



## Protocol MIRI study

*Departments of Cardio-thoracic Surgery, Surgery and Cardiology, LUMC, Leiden, The Netherlands*

### **Title**

The MIRI (Myocardial Ischemia Reperfusion Injury) study, understanding the effects of heart failure surgery to improve safety and outcome.

### **Principal Investigator**

- Dr. R.J.M. Klautz, Cardiothoracic Surgeon

### **Co-Investigator**

- Dr. J.H.N. Lindeman, Vascular Researcher

### **Research Group**

- K.A. Kortekaas, Medical Student
- J.C. Karper, Medical Student
- D.K. de Vries, Medical Student
- Dr. A.F.M. Schaapherder, Transplantation Surgeon
- Dr. J. van Pelt, CKCL (Central Clinical Chemical Laboratory)
- Drs. F.H.M. Engbers, Anesthesiologist
- Dr. D.E. Atsma, Cardiologist
- Drs. M.I.M. Versteegh, Cardiothoracic Surgeon

**Independent Physician:** Drs. J. Braun

**Institute:** Departments of Cardiothoracic Surgery, Surgery and Cardiology, Leiden University Medical Center, Leiden, The Netherlands

**Sponsors:** Departments of Cardiothoracic Surgery of the Leiden University Medical Center. The Netherlands Heart Foundation.

### **Protocol number**

P08.031

### **Date**

07 December 2007, Protocol Version 1

## Table of Contents

---

<b>Protocol Signature sheet</b>	03
<b>Synopsis</b>	04
<b>1. Introduction and Rationale</b>	05
<b>2. Study objectives</b>	06
<b>3. Methods</b>	08
3.1 Study Design	08
3.2 Study Population	08
3.3 Study Procedures	09
3.4 Required Clinical Evaluations	10
3.5 Data Handling and Record Keeping	10
<b>4. Statistical Considerations and Data Analysis</b>	12
4.1 Sample Size	12
4.1 Statistical methods to be employed	12
<b>5. Safety Reporting</b>	13
5.1 Section 10 WMO event	13
5.2 Adverse and serious adverse events	13
5.3 Data Safety Monitoring Board (DSMB)	13
<b>6. Ethical Considerations</b>	14
6.1 Regulation Statement	14
6.2 Recruitment and Consent	14
6.3 Objection by minors or incapacitated subjects	14
6.4 Benefits and risks assessment, group relatedness	14
6.5 Compensation for injury	14
<b>7. Administrative Aspects and Publication</b>	16
<b>8. List of Abbreviations</b>	17
<b>9. Reference List</b>	18
<b>Appendix A</b>	19
<b>Appendix B</b>	21



## Protocol Signature Sheet

---

Name	Signature	Date
R.J.M. Klautz, Cardiothoracic Surgeon		
J.H.N. Lindeman, Vascular Researcher		

### Contact details:

R.J.M. Klautz, MD, PhD  
*Department of Cardio-Thoracic Surgery*  
Albinusdreef 2  
2333 ZA Leiden  
Location: D-06-53, LUMC  
Telephone: 071-5264022  
Email: R.J.M.Klautz@lumc.nl



The MIRI (Myocardial Ischemia Reperfusion Injury) study, understanding the effects of heart failure surgery to improve safety and outcome.

## Synopsis

---

### Rationale

Patients with pre-existing heart failure seem to develop complications related to SIRS more often after cardiac surgery than non-heart failure patients. Those with preexisting heart failure show more often a marked temporary reduction in the post-operative pump function, have a higher release of systemic pro-inflammatory cytokines and experience a prolonged stay in ICU due to post-operative complications. These observations suggest attribution of MIRI and SIRS to the impaired outcome for heart failure patients after cardiac surgery. Suppression of the responses initiated by MIRI has been suggested as therapeutic to improve cardiac surgery outcome.

### Study Objective

The main objective of this study is to determine if patients with heart failure have a different myocardial ischemia-reperfusion injury (MIRI) and/or systemic inflammatory response (SIRS) than patients without heart failure.

### Study Design

A single center observational study.

