# Erasmus University Rotterdam CSC PhD 2013

## Project Description

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| ***School/Department:*** | Department of Experimental Cardiology  Department of Biomedical Engineering  Thorax Center  Erasmus University Medical Center, Rotterdam, The Netherlands |
| ***Project Title:*** | **Imaging the pathophysiological response to coronary interventions; an experimental and computational approach** |
| ***Abstract:*** | Atherosclerosis is a major health care burden, responsible for nearly 40% mortality in the western world. Atherosclerotic coronary artery disease, often complicated by (athero)thrombosis leading to acute myocardial infarction constitutes a dominant part of this problem. Percutaneous Coronary Intervention (PCI) by implantation of a drug eluting stent (DES) is currently the treatment of choice for acute coronary syndromes as well as stable angina.  In this project we will study the relation between the vascular environment (structures such as atheromatous plaque, fibrous intimal thickening, coronary thrombus), local and distal vascular drug uptake, vascular healing and microvascular function following DES placement. To this end, we will apply a combination of in vivo imaging in an animal model for coronary atherosclerosis, ex vivo molecular histology by means of imaging mass spectrometry (IMS), and numerical modeling of drug transport in the vascular bed.  Until now limited information is available on the concentration distribution of drugs and drug vehicles along the vessel lumen and inside the atherosclerotic vessel wall. Convection and diffusion of molecules into the blood and wall largely depends on their size, charge, and whether the compound is lipophilic or hydrophilic. We will image the pathophysiological response of the coronary circulation to the intervention by means of several intravascular imaging techniques, and match that diagnostic information to the molecular histology, studying pharmacokinetics, drug metabolites, and plaque lipidomics. A numerical model will be developed and validated based on these data, to compute the distribution of compounds with different molecular sizes at the lumen and in the vessel wall using realistic 3D reconstructions of lumen and wall of coronary arteries. At the end of this project, we will have created a tool to predict the vascular response to DES placement in patients, based on diagnostic imaging and patient-specific modeling. |
| ***Requirements of candidate:*** | In the context of the Rotterdam-China exchange program, sponsored by EUR and CSC, we are currently looking for two candidates who are interested to join our lab for a 4 year PhD program. Candidate 1 must have a solid knowledge of *biochemistry or mass spectrometry,* and should have abackground in *Chemistry, Biology, or Physics*; candidate 2 must have a solid knowledge of *Biomedical Engineering*, with affinity for finite element modeling and/or experimental studies.  Both should have a keen interest in *Medicine*, particularly cardiology, good command of English (written and oral) and have recently received, or will receive in the coming months, an MSc degree in a suitable field.  Master degree: Yes  IELTS Grade: 7.0 *(minimal 6.0 per component)*  *or*  TOEFL: *100 (minimal 20 per component)* |
| ***Supervisor information:*** | Heleen van Beusekom, PhD  Senior Scientist; h.vanbeusekom@erasmusmc.nl  Department of Experimental Cardiology  Gijs van Soest, PhD  Assistant Professor; email: g.vansoest@erasmusmc.nl  J.J. Wentzel , PhD  Associate Professor; email j.wentzel@erasmusmc.nl  Ton van der Steen, PhD, FESC  Professor; email: a.vandersteen@erasmusmc.nl  Department of Biomedical Engineering  Thorax Center  Erasmus MC  PO Box 2040  3000 CA Rotterdam  The Netherlands  Relevant publication list; all supervisors:   1. Wentzel JJ, et al., Stent implantation in coronary arteries causes alterations in 3-D geometry and distribution of 3-D shear stress at the endothelium. Journal of Biomechanics, 2000, 33:10:1287-1295. 2. Slager CJ, et al. True 3-D Reconstruction of Coronary Arteries in Patients by fusion of Angiography and IVUS (ANGUS) and its Quantitative Validation. Circulation, 2000, 102: 511-516. 3. Wentzel JJ, et al. The relationship between neointimal thickness and shear stress after Wallstent implantation in human coronary arteries at 6 months follow up. Circulation, 2000, 102: 1740-1745. 4. Thury A, et al. Focal in-stent restenosis near step-up: roles of low and oscillating shear stress? Circulation, 2002, Jun 11;105(23):e185-7. 5. Wentzel JJ, et al. Shear stress, vascular remodeling and neointimal formation. J Biomech., 2003, May;36(5):681-8. 