

# Department of Cardiac Surgery

## Chair of Cardiac Surgery

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### Director

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### Research focus

- Chronic rejection of allografts
- Therapy of end-stage heart failure: Heart transplantation or support with a left or right ventricular assist device
- Electromechanical coupling in heart failure
- Development of a non-blood contacting heart actor
- High speed camera investigations on heart valves in a pulse duplicator

### Structure of the Chair

Professorship: 1

Personnel: 100

- Doctors (of Medicine): 15
- Scientists: 3 (thereof funded externally: 0)

### Clinical focus areas

- Adult cardiac surgery
- Heart transplantation in adults and children
- Minimally invasive valve surgery
- Mechanical circulatory support
- Wound management
- Heart insufficiency therapy
- Rhythm surgery
- Surgery in grown-up with congenital heart disease
- Interventional heart valve surgery
- Interventional aortic surgery

### Research

Main research topics are on the one hand basic research in transplantation and on the other hand clinical research in mechanical circulatory support and the development of new heart assist devices.

### Chronic rejection of allografts

PI: PD Dr. C. Heim

Transplant vasculopathy is the main reason for late graft failure after heart transplantation. In order to develop effective therapeutic strategies

and translate them into clinical success, a detailed understanding of the mechanisms responsible for the development of transplant vasculopathy is essential. We have recently established and characterized the abdominal aortic allograft model as a suitable tool to study the development of transplant vasculopathy. Ongoing projects involve the role and importance of platelets and their inhibition in the development of transplant vasculopathy. Immunomodulatory effects of Clopidogrel could be shown in small animal models. The results of these preclinical studies could be translated into a multi-center study (CEDRIC). Additionally, microvascular integrity of pulmonary grafts was shown to be essential for the long-term success of animal transplant models. In cooperation with the Department of Medicine 4, another major aim of this working group is the use of antiproliferative substances to explore potential strategies to avoid the development of transplant vasculopathy in experimental transplant models.

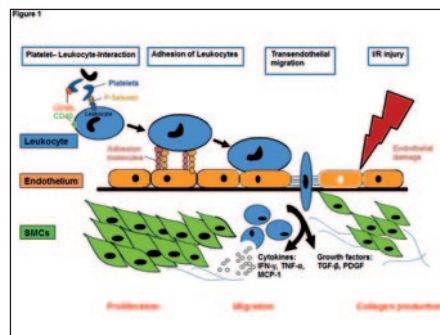


Figure 1  
Mechanisms in CAV

After I/R injury, endothelial damage is likely to occur. Adhesion molecules are upregulated and after platelet-leukocyte interaction, leukocytes transigrate through the endothelial layer. There they produce several cytokines and growth factors. As a result, SMC produce collagen, proliferate, and migrate into the neointima. This finally leads to a progressive narrowing of the transplanted vessels and to subsequent graft failure. CAV, cardiac allograft vasculopathy; IFN- $\gamma$ , interferon- $\gamma$ ; I/R, ischemia/reperfusion; MCP-1, monocyte chemoattractant protein-1; PDGF, platelet-derived growth factor; SMC, smooth muscle cell; TGF- $\beta$ , transforming growth factor- $\beta$ ; TNF- $\alpha$ , tumor necrosis factor  $\alpha$ . (Reproduced from Heim et al., *Thorac Cardiovasc Surg* 2018, with permission from Thieme)

### Therapy of end-stage heart failure: Heart transplantation or support with a left or right ventricular assist device

PI: Dr. R. Tandler

Orthotopic cardiac transplantation is the therapy of choice for cardiac insufficient patients. Due to an increasing shortage of donor organs, these cardiac insufficient patients need to be bridged with an implantable ventricular assist device until a suitable donor organ is available.

In some cases heart disease has already progressed to such an extent that the patients need to be stabilized with a left ventricular assist device or – in case of additional right heart failure – with a biventricular assist device.