### Study Population

Patients that are candidates for heart failure surgery in which restrictive mitral valve repair (RMA) is always part of the procedure and patients that are candidates for mitral valve repair for prolapse disease will be included. A total of 80 patients will be divided in 4 groups of 20 patients. Patients with pre-existent heart failure are divided in three groups: RMA + LV-reconstruction (Dor-like procedure) ± CABG, RMA + CorCap and RMA + CABG. The control group embraces patients without heart failure, namely mitral valve repair for prolapse disease.

### Study Procedures

After giving their informed consent to participate in this study blood samples and biopsies will be taken during the operation and perioperative. Anesthetic procedures in all groups will be carried out according to standard care. Various established markers in blood and tissue will be studied.

### Endpoints of the study

This study will test the hypothesis that MIRI is much more pronounced in the previously damaged heart compared to the normal heart, with left ventricular reconstruction surgery showing the most prominent injury. SIRS is related to the extent of MIRI, and can be characterized in heart failure differently than in normal patients. We assess the contribution of oxidative damage, complement, endothelial, thrombocyt and neutrophil activation and inflammation to human MIRI.

## 1. Introduction and Rationale

---

Although the efficacy in cardiothoracic-surgery has been well established<sup>1</sup>, peri-operative mortality and morbidity remain significant, especially in patients with preexisting heart failure. Reduction of mortality and morbidity is essential to increase the safety of the procedures and to extend the indications to asymptomatic patients and high risk procedures. Common occurrence of systemic complications after cardiac surgery, such as vasodilatation and ventilatory problems, indicate the role of a systemic response to the impaired outcome.

It is conceived that a vicious circle of 2 biological processes is responsible for initiating a systemic response related to the high impaired post-operative outcome: Myocardial Ischemia Reperfusion Injury (MIRI)<sup>2</sup> and the Systemic Inflammatory Response Syndrome (SIRS)<sup>3</sup>.

MIRI is the paradoxical exacerbation of myocardial damage upon restoration of blood supply to previously ischemic myocardial tissue and is considered the major, inevitable, cause of tissue damage after ischemic events such as myocardial infarction<sup>4</sup> and cardiac surgery. The pathophysiology of MIRI is complex and its exact mechanisms have not been fully elucidated yet. However, it is conceived that reperfusion results in endothelial damage, free radical production, complement and thrombocyte activation, and cytokine release, which ultimately result in an inflammatory reaction<sup>5</sup>. Release of pro-inflammatory cytokines from the myocardium induced by MIRI is not limited to the organ itself but also contributes to activation of systemic vascular endothelium, clinically recognized as SIRS.

Patients with preexisting heart failure seem to develop complications related to the systemic inflammatory response more often after cardiac surgery than non-heart failure patients. Those with preexisting heart failure show more often a marked temporary reduction in the post-operative pump function, have a higher release of systemic pro-inflammatory cytokines and experience a prolonged stay in ICU due to post-operative complications<sup>6</sup>. These observations suggest attribution of MIRI and a systemic inflammatory response to the impaired outcome for heart failure patients after cardiac surgery. Suppression of the responses initiated by MIRI has been suggested as therapeutic to improve cardiac surgery outcome.

Although studies of animal models to modify the outcome of MIRI showed promising results, the number of human studies is limited, and results thus far are disappointing. The basis for the apparent discrepancy between animal and human studies is unclear and may include species differences in mechanisms underlying MIRI or differences in organ sensitivity towards MIRI. Animal experiments are generally performed in young and healthy animals.



The MIRI (Myocardial Ischemia Reperfusion Injury) study, understanding the effects of heart failure surgery to improve safety and outcome.

This obviously contrasts to the human population exposed to MIRI indicating pitfalls in the interpretation of animal models in such a convoluted process as MIRI.

We now propose a new clinical model to obtain information about the underlying mechanisms of MIRI by measuring various established markers for each of these processes in paired arterial and venous (coronary sinus) samples. We assess the contribution of oxidative damage, complement, endothelial, thrombocyt and neutrophil activation and inflammation to human MIRI. Obtained data will provide information to understand MIRI, its possible contribution to SIRS and may provide for the development of a rational prevention or treatment strategy leading to a decline in morbidity and mortality rates.

