Department of Cardiac Surgery
Chair of Cardiac Surgery

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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
• Neuropeptide release of the heart
• Hospital-economics and management
• The arterialization of cardiac veins as an alternative myocardial revascularization strategy in an experimental long term model in pigs
• Tissue engineering of cardiovascular implants
• Development of a non-blood contacting heart actor
• High speed camera investigations on heart valves in a pulse duplicator

Structure of the Department
20 medical doctors work at the Department of Cardiac Surgery. The research is accomplished by all medical doctors, seven graduate students, and two technical assistants.

Research
Chronic rejection of allografts
Project manager: Dr. C. Heim
Transplant arteriosclerosis is the main reason for late graft failure 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 arteriosclerosis is essential. We have recently established and characterized the abdominal aortic allograft model as a suitable tool to study the development of transplant arteriosclerosis. Ongoing projects involve the role and importance of chemokines and chemokine receptors, in particular CCR7 and CXCR5, in the development of transplant arteriosclerosis. CCR7, the major homing receptor for trafficking of T and B cells, plays a crucial role in leukocyte homing. Experiments using CCR7/- mice as recipients of aortic allografts showed increased amounts of transplant arteriosclerosis during the absence of this receptor and suggest an interesting role of this receptor in this disease. Recent findings implicate an important role of human cytomegalovirus infection (HCMV) for the development of inflammatory-proliferative vascular lesions in transplanted vascularized allografts. Therefore, the major aim of this project is to develop a human peripheral blood lymphocyte (hu-PBL)/severe combined immunodeficiency (SCID) mouse xenograft-model to investigate the immunological and pathological mechanisms of HCMV in the modulation and progression of transplant arteriosclerosis.

Therapy of end-stage heart failure: Heart transplantation or support with a left or right ventricular assist device
Project manager: Dr. R. Tandler
Orthotropic 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.

Neuropeptide release of the heart
Project manager: PD Dr. T. Strecker
Calcitonin-Gene Related Peptide (CGRP) is a neuropeptide consisting of 37 amino acids and its biological action results in a strong vasodilatation. CGRP is mainly produced by the sensoric A-β and C-fibres. Recent data suggests that it may play an important role in myocardial ischemia. Neural fibres with a high CGRP content are found in both atria, the pericardium and within the adventitia of coronary arteries. Changes in CGRP production correlate with increased activity within cardiac afferent fibres. It was shown in vitro that elevated CGRP concentrations were able to increase the coronary blood flow and reduce the coronary resistance and the mean arterial blood pressure. Furthermore, CGRP was demonstrated to be cardio-protective and reduce the infarct size of myocardial infarction. The aim of our project (cooperation with Prof. Dr. K. Messlinger, Institute of Physiology and Pathophysiology) is to develop an experimental mouse model in order to investigate the effects and kinetics of CGRP production in greater detail. In addition, analyses of human CGRP production are planned by using tissue from the right ventricle or ascending aortic tissue.

Hospital-economics and management
Project managers: Prof. Dr. R. Feyrer
One of the main tasks of this group has been to face the changes in hospital reimbursement from retrospective payment to a prospective flat rate payment. Other current projects involve the development of the so called ‘clinical pathways’ in order to improve cost unit calculations and enable us to create computer-simulated scenarios of complex problems of hospital cost management. In cooperation with the Department of Anesthesiology, we perform a study analyzing the costs involving intensive care patients, and together with the German Heart Center in Berlin, we are trying to set up a database regarding long-term costs of patients on cardiac assist devices.

The arterialization of cardiac veins as an alternative myocardial revascularization strategy in an experimental long term model in pigs
Project manager: PD Dr. F. Harig
In ischemic hearts, venous retroperfusion is a potential myocardial revascularization strategy. The goal underlying retrograde coronary sinus (CS) perfusion is perfusion of the ischemic myocardium proximal to the occlusion or stenosis. The lack of suitable target vessels remains a challenge for aortocoronary bypass grafting in end stage coronary heart disease. This study aimed at investigating the arterialization of cardiac veins as an alternative myocardial revascularization strategy in an experimental long term model in pigs.

In a pig model of myocardial ischemia, selective retrograde perfusion of a coronary vein was performed. A ligation of the ramus interventricularis paracoronalis (equivalent to the left anterior descending artery (LAD) in humans) was performed in 20 German landrace pigs (Sus scrofa domestica). Retroperfusion (RP) of the concomitant vein of the LAD was performed in four pigs (RP+), but not in the other four (RP-), and the vena cordis magna (VCM) was ligated (L+) in four pigs in each of these groups, but left open (L-) in the remaining animals. Hemodynamic performance (e.g. cardiac output) was significantly better in RP+L+ pigs that underwent selective retroperfusion with proximal ligation of vena cordis magna as compared to all other animals. Long term survival was significantly better in RP+L+ pigs than in all other...
groups. Histological follow-up studies showed significantly smaller area of necrosis in all animals of the RB+L+ group.

Consequently, venous retroperfusion is an effective technique to achieve long term survival after acute LAD occlusion in a pig model. The clinical application is still pending.

**Tissue engineering of cardiovascular implants**

Project manager: Dr. C. Heim

The background for these studies is the development of an ingrowth matrix within the tissue engineering of cardiovascular grafts. The purpose of these investigations is to show whether it is possible to influence the mobility of endothelial cells, smooth muscle cells, and fibroblasts within a fully synthetic matrix by incorporating bioactive peptides. The purpose is to define a matrix which provides optimal mobility for those cells needed for a functional cardiovascular implant. Such a matrix could be integrated into a cardiovascular prosthesis in order to facilitate and direct the ingrowth of the patient’s own tissue. A single cell migration model was used to compare the influence of different cell interactive peptides on the mobility of vascular cell lines as microvascular endothelial cells (MVEC) and aortic vascular smooth muscle cells (SMC). In previous studies it could already be shown that selectively MVEC, but not SMC accelerate on a PEG matrix covered with RGD (fibronectin) and YIGSR (laminin) in comparison to a matrix covered only with RGD. These experiments were extended to the peptide sequences SIKVAV, RYVLPVR (both laminin), and DGEA (collagen) also known from the literature as being vascular cell interactive. For sufficient cellular adhesion, RGD was added to the matrix again. At an average migration speed, both cell lines showed a reduced cell speed on RGD plus RYVLPVR and RGD plus DGEA. For the combination of SIKVAV and RGD, only MVEC showed a small, but not significant increase in mobility whereas SMC did not show any difference.

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

Project manager: 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 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 new research project which will be submitted in 2015 with the DFG 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**

Project manager: 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**

Beside the traditional teaching forms (main lecture and practical courses), observerships and clinical rotations can be undertaken anytime.

**Selected Publications**


