therapy for cardiac disease		E.D. Abel	2013 - 2015
Jan Glatz	University of Jena (Jena)	Germany	Lipid metabolism in diabetic cardiomyopathy		M. Schwarzer	2013 - 2015
Jan Glatz	Boston University Medical School	USA	Fatty acid transfer across biological membranes		J.A. Hamilton	2013 - 2015
Jan Glatz	National Institutes of Health (Bethesda)	USA	CD36 in cardiac disease		M. Sack	2013 - 2015
Jan Glatz	University of Copenhagen (Copenhagen)	Denmark	Lipid metabolism in heart and skeletal muscle		B. Kiens	2013 - 2014
Jan Glatz, Joost Luiken	University of Guelph (Guelph)	Canada	Cardiac and skeletal muscle lipid metabolism		A. Bonen	2013 - 2015
Jan Glatz, Joost Luiken	University of Tromsø (Tromsø)	Norway	Effect of fish oils on cardiac lipid metabolism		T.S. Larsen	2013 - 2015
Jan Glatz, Joost Luiken	University of Oxford (Oxford)	UK	Metabolic modulation as therapy for cardiac disease		L. Heather, K. Clarke	2013 - 2015
Jeroen Frijhoff	Helmholtz Zentrum (Munchen)	Germany	Oxidation of protein tyrosine phosphataseses in tumor growth and angiogenesis		Marcus Conrad	2013 - 2015
Jeroen Frijhoff	Karolinska Institutet (Stockholm)	Sweden	Oxidation of protein tyrosine phosphatases in growth factor signaling		Arne Östman	2013 - 2015
Joachim Wildberger	Siemens	Germany	Master agreement + 1st indivual projectagreement	CTCM - 115042		2011 - present
Joachim Wildberger	Bayer	Germany	Grant Bayer	CTCM - 125003		2012 - present
Joachim Wildberger	Philips	Germany	Master agreement Philips - Radiologie	CTCM - 121097		2012 - present
Joachim Wildberger	Siemens	Germany	2nd individual projectagreement / PET MR	CTCM - 145058		2014 - present
Joachim Wildberger	Philips	Germany	Contrast Medium Reduction / Clarity IQ	CTCM - 141080		2014 - present
Joachim Wildberger	Philips	Germany	Next Generation Fusion imaging / Vessel Navigator	CTCM - 141081		2014 - present
Joachim Wildberger	Siemens	Germany	3rd individual projectagreement / Cardiac and thoracic imaging	CTCM - 155018		2015 - present
Joachim Wildberger	UK Aachen	Germany	Cardiovascular imaging		Felix Mottaghy	2013
Joachim Wildberger	CMIV, Linköpping	Sweden	Cardiovascular imaging		Anders Persson	2013

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Joachim Wildberger	Universität Marburg	Germany	Cardiovascular imaging		Andreas Mahnken	2013
Joachim Wildberger	MUSC, Charlston, SC	USA	Cardiovascular imaging		Uw Joseph Schoepf	2013
Joachim Wildberger	Duke University, Durham, NC	USA	Cardiovascular imaging		Geoff Rubin	2013
Johan Heemskerk	Laboratory for Thrombosis Research, KULAK, Kortrijk, University of Leuven	Belgium	Function of platelet glycoprotein Ib recepto	EUPLAN Consortium.	Prof. H. Deckmyn, Prof. K. Vanhoorelbeke	< 2013 - present
Johan Heemskerk	Centre for Molecular and Vascular Biology, University of Leuven	Belgium	Arterial and venous thrombosis models	Joint projects & papers, sharing expertise, animals and equipment	Prof. M. Hoylaerts	< 2013 - present
Johan Heemskerk	Université Sart-Tilman Liège	Belgium	Platelet signaling and thrombogenicity of polymeric surfaces	Joint projects & papers, sharing expertise and equipment	Dr C. Oury	2013 - present
Johan Heemskerk	University of Cambridge	UK	Platelet interaction with collagen peptides	Sharing expertise, joint papers, materials and equipment	Prof. R. Farndale	< 2013 - present
Johan Heemskerk	University of Bristol	UK	Functions of platelet kinases and procoagulant activity	Joint projects & papers, sharing expertise and regular visits	Prof. A. Poole	< 2013 - present
Johan Heemskerk	University of Birmingham	UK	Signaling of platelets in thrombus formation	EUPLAN Consortium	Prof. S.P. Watson, Prof. Y. Senis	< 2013 - present
Johan Heemskerk	University of Cambridge	UK	Complex mouse phenotyping	Joint project & paper submitted	Dr D. Adams	2015 - present
Johan Heemskerk	University of Cambridge	UK	Reactome	Joint project & paper submitted	Dr S. Jupe	2015 - present
Johan Heemskerk	University of Cambridge	UK	Blood and Transplant	BRIDGE Consortium	Prof. W.H. Ouwehand, Dr. Kate Downes	2014 - present
Johan Heemskerk	University of Leeds	UK	Platelets in fibrin formation	Joint project	Prof. R. Ariëns	2015 - present
Johan Heemskerk	INSERM, Faculté Xavier Bichat, Université Paris	France	Antithrombotic potential of glycoprotein VI antagonism	Exchange of expertise and materials, joint papers	Dr M. Jandrot-Perrus	2015 - present
Johan Heemskerk	Karolinska Institute, Stockholm	Sweden	Function of contact activation system	Joint project and joint papers	Prof. T. Renné	< 2013 - present
Johan Heemskerk	Temple University School of Medicine, Philadelphia	USA	G-proteins and platelet signaling	Collaboration and shared expertise	Prof. S. Kunapuli	< 2013 - present
Johan Heemskerk	Oregon State University, Portland, Oregon	USA	Heterogeneity in platelet responses	Joint project & papers	Dr O.W. McCarty	< 2013 - present
Johan Heemskerk	University of Würzburg	Germany	Platelet-collagen interactions and calcium signaling in mice	EUPLAN Consortium	Prof. B. Nieswandt, Dr. A. Braun	< 2013 - present