## 2. Study Objectives

---

The aim of the study is to understand the effects of heart failure surgery compared to non heart failure surgery to improve safety and outcome.

- The primary objective is to determine if patients with heart failure have a different myocardial ischemia-reperfusion injury (MIRI) and/or systemic inflammatory response (SIRS) than patients without heart failure.
- The secondary objectives are:
  - Do patients with ischemic heart failure have a different MIRI and/or SIRS than patients with idiopathic (non-ischemic) heart failure?
  - Do patients with left ventricular reconstruction surgery have a different MIRI and/or SIRS than patients in whom the left ventricle is not opened?
  - Is MIRI related to SIRS?

### Hypothesis

This study will test the hypothesis that myocardial ischemia reperfusion injury is much more pronounced in the previously damaged heart compared to the normal heart, with left ventricular reconstruction surgery showing the most prominent injury. SIRS is related to the extent of myocardial-reperfusion injury, and can be characterized in heart failure differently than in normal patients.

## 3. Methods

---

### 3.1 Study design

This is a single center observational study in the LUMC in Leiden, the Netherlands. In this study arteriovenous differences for measurements of systemic and myocardial biomarkers of MIRI and myocardial damage will be assessed in patients undergoing mitral valve surgery.

MIRI is an inevitable part of the surgical procedure with the ischemic period during CPB and reperfusion after declamping of the aorta. Paired blood samples will be obtained before, during and after surgery. Furthermore two biopsies will be performed, one just after the cardioplegic arrest of the heart and the other just before release of the cross-clamp and thus restoring normal blood flow to the coronary circulation.

Please refer to section 4 for justification of the sample size.

### 3.2 Study Population

Patients that are candidates for heart failure surgery in the LUMC in which restrictive mitral valve repair (RMA) is always part of the procedure and patients that are candidates for mitral valve repair for prolapse disease will be included. All indications for surgery are made during a weekly medico-surgical conference. A total of 80 patients will be divided in 4 groups of 20 patients. All patients will be entered consecutively until each group has 20 patients.

Patients with pre-existent heart failure are divided in three groups:

- RMA + LV-reconstruction (Dor-like procedure) ± CABG
- RMA + CorCap
- RMA + CABG.

The control group embraces patients without heart failure, namely mitral valve repair for prolapse disease.

All preoperative examinations will be done according to the currently valid treatment and preoperative evaluation protocol.

Additional procedures like tricuspid valve annuloplasty, ablation procedures and placement of LV-lead for biventricular pacing will be performed as indicated. Heart failure is defined as EF < 35% and referred for surgery through the "Mission! Heart Failure Program"<sup>7</sup>.



*Inclusion criteria:*

- Acceptation for mitral valve surgery via sternotomy

*Exclusion criteria:*

- Acceptation for minimal invasive mitral valve surgery
- Inability to sign informed consent
- Less than 18 years old
- Emergency operations
- Inability to introduce coronary sinus catheter

### **3.3 Study Procedures**

Eligible patients seen at the outpatient clinic meeting our in- and exclusion criteria will receive written and oral information during their first visit. Patients transferred from other hospitals than the LUMC will receive this information, written and oral, the day before surgery. Informed consent from all patients will be sought the day before surgery. No screening, except for the in- and exclusion criteria will be done.

After giving his or her informed consent to participate in the study, each patient will be assigned a unique study number. This number is for example necessary when blood is transferred to the central clinical chemical laboratory (CKCL).

*Pre operative*

Pre-operative blood samples will be drawn at least more than 24 hours before surgery (only venous systemic sample). This whole blood sample will be brought to the CKCL, where a whole blood stimulation (WBS) will be performed.

*Anesthesia*

Administration of anesthetics will be performed according to the fast-track protocol

- Administration allowed:
  - Propofol
  - Remiventanil
  - Suventanil
  - Dobutamin
  - Enoximone
  - Noradrenalin

All patients will be administrated Tranexamic acid.