### Electromechanical coupling in heart failure

PI: PD Dr. C. Heim

Remodelling of cardiomyocytes in heart failure patients is well described in the literature, but not completely understood. The calcium delivery in cardiomyocytes may be altered in heart failure patients. In previous studies the remodeling of the T-system of the cardiomyocytes was discussed as responsible for cardiac recovery in ventricular assist device patients. Therefore the aim of the ongoing projects in cooperation with the Institute of Physiology and Pathophysiology is to further analyze underlying mechanisms of the T-system remodeling using human heart tissue from VAD or transplant patients.

### Development of a non-blood contacting heart actor

PI: Prof. Dr. M. Weyand

The support of the insufficient heart muscle function by artificial support systems is worldwide an intensive field of research and an aim sought for for about 60 years. Rising life expectancy and the growing number of heart-insufficient patients on the one hand as well as restricted availability of donor organs and damping of the increase of the health costs will further raise the need in innovative support systems in the future. On account of the risks of the existing, invasive, clinical methods, a carefully implantable technology is necessary. It must be functioning reliably as well as permanently and intervene not invasive in the heart-circulatory system. Within a clinical-medical setting, the investigation of a research project pursues from the interpretation over the production up to the clinical validity of the system function more new, actoric, and patient-individual heart muscle support systems for the purposes of an external compression of the heart. Therefore the main focuses are the investigation of a biomechanically efficient, mechanical system as well as the development of di- or piezoelectric based actor material patterns.

### High speed camera investigations on heart valves in a pulse duplicator

PI: Dr. M. Kondruweit

High-speed camera investigations on heart valves in an animal model are an already established model. In this project these proceedings

are applied into a pulse duplicator to be able to compare several heart valve types in a standardized procedure. Special situations, as for example the Ventricle Assist Devices support and the effect on the hemodynamic on the heart valves, are examined. The results should show possible reasons for heart valve attrition by measuring power vectors. If possible, these reasons shall be corrected by changing the valve design.

## Teaching

The Department of Cardiac Surgery takes part in compulsory and elective subjects for the curricular teaching of the Medicine and Dentistry. Bachelor's and Master's theses are supervised as well as MD and PhD theses.

## Selected publications

Heim C, Tandler R, Kondruweit M, Weyand M. Chirurgische Therapiemöglichkeiten bei Herzinsuffizienz. CHAZ. 2018; 4:209-215

Gocht A, Spriewald B, Distler JHW, Ramsperger-Gleixner M, Ensminger SM, Weyand M, Heim C. Small Molecule Tyrosine Kinase Inhibitor Nintedanib Reduces Development of Cardiac Allograft Vasculopathy in Murine Aortic Allografts. Transplantation Direct. 2018 Jun 18;4(7):e367

Gocht A, Distler JHW, Spriewald B, Ramsperger-Gleixner M, Weyand M, Ensminger SM, Heim C. Effects of different serotonin receptor subtype antagonists on the development of cardiac allograft vasculopathy in murine aortic allografts. Transpl Immunol. 2018; 49:43-53

Ghaderi S, Alidadiani N, SoleimaniRad J, Heidari HR, Dilaver N, Heim C, Ramsperger-Gleixner M, Baradaran B, Weyand M. DJ1 and microRNA-214 act synergistically to rescue myoblast cells after ischemia/reperfusion injury. J Cell Biochem. 2018;119(9):7192-7203

Heim C, Tandler R, Weyand M. ESC-leitlinienbasierte Therapieempfehlungen für herzinsuffiziente Patienten in der Herzchirurgie. 2018; 32(5), 391-401

Heim C, Gocht A, Weyand M, Ensminger SM. New Targets for the Prevention of Chronic Rejection after Thoracic Organ Transplantation. Thorac Cardiovasc Surg. 2018; 66(01):31-41

## International cooperation

Dr. M. Nicolls, Professor in Pulmonary and Critical Care Medicine, Stanford University, CA: USA