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CONTACT PERSON MAASTRICHT	NAME OF INTERNATIONAL INSTITUTE/ ORGANISATION (CITY)	COUNTRY	TOPIC	NAME OF NETWORK (IF APPLICABLE)	CONTACT PERSON ABROAD	PERIOD
Johan Heemskerk	Ludwig-Maximilians-University & DZHK partner site Munich Heart Alliance, Munich	Germany	Platelets in inflammation and atherothrombosis	Joint projects & papers	Prof. C. Weber, Prof. O. Soehnlein	< 2013 - present
Johan Heemskerk	Johannes Gutenberg University Mainz	Germany	Platelet Proteomics Consortium	Joint project & papers, student visits	Prof. U. Walter, Prof. W. Ruf, Dr K. Jurk	< 2013 - present
Johan Heemskerk	Universitäts Klinikum Freiburg	Germany	STIM1 and Orai1 in platelet function	Joint project & paper	Prof. B. Zieger	< 2013 - present
Johan Heemskerk	University of Tübingen	Germany	Whole-blood thrombus formation in drug-treated patients	Sharing materials, joint project and papers	Dr. O. Borst, Prof. M. Gawaz	2013 - 2015
Johan Heemskerk	RWTH Universitäts Klinikum Aachen	Germany	DPPs and platelet function	Joint project & paper in preparation	Dr. H. Noels	2014 - 2015
Johan Heemskerk	Ludwig-Maximilians-Universität München	Germany	Role of platelet MIF	Joint project & paper	Prof. J. Bernhagen	2013 - 2015
Johan Heemskerk	Leibniz-Institut für Analytische Wissenschaften-ISAS, Dortmund	Germany	Platelet Proteomics Consortium	Joint projects & papers, joint PhD student	Prof. A. Sickmann, Dr. R. Zahedi	< 2013 - present
Johan Heemskerk	Hospital Papa Giovanni XXIII, Bergamo	Italy	Thrombocytosis	Joint project & paper submitted	Dr. A. Falanga	< 2013 - present
Johan Heemskerk	University of Pavia	Italy	Role of platelet PI3Ks	EUPLAN Consortium	Prof. M. Torti	< 2013 - present
Johan Heemskerk	University of Berne	Switzer-land	Platelet adhesion and flow	Joint papers, sharing expertise and materials	Prof. K. Clemetson, Prof. A. Angelillo-Scherrer	< 2013 - present
Johan Heemskerk	Hacettepe University, Ankara	Turkey	Dietary modulation of thrombosis	Joint project, student exchange	Dr. R. Nergiz-Unal	2015 - present
Joost Luiken	German Institute of Human Nutrition (Berlin)	Germany	Lipid metabolism in diabetic cardiomyopathy		R.W. Schwenk	2013 - 2014
Joost Luiken	University of Barcelona (Barcelona)	Spain	Mitochondrial function in cardiac disease		A. Zorzano	2014 - 2015
Joost Lumens	Université de Bordeaux	France	Computer Modeling in Cardiac Resynchronization Therapy		Prof. Bordachar	2013 - present
Joost Lumens	University of Pittsburgh	USA	Computer Modeling in Cardiac Resynchronization Therapy		Prof. Gorcsan	2013 - present
Joost Lumens	Kings College London	UK	Computer Modeling in Cardiac Resynchronization Therapy		Prof. Frances	2013 - present
Judith Cosemans	Chapel Hill	USA	Biochemistry		Dr Wolfgang Bergmeier	

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INTERNATIONAL COLLABORATIONS