- No administration of:
  - Ketamine
  - Sevofluran
  - Dexamethason

### *Operation*

A coronary sinus catheter is placed by the anesthesiologist through a jugular vein into the right atrium and placed by the surgeon in the coronary sinus during the mitral procedure (the mitral valve is reached by the transseptal approach in Leiden as a standard procedure). The procedure will not interfere with the duration or procedure of the operation. The catheter is removed if the patient recovered well enough to leave the intensive care unit or 24 hours postoperative. Collected blood, as described below, will be placed on ice immediately and transported to the laboratory (CKCL), where it is centrifuged twice and stored at -80°C in aliquots. The first time that the blood is centrifuged will be at 4°C with 2990RPM. The second time will be in a Eppendorf centrifuge at 4°C with 10.000RPM. Finally it will be stored at -80°C. The analysis of the samples will be with a human-multiplex panel of Bio Rad.

In addition, two biopsies will be performed, one just after the cardioplegic arrest of the heart and the other just before release of the cross-clamp and thus restoring normal blood flow to the coronary circulation, and the tissue will be divided in two parts and stored in both formalin and snap frozen to -80°C.

Sampling of blood will take place at the following moments:

- 1: Pre-operative blood samples (only venous systemic sample).
- 2: After induction of anesthesia / before cardiopulmonary bypass (only systemic sample).
- 3: At 1, 5, 15, 30, 45, 60 min. 4, 6, 10, 18 and 24 hours after release of the aortic cross clamp from the coronary sinus catheter. At 0, 15, 30, 60 min. 4, 6, 10, 18 and 24 hours after release of the aortic cross clamp from the systemic circulation (arterial line).
- 4: Venous systemic samples will be obtained on day 3 and 5 after surgery.

### *Measurements*

We will examine the following:

- A. Factors related to the acute inflammatory response (e.g IL-6, ICAM1, vWF)
- B. Factors that are likely involved in the pathophysiology of ischemia-reperfusion injury (e.g cytokines, p-selectin, ICAM1)
- C. Markers of myocardial injury (e.g CPK-MB, troponins)
- D. Evaluation of endomyocardial biopsies will be performed, guided by the findings of the biomarkers essays (for example Toll-Like Receptors)



The MIRI (Myocardial Ischemia Reperfusion Injury) study, understanding the effects of heart failure surgery to improve safety and outcome.

#### *Withdrawal of individual subjects*

Subjects can leave the study at any time for any reason if they wish to do so without any consequences.

#### *Intention to treat*

Not applicable.

### **3.4 Required Clinical Evaluations**

Measurements during the patient's ICU- (Intensive Care Unit) and OR (Operation Room) stay will be obtained from the hospital's EPD system.

The total amount of extra blood samples taken, are:

- Pre operative (nursing staff): max. 3.5 ml (Heparine tube) + 10 ml (EDTA-tube)
- Operative (OR): 100 ml (10 ml per sample)
- Post operative (ICU): 100 ml
- Day 3 and 5 post operative: max. 2 x 10 ml (EDTA tube)

### **3.5 Data Handling and Record Keeping**

Data will be obtained from the Metavision computer system of the ICU and OR, and from the patient's medical record. The blood samples and biopsies will be stored at -80°C.

All data will be entered after validation in a computer system for subsequent tabulation and statistical analysis. The data will be handled confidentially and anonymously.

## 4. Statistical Considerations and Data Analysis

---

### 4.1 Sample size

The large number of biomarkers, all with different biological variation and the various comparisons makes an exact calculation of patients needed difficult. The number of 4 x 20 patients is based on what is found in other studies and it reflects roughly our yearly number of operations performed in each group.

After 5 patients are included in each group, initial biological essay-studies will be started to confirm:

- 1) The number of patients needed to draw adequate conclusions on ischemia-reperfusion injury and systemic inflammatory response
- 2) That the number and timing of sampling is adequate. If the sample size or -time seems to be inaccurate, it will be adjusted.

### 4.2 Statistical methods to be employed

A parametric test should be obtained if the data are sampled from a population that follows a Gaussian distribution (at least approximately). A non-parametric test or repeated measures ANOVA will be obtained if the data will not be sufficient to the mentioned assumption above.

$P < 0.05$  will be considered statistically significant for the primary outcome measure.

The statistical analysis will be conducted using the SPSS (Statistical Package for the Social Sciences) statistical package, release 12.0.1 (SPSS Inc., Chicago, IL).



