

# An Investigation into the role of Matrix Metalloproteinases (MMPs) in Lower Limb Vascular Restenosis

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<b>Registration date</b> 29/09/2006	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 20/04/2015	<b>Condition category</b> Surgery	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

Not provided at time of registration

## Contact information

### Type(s)

Scientific

### Contact name

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### Contact details

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## Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

N0544170118

# Study information

## Scientific Title

An Investigation into the role of Matrix Metalloproteinases (MMPs) in Lower Limb Vascular Restenosis

## Study objectives

Does blocking enzymes in the wall of the artery - matrix metalloproteinases (MMPs) - prevent the artery from narrowing after angioplasty (balloon treatment) or surgery (bypass graft)?

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Not provided at time of registration

## Study design

Randomised controlled trial

## Primary study design

Interventional

## Secondary study design

Randomised controlled trial

## Study setting(s)

Hospital

## Study type(s)

Treatment

## Participant information sheet

## Health condition(s) or problem(s) studied

Surgery: Cardiovascular

## Interventions

Patients under the care of the Cambridge Vascular Unit undergoing femoro-popliteal angioplasty or femoro-popliteal/tibial bypass will be eligible for the study. The indication for intervention will be severe limb ischaemia (rest pain, ulceration, gangrene) or short distance claudication failing to respond to medical and exercise therapy.

### Pre-procedural Noninvasive Assessments:

Following informed consent the degree of ischaemia will be measured using ankle brachial pressure index (ABPI) measurements and transcutaneous oxygen measurements (TcPO<sub>2</sub>). Arterial stiffness and Endothelial Function will also be determined by applying a pressure probe to the carotid and radial arteries in turn with concomitant ECG gating.

### Percutaneous Angioplasty:

These procedures are routinely carried out as either day cases or with overnight stay. During the

procedure two 40 ml blood samples will be taken for plasma MMP analysis, plus CRP level, cholesterol, U&Es, elastin breakdown products, elastase activity and genetic analyses. One 40 ml sample will be systemic venous blood taken from the venous access cannula inserted for the procedure. A second 40 ml sample will be taken from the femoral vein in the leg undergoing the procedure. This is blood returning from the treated leg, and is more likely to reflect the local MMP activity potentially related to restenosis. On the same day as the PTA procedure the patients will be commenced on the SDD/placebo medication in a double blind randomised design. One tablet (25 mgs SDD) twice per day. This will be continued for 24 weeks post procedure.

#### **Post Procedure Follow Up:**

Colour duplex ultrasound assessment of the angioplasty site will be used to document blood velocities across the lesion and percentage of restenosis. These measurement will take place in the Vascular Laboratory at the following intervals: 1, 6, 12, 24, 36, 52 weeks. At 24 and 52 weeks repeat blood samples will be taken.

#### **Femoro-distal bypass:**

The same pre-procedural assessments will be performed as for PTA. These assessments will be co-ordinated with the patients pre-clerking clinic visit, usually 1 week prior to surgery. During surgery 2 tissue samples will be taken. One will be an arterial wall biopsy, to be analysed for arterial tissue MMP status. This will be taken from the proximal anastomosis site as a small ellipse avoiding any stenosis/narrowing of the anastomosis. A second sample will be taken from the venous tissue used for the bypass for MMP analysis.

As soon as patients are taking oral medication post operatively (usually 12-24 hours) the SDD /placebo medication will be commenced. As for PTA this will be for 24 weeks.

Prior to discharge the graft will be scanned to establish baseline graft velocities and any early abnormalities. As with the PTA protocol, further graft monitoring for stenosis, ABPI, and TcPO<sub>2</sub> measurements will occur at 6, 12, 24, 36 and 52 weeks. Surveillance of vein grafts at these intervals is normal clinical practice. Blood samples will be taken at 24 and 52 weeks.

#### **Intervention Type**

Mixed

#### **Primary outcome measure**

1. MMP activities SDD versus placebo
2. CRP levels
3. Endothelial function and re-stenosis
4. Arterial wall stiffness and re-stenosis.

#### **Secondary outcome measures**

Not provided at time of registration

#### **Overall study start date**

18/07/2005

#### **Completion date**

18/07/2008

## **Eligibility**

**Key inclusion criteria**

Serum samples collected at the time of vascular intervention (radiologist or surgeon). Follow up samples by vascular research fellow.

Arterial wall and vein biopsies taken at the time of surgery by operating surgeon.

**Participant type(s)**

Patient

**Age group**

Adult

**Sex**

Both

**Target number of participants**

35 in each trial arm, ie 270

**Key exclusion criteria**

1. Patient unable to give informed consent
2. Age < 18 years
3. Pregnancy, planned pregnancy
4. Life expectancy less than 12 months
5. Inability to monitor the angioplasty site or graft with ultrasound for stenosis
6. Unable to take SDD (ie allergic reaction) or currently taking tetracyclines
7. Unable to take adjuvant treatment with antiplatelet/anticoagulant agent and statin

**Date of first enrolment**

18/07/2005

**Date of final enrolment**

18/07/2008

**Locations****Countries of recruitment**

England

United Kingdom

**Study participating centre**

Addenbrooke's NHS Trust

Cambridge

United Kingdom

CB2 2QQ

# Sponsor information

## Organisation

Record Provided by the NHSTCT Register - 2006 Update - Department of Health

## Sponsor details

The Department of Health, Richmond House, 79 Whitehall  
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United Kingdom  
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## Sponsor type

Government

## Website

<http://www.dh.gov.uk/Home/fs/en>

# Funder(s)

## Funder type

Government

## Funder Name

Cambridge Consortium - Addenbrooke's (UK), NHS R&D Support Funding

# Results and Publications

## Publication and dissemination plan

Not provided at time of registration

## Intention to publish date

## Individual participant data (IPD) sharing plan

## IPD sharing plan summary

Not provided at time of registration