CONTACT PERSON MAASTRICHT	NAME OF INTERNATIONAL INSTITUTE/ ORGANISATION (CITY)	COUNTRY	TOPIC	NAME OF NETWORK (IF APPLICABLE)	CONTACT PERSON ABROAD	PERIOD
Judith Sluimer	Transatlatic Network of Excellence, Fondation Leducq	EU/USA	Autophagy	Modulating autophagy to treat cardiovascular disease	Jun Sudoshima, Beth Levine, Guido Kroemer, Ana-maria Cuervo, Kinja Otsu, Richard Kitsis	2015 - 2020
Judith Sluimer	University Eastern Finland (Kuopio)	Finland	Angionesis in atherosclersois		Seppo Yla-Herttuala	2012 - 2015
Judith Sluimer	NYU (NY)	USA	Hypoxia, cholesterol metabolism		Ed Fisher	2011- present
Judith Sluimer	Freiburg University (Freiburg)	Germany	Hypoxia-inducble factor 1		Alma Zernecke	2012 - 2015
Judith Sluimer	VIB Vesalius Research Centre (Leuven)	Belgium	Hypoxia, angiogenesis, prolyl hydroxylases		Peter Carmeliet	2010 - present
Judith Sluimer	Universiity Helsinki	Finland	Angionesis in atherosclersois		Kari Alitalo	2013 - 2015
Judith Sluimer	Karolinska Instituur (Stockholm)	Sweden	Dietary Nitrate		Jon Lundberg	2013 - 2015
Judith Sluimer	Cambridge University	UK	Hypoxia in atherosclerosis, MerTK		Ziad Mallat	2012 - 2014
Julie Staals	University of Edinburgh	UK / Scotland	Imaging of cerebral small vessel disease		J. Wardlaw	2014 - present
Koen Reesink	Macquarie University	Australia	Arterial Stiffness		Prof. Avolio	2013 - present
Koen Reesink	Imperial College London	UK	Arterial Stiffness		Prof. Hughes	2013 - present
Koen Reesink	Université Paris Descartes	France	Arterial Stiffness		Prof. Boutouyrie	2013 - present
Koen Reesink	Macquarie University	Australia	Arterial Stiffness		Prof. Avolio	2013 - present
Laurent Pison	Uppsala University	Sweden	Epicardial AF ablation		Prof. Blomström-Lundqvist	2013 - present
Laurent Pison	Barcelona, Hospital Clinic	Spain	Imaging in ablation procedures		Prof. Lluis Mont	2015 - present
Leon de Windt	Hannover Medical School	Germany	Circulating noncoding RNAs as diagnostic biomarkers	Marie Sklodowska Curie Fellowship to Martina Calore	Thomas Thum	2015 - present
Leon de Windt	ICGEB, Trieste	Italy	Adeno-associated viral vectors as gene therapy tools (has led to an EMBO Long Term Fellowship and a Marie Sklodowska Curie Fellowship to Ellen Dirkx)	EMBO Long Term Fellowship & Marie Sklodowska Curie Fellowship to Ellen Dirkx	Mauro Giacca	2014 - present

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Leon de Windt	University of Padua	Italy	Epigenetics of arrhythmogenic cardiomyopathy (has led to a Marie Sklodowska Curie Fellowship to Martina Calore)	Marie Sklodowska Curie Fellowship to Martina Calore	Allesandra Rampazzo	2014 - present
Leon Schurgers	Kings College London	UK	VSMC calcification		Prof C. Shanahan	2013 - 2015
Leon Schurgers	Klinikum Aachen	Germany	Calcification	VitaVask (ERA-EDTA)	Prof. J. Floege	2013 - 2015
Leon Schurgers	Klinikum Aachen	Germany	Calcification		Prof. W. Jahnen-Dechent	2013 - 2015
Leon Schurgers	Klinikum Aachen	Germany	Post-doc (M Burgmaier, R Stohr)		Prof. N. Marx	2013 - 2015
Leon Schurgers	VU Amsterdam	Nether-lands	Joined PhD	Dutch Kidney Foundation	Dr M. Vervloet	2014 - 2015
Leon Schurgers	GSTT/ Kings College London	UK	Vitamin K measurement		Dr M. Shearer	2013 - 2015
Leon Schurgers	Jefferson Medical College	USA	PXE		Prof. Uitto	2013 - 2015
Marc van Zandvoort	Sheffield University	UK	Microvesicles in atherosclerosis	NIH	Vikki Ridger	2015 - present
Marc van Zandvoort	Cambridge University	UK	Optical and non-invasive imaging of atherosclerosis	Cambridge Neuroscience	Umar Sadat/ Farouc Jaffer	2013 - 2015
Marc van Zandvoort	Universitatsklinikum Aachen	Germany	Combined optical and non-invasive imaging (US)	ExMi-CARIM	Fabian Kiessling/Twan Lammers	2013 - present
Marc van Zandvoort	Ludwig Maximilian University Munich	Germany	Microscopy of atherosclerosis	LMU-CARIM	Christian Weber/Remco Megens	2013 - present
Marc van Zandvoort	Universitatsklinikum Aachen	Germany	Cardiac microscopic imaging	IMCAR-CARIM	Elisa Liehn/ Joachim Jankowski	2013 - present
Marc van Zandvoort	Universitatsklinikum Aachen	Germany	Tissue Engineering/heart valves	Helmholtz Institute for Biomedical Techniques	Stefan Jockenhovel	2014 - present
Marc van Zandvoort	Universitatsklinikum Aachen	Germany	Cell scaffolds	Helmholtz Institute for Biomedical Techniques	Martin Zenke	2014 - present
Marco Das	Siemens	Germany	Master agreement + 1st indivual projectagreement	CTCM - 115042		2011 - present
Marco Das	Bayer	Germany	Grant Bayer	CTCM - 125003		2012 - present
Marco Das	Philips	Germany	Master agreement Philips - Radiologie	CTCM - 121097		2012 - present
Marco Das	Siemens	Germany	2nd individual projectagreement / PET MR	CTCM - 145058		2014 - present
Marco Das	Philips	Germany	Contrast Medium Reduction / Clarity IQ	CTCM - 141080		2014 - present