The MIRI (Myocardial Ischemia Reperfusion Injury) study, understanding the effects of heart failure surgery to improve safety and outcome.

## **5. Safety reporting**

---

### **5.1 Section 10 WMO event**

In accordance to section 10, subsection 1, of the WMO, the investigator will inform the subjects and the reviewing accredited METC if anything occurs, on the basis of which it appears that the disadvantages of participation may be significantly greater than was foreseen in the research proposal. The study will be suspended pending further review by the accredited METC, except insofar as suspension would jeopardise the subjects' health. The investigator will take care that all subjects are kept informed.

### **5.2 Adverse and serious adverse events**

Not applicable

### **5.3 Data Safety Monitoring Board (DSMB)**

Not applicable

## 6. Ethical considerations

---

### 6.1 Regulation Statement

The study will be conducted according to the principles of the Declaration of Helsinki (accepted by the WMA General Assembly, 9 October 2004, Tokyo) and in accordance with the Medical Research Involving Human Subjects Act (WMO).

### 6.2 Recruitment and Consent

The protocol of this study will be submitted to the Medical Ethics Committee of the Leiden University Medical Centre. The study will not commence before formal approval has been granted. After assessment of eligibility, the subjects will receive oral and written explanation about the study. Only patients who give their written acknowledgement of informed consent will participate to this study.

### 6.3 Objection by minors or incapacitated subjects

Patients younger than 18 years and adults unable to sign the informed consent are excluded.

### 6.4 Benefits and risk assessment, group relatedness

The proposed study aims to optimize the surgical treatment. The measurements necessary to assess the defined study endpoints are not expected to negatively influence the result of treatment. The use of the catheter will have an insignificant risk.

### 6.5 Compensation for injury

The Leiden University Medical Center has a liability insurance which is in accordance with article 7, subsection 6 of the WMO.

The LUMC (also) has an insurance which is in accordance with the legal requirements in the Netherlands (Article 7 WMO and the Measure regarding Compulsory Insurance for Clinical Research in Humans of 23th June 2003). This insurance provides cover for damage to research subjects through injury or death caused by the study.

1. € 450.000,-- (i.e. four hundred and fifty thousand Euro) for death or injury for each subject who participates in the Research;
2. € 3.500.000,-- (i.e. three million five hundred thousand Euro) for death or injury for all subjects who participate in the Research;
3. € 5.000.000,-- (i.e. five million Euro) for the total damage incurred by the organisation for all damage disclosed by scientific research for the Sponsor as 'verrichter' in the meaning of said Act in each year of insurance coverage.



The MIRI (Myocardial Ischemia Reperfusion Injury) study, understanding the effects of heart failure surgery to improve safety and outcome.

The insurance applies to the damage that becomes apparent during the study or within 4 years after the end of the study.



The MIRI (Myocardial Ischemia Reperfusion Injury) study, understanding the effects of heart failure surgery to improve safety and outcome.

## **7. Administrative aspects and publication**

---

### **Access to source data and documents**

All study data will be handled confidentially. The investigator will retain the original of all source documents for a period of two years after the report of the study has been finalized, after which all study-related documents will be archived and kept on microfilm, which will be kept according to GRP regulations. The results of this study will be published in an international scientific journal.

## 8. List of Abbreviations

---

CABG	Coronary Artery Bypass Graft
CKCL	Central Clinical Chemical Laboratory
CPB	Cardio Pulmonary Bypass
GRP	Good Research Practice
ICAM1	Intercellular Adhesion Molecule - 1
ICU	Intensive Care Unit
IL-6	Interleukine-6
LUMC	Leiden University Medical Centre
LV EF	Left Ventricular Ejection Fraction
METC	Medical Research Ethics Committee (MREC); in Dutch: Medisch Ethische Toetsing Commissie
MIRI	Myocardial Ischemic Reperfusion Injury
OR	Operation Room
RMA	Restrictive Mitral Valve Repair
SAE	Serious Adverse Event
SIRS	Systemic Inflammatory Response Syndrome
vWF	von Willebrand Factor
WBS	Whole Blood Stimulation
WMO	Medical Research Involving Human Subjects Act (Wet Medisch-Wetenschappelijk Onderzoek met Mensen)

