# Ablation of slow conducting anatomical isthmuses in patients with repaired Tetralogy of Fallot, who undergo reoperation for pulmonary valve replacement and who are at risk for isthmus related ventricular arrhythmias.

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1) To evaluate the feasibility and the acute effect of intra-operative cryoablation of the slow conducting anatomical isthmuses (endpoint bidirectional conduction block) and on the re-inducibility of monomorphic isthmus dependent VT. 2) To study the...

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| **Ethical review** | Approved WMO |
| **Status** | Completed |
| **Health condition type** | Other condition |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON39860

**Source**
ToetsingOnline

**Brief title**
Tetralogy of Fallot

### Condition

- Other condition
- Cardiac arrhythmias

**Synonym**
Tetralogy of Fallot

**Health condition**

hartaandoeningen, congenitaal

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Leids Universitair Medisch Centrum
**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** Cryoablation, Intra-operative Ablation, Tetralogy of Fallot, Ventricular Tachycardia

## Outcome measures

**Primary outcome**

The main study parameters are: (1) prevalence and characteristics of slow conducting anatomical isthmuses, (2) inducibility of monomorphic isthmus related VT before intra-operative cryoablation, (3) histological and electrophysiological characteristics of the biopsies taken from slow conducting isthmuses (re-operation) and the unfundibular muscle which is the most frequent location of a potential slow conducting isthmuses later in life (initial repair).

The main study endpoints are: (1) achievement of bidirectional conduction block after intra-operative cryoablation, (2) re-inducibility of isthmus dependent monomorphic VT after intra-operative cryoablation and (3) occurrence and recurrence of VA during follow-up.

**Secondary outcome**

Not applicable.

# Study description

### Background summary

Tetralogy of Fallot (TOF) is the most common severe congenital heart disease and is associated with late morbidity and mortality due to ventricular arrhythmias (VA). Patients with documented or suspected VA usually receive implantable cardioverter defibrillators (ICDs). However, not all VA are life-threatening although an important source of morbidity. In addition, ICDs do not prevent VA therefore additional and/or alternative treatment options are required. Of importance, the majority of VA associated with TOF are monomorphic ventricular tachycardias (VT). We recently could demonstrate that the substrate for the majority of these monomorphic VTs are slow conducting anatomical isthmuses bordered by unexcitable tissue. These slow conducting isthmuses may be the consequence of the initial repair in childhood but may also be due to the abnormal myocardium of the malformation itself. Targeting these isthmuses by catheter ablation has been shown to prevent VT recurrence and is the accepted current approach in clinical practice. Patients after initial total repair of TOF may require a reoperation for pulmonary valve regurgitation. However, simply replacing the valve does not affect the risk for VT. During reoperation potential slow conducting isthmuses can be ablated with the potential to prevent VT recurrence but also VT occurrence and thereby *curing* the isthmus dependent monomorphic VT provided that isthmus block is achieved. Preventive ablation of the slow conducting isthmuses during surgery becomes particular important if pulmonary valve replacement (PVR) by a homograft is performed. In this case, the homograft may cover important parts of the slow conducting isthmus which makes catheter ablation at a later stage impossible and is the most important reason for ablation failure in patients that present with VT after PVR.

### Study objective

1) To evaluate the feasibility and the acute effect of intra-operative cryoablation of the slow conducting anatomical isthmuses (endpoint bidirectional conduction block) and on the re-inducibility of monomorphic isthmus dependent VT.
2) To study the pathomechanism of slow conduction within these isthmuses by comparing histological and electrophysiological characteristics of biopsies in patients after repair of TOF who undergo re-operation and of patients who undergo first total correction.
3) To assess the long-term results of intra-operative cryoablation of the slow conducting anatomical isthmuses on recurrence and occurrence of monomorphic VT.

### Study design

A prospective duo-centre cohort study.

### Intervention

Intra-operative cryoablation of the slow conducting anatomical isthmuses.

### Study burden and risks

Group A: All patients with repaired TOF who are accepted for PVR will undergo electrophysiologic evaluation consisting of programmed electrical stimulation (PES) and right ventricular electro-anatomical mapping (EAM) before operation. Only EAM is part of the research protocol, except for patients who previously experienced an episode of spontaneous VA. Right ventricular mapping is performed through the same venous access already obtained for PES and performed using a standard non-fluoroscopic 3D mapping system (CARTO 3). EAM takes additional 10-15min procedure time and has no specific additional risks. During operation, a biopsy will be taken from the infundibular septum in all patients which is the most frequent location of slow conducting myocardium. The intra-operative biopsy is a study procedure, which is associated with minimal risks and taken from an already diseased area. Furthermore, intra-operative cryoablation will be performed in patients with slow conducting anatomical isthmuses and/or VA. The intra-operative cryoablation is part of the investigational treatment in patients with slow conducting anatomical isthmuses but without documented or induced VA. However, these patients are still at high risk to develop arrhythmias from these areas after re-operation. Of importance, these specific areas are difficult to target or impossible to target by catheter ablation after valve replacement as the homograft covers important parts. Cryoablation is associated with minor risks and the standard intra-operative treatment for other arrhythmias. In patients inducible for VA and/or patients with slow conducting anatomical isthmuses postoperative EP study and EAM will be performed to evaluate the results of surgical cryoablation. For patients with a slow conducting isthmus only as potential substrate for future VTs, EPS and EAM is part of the research protocol. The specific risks of the tests are described in detail in the protocol.
Group B: The tissue that will be investigated regarding histological and electrophysiological characteristics is tissue that will be removed as part of the repair operation, therefore there is no additional risk.

## Contacts

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

## Inclusion criteria

1. Patients with Tetralogy of Fallot, who will undergo pulmonary valve replacement.
2. Patients from the age of eight years.

## Exclusion criteria

1. Inability to sign informed consent by the patient or his legal representative.
2. Inability to comply with the protocol due to hemodynamic instability.

# Study design

## Design

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| Study type: | Interventional |
| Intervention model: | Other |
| Allocation: | Non-randomized controlled trial |
| Masking: | Open (masking not used) |

**Primary purpose:** Basic science

## Recruitment

NL

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|---|---|
| Recruitment status: | Completed |
| Start date (anticipated): | 15-05-2013 |
| Enrollment: | 60 |
| Type: | Actual |

# Ethics review

Approved WMO

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| Date: | 01-05-2013 |
| Application type: | First submission |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden) |
| | metc-ldd@lumc.nl |

Approved WMO

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|---|---|
| Date: | 12-11-2013 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden) |
| | metc-ldd@lumc.nl |

Approved WMO

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|---|---|
| Date: | 12-12-2013 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden) |
| | metc-ldd@lumc.nl |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

ID: 21437
Source: Nationaal Trial Register
Title:

## In other registers

| Register | ID |
|---|---|
| CCMO | NL41727.058.12 |
| Other | Volgt |
| OMON | NL-OMON21437 |