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Marco Das	Philips	Germany	Next Generation Fusion imaging / Vessel Navigator	CTCM - 141081		2014 - present
Marco Das	Siemens	Germany	3rd individual projectagreement / Cardiac and thoracic imaging	CTCM - 155018		2015 - present
Marjo Donners	Christian-Albrechts University, Kiel	Germany	A Disintegrin and Metalloproteases			
Marjo Donners	RWTH, Aachen	Germany	A Disintegrin and Metalloproteases			
Marjo Donners	Heart Research Institute/ University of New South Wales, Sydney	Australia	High Density Lipoproteins			
Mark Post	King's College, London	UK	Tissue engineering		Dr Lucy Di-Silvio	2015 - present
Mark Post	KU Leuven	Belgium	Angiogenesis		Dr Vincenza Caolo	2013 - present
Matthijs Blankesteijn	Cardiovascular Research Institute, Ioannina/Athens	Greece	Effect of Growth hormone administration on infarct healing		T.M. Kolettis	2013 - 2015
Matthijs Blankesteijn	Studies Coordinating Centre, Research Unit Hypertension and Cardiovascular Epidemiology, KU Leuven Department of Cardiovascular Sciences, University of Leuven, Leuven, Belgium	Belgium	Left Ventricular Dysfunction and CXCR3 ligands in hypertension		J. Staessen	2013 - 2014
Matthijs Blankesteijn	UC San Diego School of Medicine, Div. of cardiovascular Medicine	USA	Joint PhD project of Dimosthenis Giamouridis		K. Hammond	2014 - 2018
Miranda Nabben	University of Washington (Seattle)	USA	Energy metabolism in cardiac hypertrophy		R. Tian	2013 - 2015
Miranda Nabben	University of Münster (Münster)	Germany	MR imaging of cardiovascular disorders		C. Faber	2013 - 2015
Miranda Nabben	Mount Sinai School of Medicine (New York)	USA	Cardiac energy metabolism in a CPT1 knockin mouse model		S.M. Houten	2013 - 2014
Neumann D	University of Grenoble (Grenoble)	France	AMPK as target for cardiac metabolic disease		U. Schlattner	2013 - 2015
Neumann D	University of Valencia (Valencia)	Spain	AMPK as target for cardiac metabolic disease		P. Sanz	2013 - 2015
Neumann D	Institute Cochin (Paris)	France	AMPK as target for cardiac metabolic disease		B. Viollet	2013 - 2015
Neumann D	Johns Hopkins University (Baltimore)	USA	AMPK as target for cardiac metabolic disease		G.W. Hart	2013 - 2014
Neumann D	Tsinghua University (Tsinghua)	China	AMPK as target for cardiac metabolic disease		J-W. Wu	2013 - 2015
Neumann D	University of Melbourne (Melbourne)	Australia	AMPK as target for cardiac metabolic disease		D. Stapleton	2013 - 2015