## 9. Reference List

---

1. Bax JJ. *Restrictive annuloplasty and coronary revascularization in ischemic mitral regurgitation results in reverse left ventricular remodelling*. *Circulation*, 2004;110(11 Suppl 1):II103-8
2. Ruel M. *Vasomotor dysfunction after cardiac surgery*. *Eur J CardioThorac Surg* 2005;26:1002-14
3. Laffey JG. *The systemic inflammatory response to cardiac surgery*. *Anesthesiology* 2002;97:215-252
4. Neumann FJ. *Cardiac release of cytokines and inflammatory response in acute myocardial infarction*. *Circulation*, 1995;92:748-553
5. Carden DL. *Pathophysiology of ischaemia-reperfusion injury*. *J Pathol*, 2000;190:255-66
6. Deng MC. *Impact of left ventricular dysfunction on cytokines, hemodynamics and outcome in bypass grafting*. *Ann Thorac Surg* 1996;62:184-190
7. [http://www.eindhoven.nl/Mission!/professional/Mission\\_prof\\_index\\_flowchart\\_HF.htm](http://www.eindhoven.nl/Mission!/professional/Mission_prof_index_flowchart_HF.htm)

## Appendix A: Patiënteninformatie LUMC

Versie 1, d.d. 7 december 2007

Patiënteninformatie ten behoeve van een wetenschappelijk onderzoek naar:

### **De invloed van de functieovername van het hart op het herstel na de hartoperatie**

Geachte mevrouw / mijnheer,

In aansluiting op het gesprek met uw behandeld arts ontvangt u hierbij de schriftelijke informatie die betrekking heeft op het wetenschappelijk onderzoek waarvoor uw medewerking is gevraagd. Dit onderzoek wordt verricht om inzicht te krijgen waarom het herstel na een hartoperatie voor een kleine groep patiënten gecompliceerder is dan voor de meeste patiënten.

#### **Inleiding**

U ondergaat binnenkort een operatie aan de mitraalklep van het hart. Tijdens deze operatie worden de functies van het hart en de longen tijdelijk overgenomen door een hart-longmachine. In een kleine groep patiënten zien we dat het herstel na de operatie bemoeilijkt wordt door complicaties die door de functieovername door de machine kunnen optreden. Deze complicaties ontstaan mogelijk doordat, als reactie op de functieovername, er stoffen in het bloed vrijkomen. Het is onbekend welke specifieke stoffen er vrijkomen en of ze uit het hart komen.

#### **Doel van de studie**

Bij gebruik van de hart-longmachine ontstaat er een periode waarin er geen bloed door het hart stroomt en waardoor er lichte schade aan het hart zou kunnen ontstaan (ischemie). Deze schade aan het hart blijft beperkt doordat aan het einde van de operatie het hart weer opnieuw van zuurstofrijk bloed wordt voorzien (reperfusie). Het is bekend dat de tijdelijke periode van ischemie bij een klein aantal mensen problemen veroorzaakt waardoor zij mogelijk langer in het ziekenhuis moeten blijven. Hoe deze problemen precies ontstaan is nog onduidelijk.

Met dit onderzoek willen we achterhalen of het hart, nadat er weer bloed door stroomt, stoffen aan het bloed gaat afgeven die verantwoordelijk kunnen zijn voor de problemen. Door deze informatie hopen we dat we in de toekomst beter in staat zullen zijn om dergelijke complicaties na de operatie te voorkomen en het herstel te bevorderen.

#### **Opzet van de studie**

Om het effect van de ischemische periode op het hart te bestuderen zal er ten behoeve van dit onderzoek aan het einde van deze periode een zeer kleine hoeveelheid hartweefsel worden weggenomen. Wanneer er vervolgens weer bloed door het hart stroomt, wordt er op vaste tijdstippen een kleine hoeveelheid bloed afgenomen. Hiertoe wordt er tijdens de operatie een extra catheter (dun slangetje) via de hals tot in het hart gebracht. Via deze kleine catheter kan direct uit een ader van het hart het bloed worden afgenomen. De catheter zal 24 uur in het hart blijven zitten om ook na de operatie op een vast aantal tijdstippen een buisje bloed te kunnen afnemen. Hierna zal de catheter worden verwijderd. In totaal zal de hoeveelheid bloed die wordt afgenomen ongeveer 230 ml zijn (ter vergelijking: bij donatie voor een bloedtransfusie wordt 500 ml afgenomen). Dit vormt geen serieuze belasting voor uw lichaam. Uw gegevens zullen verzameld en vergeleken worden met de andere patiënten die aan het onderzoek deelnemen.