6. Gijsen FJH, et al. Tissue regression in sirolimus-eluting stents in human coronary arteries is localized and correlates with shear stress. Am J Cardiol., 2003, Dec 1;92(11):1325-8. 7. ten Have AG, et al. Temperature distribution in atherosclerotic coronary arteries: influence of plaque geometry and flow (a numerical study). Phys Med Biol., 2004, Oct 7;49(19):4447-62. 8. Slager CJ, et al. The role of shear stress in the generation of rupture-prone vulnerable plaques. Nat Clin Pract Cardiovasc Med., 2005, Aug;2(8):401-7.   10. Slager CJ, et al. The role of shear stress in destabilization of vulnerable plaques and related therapeutic implications. Nat Clin Pract Cardiovasc., 2005, Sept;2(9):456-64.   1. ten Have A, et al. Intracoronary thermography: Heat generation, transfer and detection, EuroIntervention 1(1); May 2005: 105-114 2. Ten Have AG, et al. Influence of catheter design on lumen wall temperature distribution in intracoronary thermography. J Biomech. 2007;40(2):281-8. 3. Ten Have AG, et al. A numerical study on the influence of vulnerable plaque composition on intravascular thermography measurements. Phys Med Biol. 2006 Nov 21;51(22):5875-87. 4. Wentzel JJ, et al. In vivo 3D distribution of lipid-core plaque in human coronary artery as assessed by fusion of near infrared spectroscopy-intravascular ultrasound and multislice computed tomography scan.Circ Cardiovasc Imaging. 2010 Nov 1;3(6):e6-7. 5. Commandeur S, et al. [Polymers, drug release, and drug-eluting stents.](http://www.ncbi.nlm.nih.gov/pubmed/17107364) J Interv Cardiol. 2006 Dec;19(6):500-6. Review 6. van Beusekom HM, et al. [Drug-eluting stents show delayed healing: paclitaxel more pronounced than sirolimus.](http://www.ncbi.nlm.nih.gov/pubmed/17434882) Eur Heart J. 2007 Apr;28(8):974-9. 7. van Beusekom et al. [The neointimal response to stents eluting tacrolimus from a degradable coating depends on the balance between polymer degradation and drug release.](http://www.ncbi.nlm.nih.gov/pubmed/19112791) EuroIntervention. 2008 May;4(1):139-47. 8. Onuma Y, et al [The paradigm of endothelium and stent thrombosis in DES.](http://www.ncbi.nlm.nih.gov/pubmed/19202686) EuroIntervention. 2008 Aug;4 Suppl C:C17-21. 9. Ertaş G, van Beusekom HM, van der Giessen WJ. [Late stent thrombosis, endothelialisation and drug-eluting stents.](http://www.ncbi.nlm.nih.gov/pubmed/19421365) Neth Heart J. 2009 Apr;17(4):177-80. 10. van den Heuvel M, et al. [Endothelial dysfunction after drug eluting stent implantation.](http://www.ncbi.nlm.nih.gov/pubmed/19838153) Minerva Cardioangiol. 2009 Oct;57(5):629-43. Review. 11. van Beusekom HM, et al. [Endothelial function rather than endothelial restoration is altered in paclitaxel- as compared to bare metal-, sirolimusand tacrolimus-eluting stents.](http://www.ncbi.nlm.nih.gov/pubmed/20542807) EuroIntervention. 2010 May;6(1):117-25. doi: 10.4244/. 12. van den Heuvel M, et al. [Specific coronary drug-eluting stents interfere with distal microvascular function after single stent implantation in pigs.](http://www.ncbi.nlm.nih.gov/pubmed/20650434) JACC Cardiovasc Interv. 2010 Jul;3(7):723-30. Erratum in: JACC Cardiovasc Interv. 2010 Sep;3(9):994. 13. Van Der Giessen WJ, Van Beusekom HM. [New drug-eluting stents with biodegradable polymers.](http://www.ncbi.nlm.nih.gov/pubmed/21285929) Minerva Cardioangiol. 2011 Feb;59(1):31-8.   24. Gonzalo N, et al. Optical coherence tomography patterns of stent restenosis. *Am Heart J.* 2009;158(2):284-293.  25. van Soest G, et al. Atherosclerotic tissue characterization in vivo by optical coherence tomography attenuation imaging. *J Biomed Opt.* 2010;15(1):011105-011109.  26. Goderie TPM, et al. Combined optical coherence tomography and intravascular ultrasound radio frequency data analysis for plaque characterization. Classification accuracy of human coronary plaques in vitro. *International Journal Of Cardiovascular Imaging.* 2010;26(8):843-850.  27. Garg S, et al. First use in patients of a combined near infra-red spectroscopy and intra-vascular ultrasound catheter to identify composition and structure of coronary plaque. *EuroIntervention.* 2010;5(6):755-756.  28. Regar E, et al. Optical coherence tomography in patients with acute coronary syndrome. *EuroIntervention.* 2010;6 Suppl G:G154-160.  29. Gonzalo N, et al. Witnessed Coronary Plaque Rupture During Cardiac Catheterization. *JACC Cardiovasc Imaging.* 2011;4(4):437-438.  30. Regar E, et al. The diagnostic value of intracoronary optical coherence tomography. *Herz.* 2011;36(5):417-429.  31. van Soest G, et al. Pitfalls in Plaque Characterization by OCT: Image Artifacts in Native Coronary Arteries. *J Am Coll Cardiol Img.* 2011;4(7):810-813.  32. Jansen K, et al. Intravascular photoacoustic imaging of human coronary atherosclerosis. *Opt. Lett.* 2011;36(5):597-599. |