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Paola van der Meijden	CTH Mainz	Germany			Prof. Wolfram Ruf	
Paul Volders	Cardiac Bioelectricity and Arrhythmia Center, Washington University (St. Louis, MO)	USA	Computational modeling of cardiac cellular electrophysiology		Prof. Y. Rudy	2013 - 2015
Paul Volders	Research Hospital Istituto Auxologico Italiano, Center for Cardiac Arrhythmias of Genetic Origin (Milano)	Italy	Inherited cardiac arrhythmias and genetic testing		Prof. P. Schwartz	2013 - 2015
Paul Volders	Westfälische Wilhelms-Universität, Institut für Humangenetik, Genetische Epidemiologie (Münster)	Germany	Genetic epidemiology and statistical genetics		Prof. M. Stoll	2013 - 2015
Paula da Costa Martins	University of Porto	Portugal	Post-transcriptional regulation of right ventricular remodeling	FCT (Portuguese Foundation for Science and Technology) grant to Paula da Costa Martins	Adelino Leite Moreira	2015 - present
Paula da Costa Martins	University of Coimbra	Portugal	Noncoding RNAs as regulators of angiogenesis in heart	Erasmus fellowship to Ricardo Abreu	Carlos Duarte	2015 - present
Paula da Costa Martins	University of Manchester	UK	Circadian clock and microRNAs	ESC First Contact Initiative grant	Alicia D'Souza	2014 - present
Robert van Oostenbrugge	University of Calgary	Canada	Imaging of cerebral small vessel disease	Center Of Excellence in Neurodegeneration (COeN)	E. Smith	2013 - present
Robert van Oostenbrugge	Ludwig Maximillian University Munich	Germany	Cerebral small vessel disease	SVD@TARGET	M. Dichgans	2015 - present
Rory Koenen	RWTH Aachen, University Hospital	Germany	Platelets as initiators and mediators of liver fibrosis		Dr. Hacer Sahin	2012 - present
Rory Koenen	LMU Munich University, Munich	Germany	Structure-function mapping of the chemokine interactome enables tailored intervention in acute and chronic inflammation		Prof. Christian Weber	2012 - present
Rory Koenen	University Hospital Tübingen	Germany	Characterization of the JAM-A EMMPRIN interaction		Prof. Harald Langer	2014 - present
Sander Verheule	University of Oxford	UK	Adipocyte signalling in AF	Joint publication	Prof. C. Antoniades	2013 - present
Sander Verheule	University of Greifswald	Germany	Adipocyte signalling in AF	Joint publication	Prof. U Lendeckel	2012 - present
Stephane Heymans	Mayo Clinics, Florida	USA	Collaboration on myocarditis: immune mechanisms and genetics	common Leducq application	Prof. Leslie Cooper	2015 - present

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Stephane Heymans	Berlin University Hospital	Germany	Working together on inflammatory mechanisms of diastolic dysfunction & diabetes, myocarditis and dilated cardiomyopathies	FP7-MEDIA	Prof. C. Tschoeppe, Prof. HP Schultheiz & Prof. W. Poller	2009 - present
Stephane Heymans	Zurich	Switzer-land	Expert in experimental models of myocarditis and immune mechanisms	Leducq application	Prof. Urs Eriksson	2015 - present
Stephane Heymans	Hull	Germany	Recent collaboration on monocytes/macrophages in cardiac diseases, isolation and sorting of monocytes and cardiac macrophages.		Prof. Stefan Frantz	2013 - present
Stephane Heymans	Nancy	France	Collaborations on biomarker validation studies in heart failure. Discovery on novel protein and microRNA therapeutic targets for cardiac fibrosis	FP7-project Homage & Fibrotargets	Prof. Faiez Zannad	
Stephane Heymans	Institute of Cardiovascular and Medical Sciences Glasgow	UK	Clinical studies in heart failure	FP7-Homage	Prof. J. Cleeland	
Stephane Heymans	Leuven University & Hosptial	Belgium	Epidemiologist and specialist in cohort/ population studies	FP7-MEDIA, EU-Mascara and FP6-Ingenious Hypercare	Prof. J. Staessen	
Stephane Heymans	Hannover University	Germany	Common project on microRNAs in cardiac transplant rejection.	FP7-Homage & FP7-Fibrotargets	Prof. T. Thum	2009 - present
Stephane Heymans	ICGEB Trieste	Italy	Different visits and collaboration for Adenovirus-associated vector (AAV)-technology for cardiac-specific protein/ miRNA overexpression		Prof. M. Giacca	
Stephane Heymans	Kings College, London	UK	Collaboration on novel proteomics techniques to establish the glycome and membranome of monocytes/macrophages		Prof. M. Mayr	2009 - present
Stephane Heymans	Leipniz Institute at Munster University, Münster	Germany	International collaboration on next generation sequencing platform and post-sequencing computational pipeline		Prof. Monika Stoll	2014 - present
Tammo Delhaas	Narayana Institute of Cardiac Sciences	India	Pre-conditioning in Pediatric Cardiac Surgery		Dr. Suresh	2013 - present
Tammo Delhaas	Cardio Centro Ticino / Unversity of Lugano	Switzer-land	Computer Modeling in Cardiac Resynchronization Therapy		Profr. Auricchio	2013 - present
Tammo Delhaas	Justus Liebig University	Germany	Computer Modeling in Congenital Heart Disease		Prof. Schranz	2013 - present