#### **Wat betekent meedoen aan deze studie?**

Wanneer u besluit mee te doen aan dit onderzoek zal de behandeling van uw ziekte niet anders zijn dan wanneer u besluit niet mee te doen. Deelname aan dit onderzoek heeft voor u persoonlijk geen voordeel of nadeel. Het wegnemen van het hartweefsel en het inbrengen van de extra catheter brengen geen onnodige risico's met zich mee.



The MIRI (Myocardial Ischemia Reperfusion Injury) study, understanding the effects of heart failure surgery to improve safety and outcome.

### **Vrijwilligheid van deelname**

Uw medewerking aan dit onderzoek is geheel vrijwillig. U kunt zich te allen tijde terugtrekken uit het onderzoek, zonder dat dit nadelige consequenties heeft voor uw verdere behandeling. U bent niet verplicht de reden van uw terugtrekken aan de behandelend specialist te melden.

### **Privacy**

Alle gegevens die we voor dit onderzoek over u en uw ziekte worden verzameld, zullen strikt vertrouwelijk worden behandeld. Deze vallen onder het medisch beroepsgeheim. Uw privacy zal zorgvuldig worden bewaakt. Uw gegevens zullen anoniem worden verwerkt en de resultaten van het onderzoek zullen bij publicatie in een wetenschappelijk tijdschrift niet tot u te herleiden zijn. Het materiaal, zowel het bloed als de stukjes hartweefsel, worden onder een speciaal nummer opgeslagen waardoor het niet meer tot u herleidbaar is. Aangezien de uitkomsten van het onderzoek pas een jaar na deelname van de laatste patiënt bekend zullen zijn, hebben deze voor u als patiënt geen betekenis meer. Daarom is besloten deze resultaten niet aan u terug te koppelen.

### **Verzekering**

Zoals wettelijk is voorgeschreven, is er door het LUMC een verzekering afgesloten waaruit eventuele schade als gevolg van het onderzoek betaald kan worden. Wanneer u vindt dat u schade heeft ondervonden als gevolg van deelname aan het onderzoek kunt u contact opnemen met de arts onderzoeker, vermeld onder aan de brief.

### **Tot slot**

Dit onderzoek is ter beoordeling voorgelegd aan en na beoordeling goedgekeurd door de Medisch Ethische Commissie van het Leids Universitair Medisch Centrum en na beoordeling goedgekeurd op ..-.-..

Als u nu of op een later tijdstip vragen of twijfels hebt ten aanzien van uw deelname, het verloop van het onderzoek, het risico of uw rechten, dan kunt u zich wenden tot de arts onderzoeker, uw behandelend arts of een onafhankelijk arts. De laatstgenoemde arts is niet bij de uitvoering van dit onderzoek betrokken, maar wel goed op de hoogte van het onderzoek.

De onafhankelijk arts voor dit onderzoek is J. Braun, thoraxchirurg, telefoon: 071-5264022.

Bij voorbaat hartelijk dank voor uw deelname,

Dr. R.J.M. Klautz  
Thoraxchirurg  
Afdeling Thoraxchirurgie  
Telefoon: 071-5264022





The MIRI (Myocardial Ischemia Reperfusion Injury) study, understanding the effects of heart failure surgery to improve safety and outcome.

Ondergetekende verklaart dat de hierboven genoemde persoon zowel mondeling als schriftelijk over het bovenvermelde onderzoek is geïnformeerd. Hij/zij verklaart tevens dat voortijdige beëindiging van de deelname door bovengenoemde persoon, van geen enkele invloed zal zijn op de zorg die hem of haar toekomt.

Naam: ..... (duidelijk schrijven aub)

Functie: .....

Handtekening: .....

Datum:                    -            -            (dag-maand-jaar)