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Tammo Delhaas	University Hospital in Motol	Czech Republic	Cardiac Pacing in Children		Prof. Janousek	2013 - present
Tilman Hackeng	LMU Munich University, Munich	Germany	Structure-function mapping of the chemokine interactome enables tailored intervention in acute and chronic inflammation		Prof. Christian Weber	2012 - present
Tilman Hackeng	Scripps Research Institute, Ja Jolla, CA	USA	Structure function analysis of anticoagulant proteins		Prof. Philip Dawson	1998 - present
Tilman Hackeng	Scripps Research Institute, Ja Jolla, CA	USA	Chemical protein synthesis			
Uli Schotten	St. Gorge's Hospital, University of London	UK	AF pathophysiology, non-invasive assessment of AF mechanisms	European Network for Translational Research on Atrial Fibrillation	Prof. J. Camm	2010 - 2015
Uli Schotten	Radcliffe Hospital, Oxford	UK	ROS signaling in AF	European Network for Translational Research on Atrial Fibrillation	Prof. B. Casadei	2010 - 2015
Uli Schotten	INSERM Paris	France	Fatty infiltration in atrial myocardium	European Network for Translational Research on Atrial Fibrillation	Prof. S. Hatem	2010 - 2015
Uli Schotten	University of Essen Duisburg	Germany	Ca handling in AF	European Network for Translational Research on Atrial Fibrillation	Prof. D Dobrev	2010 - 2015
Uli Schotten	University of Birmingham	UK	Classification of AF	European Network for Translational Research on Atrial Fibrillation	Prof. P. Kirchhof	2010 - 2015
Uli Schotten	University of Bern	Switzer-land	Fibrosis and AF	European Network for Translational Research on Atrial Fibrillation	Prof. S. Rohr	2010 - 2015
Uli Schotten	University of Magdeburg	Germany	Role of different etiologies in AF	European Network for Translational Research on Atrial Fibrillation	Prof. A. Götte	2010 - 2015
Uli Schotten	University of Münster	Germany	Transgenic mouse models of AF	European Network for Translational Research on Atrial Fibrillation	Prof. FU Müller	2010 - 2015
Uli Schotten	University Hospital Bordeaux	France	Non-invasive quantification of AF	European Network for Translational Research on Atrial Fibrillation	Prof. P. Jais	2010 - 2015
Uli Schotten	University Hospital Bordeaux	France	Ablation strategies in AF	European Network for Translational Research on Atrial Fibrillation	Prof. M Haissaguerre	2010 - 2015
Uli Schotten	ERKEM TIBBI YAYINCILIK YAZILIM GELISTIRME VE EGITIM HIZMETLERI, University Ankara	Turkey	Machine learning algirithms	European Network for Translational Research on Atrial Fibrillation	Prof. A. Oto	2010 - 2015
Uli Schotten	University Montreal	Canada	Ca handling in AF	Leducq Network ENAFRA: European North American Atrial Fibrillation Research Alliance	Prof. S. Nattel	2007 - 2013

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Uli Schotten	University of Maryland	USA	Ca handling in AF	Leducq Network ENAFRA: European North American Atrial Fibrillation Research Alliance	Prof. J Lederer	2007 - 2013
Uli Schotten	Cleveland Clinic	USA	Ca handling in AF	Leducq Network ENAFRA: European North American Atrial Fibrillation Research Alliance	Dr. D. Van Wagoner	2007 - 2013
Uli Schotten	Technical University Dresden	Germany	Ca handling in AF	Leducq Network ENAFRA: European North American Atrial Fibrillation Research Alliance	Prof. U. Ravens	2007 - 2013
Uli Schotten	Harvard Medical School, Boston	USA	Genetics of AF	Leducq Network ENAFRA: European North American Atrial Fibrillation Research Alliance	Dr. P. Ellinor	2007 - 2013
Uli Schotten	University München (LMU)	Germany	Genetics of AF	Leducq Network ENAFRA: European North American Atrial Fibrillation Research Alliance	Prof. S. Kääb	2007 - 2013
Uli Schotten	Charite, Berlin	Germany	ROS signaling in AF	ITN Network: RADOX: RADical reduction of OXidative stress in cardiovascular diseases	Prof. V. Regitz-Zagrosek	2012 - present
Uli Schotten	KU Leuven	Belgium	ROS signaling in AF	ITN Network: RADOX: RADical reduction of OXidative stress in cardiovascular diseases	Prof. S. Janssens	2012 - present
Uli Schotten	University Cambridge	UK	ROS signaling in AF	ITN Network: RADOX: RADical reduction of OXidative stress in cardiovascular diseases	Prof. T. Krieg	2012 - present
Uli Schotten	University Glasgow	UK	ROS signaling in AF	ITN Network: RADOX: RADical reduction of OXidative stress in cardiovascular diseases	Prof. R. Touys	2012 - present
Uli Schotten	Radcliffe Hospital, Oxford	UK	ROS signaling in AF	ITN Network: RADOX: RADical reduction of OXidative stress in cardiovascular diseases	Prof. K. Channon	2012 - present

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Uli Schotten	University Padua	Italy	ROS signaling in AF	ITN Network: RADOX: RADical reduction of OXidative stress in cardiovascular diseases	Prof. F. DiLisa	2012 - present
Uli Schotten	University Barcelona	Spain	Exercise and AF	EU project: CATCH ME: Characterizing Atrial Fibrillation by Translating ist Causes into Health Modifiers in the Elderly	Prof. L Mont	2015 - present
Uli Schotten	Network of competence of AF	Germany	AF Classification	EU project: CATCH ME: Characterizing Atrial Fibrillation by Translating ist Causes into Health Modifiers in the Elderly	Prof. G. Breithardt	2015 - present
Uli Schotten	University of Copenhage	Denmark	Animal models of AF	AFib-TrainNet: EU Training Network in Novel Targets and Methods in Atrial Fibrillation	Prof. T. Jespersen	2015 - present
Uli Schotten	University Clinic Eppendorf	Germany	HiPS for AF	AFib-TrainNet: EU Training Network in Novel Targets and Methods in Atrial Fibrillation	Prof. T. Eschenhagen	2015 - present
Uli Schotten	University Glasgow	UK	Cellular electrophysiology of AF	AFib-TrainNet: EU Training Network in Novel Targets and Methods in Atrial Fibrillation	Prof. G. Smith	2015 - present
Uli Schotten	Universita Svizzera Italiana Lugano	Switzer-land	Modeling and singal analysis	AFib-TrainNet: EU Training Network in Novel Targets and Methods in Atrial Fibrillation	Prof. A. Aurrichio	2015 - present
Uli Schotten	University Freiburg	Germany	Structure-function relationship in AF	Several joint publications	Prof. P. Kohl	2002 - present
Uli Schotten	Stanford University	USA	Rotors in AF	Joint publications	Prof. S. Narayan	2010 - present
Vu Thao-Vi Dao	Heinrich Heine University Düsseldorf	Germany	Impact of eNOS-Dependent Oxidative Stress on Endothelial Function and Neointima Formation; Stability of murine bradykinin type 2 receptor despite treatment with NO, bradykinin, icatibant or C1-INH		Georg Kojda	2015 - present
Wouter Huberts	University of Sheffield	UK	Modeling in Vascular Access Surgery		Prof. Hose	2013 - present

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Wouter Huberts	University of Bergamo	Italy	Modeling in Vascular Access Surgery		Dr Remuzi	2013 - present
Wouter Huberts	Norwegian University of Science and Technology	Norway	Uncertainty Quantification and Sensitivity Analysis		Prof. Hellevik	2013 - present
Wouter Huberts	Ghent University	Belgium	Experimental Validation of Computational Cardiovascular Models		Prof. Verdonck	2013 - present

ANNEX
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NARRATIVE SOCIETAL IMPACT OF RESEARCH IN THE THEME ELECTRO-MECHANICS OF THE HEART – PROFESSOR FRITS PRINZEN

When within a short period of time
1. animal activists protest against your experiments,
2. the university forces you to stop those experiments,
3. the local newspaper spends a 2-page interview about your work and
4. you get a phone call from the grandmother of the first patient benefiting from "your" therapy to thank you.....
... you know that your research has societal impact,
... albeit not always in the way you like.

An important phase in this research line was my sabbatical leave at the Johns Hopkins University, 20 years ago, where for the first time MRI tagging studies were performed in the paced (animal) heart. We were able to determine the enormous regional differences in mechanical loading within a paced heart. This resulted in a still *frequently cited article in JACC*[1].

In subsequent years we continued to contribute to the evidence that the conventional pacemakers create abnormal contraction patterns and, while correcting heart rate, created a loss of pump function. And we sought for better sites for ventricular pacing, in order to avoid these problems. In 2003 we published the first evidence in animal experiments that pacing at the apex (=tip) of the left ventricle (LV) or at the left side of the interventricular septum provides the best pump function[2]. In 2007 we published in *the New England Journal of Medicine* how LV apex pacing cured one child[3] and this was confirmed five years later in a large clinical trial, *published in Circulation*[4]. Currently, proper positioning of the pacemaker electrode in children is *almost routine around the world*, as shown for example by an article from Cuba[5].

Together with the Bakken Research Center Medtronic we *developed (and patented) a novel pacemaker electrode* that can be implanted chronically at the LV septum in a very easy way. We demonstrated feasibility and functional excellence in chronic animals in 2009. It took a few years to achieve sufficient permission to move to a first-in-man study. When the permission was granted in 2012, the study was performed by Dr. Kevin Vernooy and colleagues in the MUMC+ and was completed in 2015. *The article, in Circulation Arrhythmia and Electrophysiology, was selected as the "editor's pick" in the issue where it appeared*[6]. Currently we are preparing further continuation of the development of LV septal pacing in patients.

Another aspect of research is that sometimes the results open up an entirely new and previously unexpected field. The animal research on ventricular pacing increased the awareness that any abnormal ventricular conduction has an adverse effect on function of the heart. Clinical studies showed that this is particularly true in patients with heart failure. A novel pacemaker therapy (cardiac resynchronization therapy, CRT) evolved in the late 1990's. In a selected subgroup of heart failure patients CRT significantly improves quality of life and prolongs life expectancy. Our research group contributed significantly to this field[7][8].

One of the interesting achievements during the last years is the finding that the 3-dimensional vectorcardiogram (VCG) can be calculated from the regular 12-lead ECG and that this VCG provides better clues for application of CRT than the regular ECG. Because such VCG measurements are non-invasive and can be performed in every center, these findings will have major clinical impact. Due to this experience, we are currently the *core-lab ECG and VCG for two clinical trials*. We also achieved a *valorization grant from the Center for Translational Molecular Medicine* for further development of concepts derived from our understanding of the VCG.

Moreover, close collaboration with the department of Biomedical Engineering resulted in the use and rapid further development of *the CircAdapt computer program for CRT research*, solving questions like how to optimize CRT and development of a new echocardiographic parameter for better selection of candidates for CRT (collaboration with Prof. Tammo Delhaas and Dr. Joost

1 Prinzen FW, Hunter WC, Wyman BT and McVeigh ER. Mapping of regional myocardial strain and work during ventricular pacing: experimental study using Magnetic Resonance Imaging tagging. J Am Coll Cardiol. 1999;33:1735-1742.
2 Peschar M, de Swart H, Michels KJ, Reneman RS and Prinzen FW. Left ventricular septal and apex pacing for optimal pump function in canine hearts. J Am Coll Cardiol. 2003;41:1218-1226.
3 Vanagt WY, Prinzen FW and Delhaas T. Reversal of pacing-induced heart failure by left ventricular apical pacing. N Engl J Med. 2007 357:2637-8.
4 Janoušek J, van Geldorp IE, Krupičková S, Rosenthal E, Nugent K, Tomaske M, Früh A, Elders J, Hiippala A, Kerst G, Gebauer RA, Kubuš P, Frias P, Gabbarini F, Clur SA, Nagel B, Ganame J, Papagiannis J, Marek J, Tisma-Dupanovic S, Tsao S, Nürnberg JH, Wren C, Friedberg M, de Guillebon M, Volaufova J, Prinzen FW, Delhaas T and Cardiology. WGfCDaEotAfEP. Permanent cardiac pacing in children: choosing the optimal pacing site: a multicenter study. Circulation. 2013;127:613-23.
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NARRATIVE SOCIETAL IMPACT OF RESEARCH IN THE THEME ELECTRO-MECHANICS OF THE HEART – PROFESSOR FRITS PRINZEN

Lumens). *Several publications*[9][10] describe studies that are close to clinical trials and approach the goals described in the Avicenna document on "how computer simulations will transform the biomedical industry". The CircAdapt program is also currently adopted and coupled to programs of other computer scientists. *A simplified version is publically available and frequently used for teaching (bio)medical students (www.circadapt.org).*

With all the experience in the field of CRT, *Dr. Prinzen participated in the committee writing the 2012 Expert Consensus Statement for CRT, of EHRA/HRS, the European and American organizations for cardiac arrhythmia*. This statement supports the guidelines for professionals in the field. As of 2014 he is the *chairman of the EHRA Innovation Committee*.

Dr. Lumens is *member of the working group on eCardiology of the ESC*. In this working group all novel digital technologies, for therapies and training in cardiology, are discussed and stimulated, ranging from information provided by smart phones to computer models.

The extensive international network also leads to close scientific collaboration with, among others, the Universities of Lugano and Bordeaux, resulting in many joint publications, exchange of young investigators and visiting professorships. The broader societal impact of the research group is also expressed by a large number of scientific grants and industry contracts, as well as the *five personal ("Dekker") grants provided by the Netherlands Heart Foundation*. Finally, members of the team frequently give *talks for health care professionals, including allied professionals, and for organizations of heart failure patients*.

The abovementioned history of research on pacing therapies may be characteristic for many medical discoveries: starting in experimental animals and continuing on to patients. Even though in this particular case the line was fairly straightforward, it took more than a decade to come from animal research to clinical application. Nevertheless, these important medical developments would not have been possible without animal experiments. Notably, these studies were performed in a species of which the heart is most similar to man, being the dog.

Experiments in dogs are a sensitive topic to the general public, related to the strokability of these animals. However, there was considerable literature and experience from the own laboratory that effects of ventricular pacing were significantly different when testing in other large animals, like pigs and goats. Therefore, doing the studie[1]s in dogs was the only way to reach the goal of a better treatment for pacemaker patients.

The ethical question raises whether it ethically acceptable to take a dog's life to save a human life. A university employee, commenting on the discussions about the dog experiments, addressed this question impressively: "I have a dog and I have been diagnosed with heart failure. I really love my dog, but if I have to choose between his life or mine, I chose mine." Of course, it is the heavy responsibility of the investigator to perform the experiments in the most ethical way, more specifically respecting the three "R's": replacement (if possible), reduction and refinement. In addition, it is the joint responsibility of the investigator and the university to be pro-active and inform the public sufficiently and preferably ahead of time, to explain why such studies are performed. Here clearly some work is to be done.

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