PARTICIPANT INFORMATION SHEET FOR HEART ATTACK PATIENTS

Study Title: *Oxford Acute Myocardial Infarction Study – OXAMI study*

You are being invited to continue being part of a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives or nursing staff on the ward if you wish. Part 1 tells you the purpose of this study and what will happen to you if you take part. Part 2 gives you more detailed information about the conduct of the study.

Please ask us if there is anything that is not clear or if you would like more information. Thank you for reading this

PART 1

What is the purpose of the study?

- To study in more detail heart disease in patients attending the John Radcliffe Hospital for standard investigations and treatments.
- To examine some of the latest clinical investigation methods used to assess heart artery disease, and
- To see how these combining results from these investigations may improve the way we manage patients with heart artery disease.

Why have I been invited?

You have just received coronary angioplasty/stent procedure at John Radcliffe Hospital to treat your heart attack. During the procedure, we included you in this clinical research study, which involved taking some blood samples and making some additional measurements. With the emergency treatment over, we now wish to invite you to continue participation in this study.

Your participation is important to us as researchers because we are aiming to get a clearer idea of what happens during heart attacks. Please be assured that at all times your safety is the number one priority and your standard treatment is in no way compromised by being included in any part of this study.

What would happen to me if I continue to take part?

You will join up to 500 patients who will be taking part in a research programme at the John Radcliffe Hospital in Oxford. We want to monitor your recovery from the heart attack by carrying out some investigations which are additional to the standard care pathway. ***Please note that all these investigations are proven and safe techniques used by clinicians*.**

How is this experience different from standard care?

Typically, a patient with a heart attack may undergo some or all of these investigations:

Whilst in hospital:
- Angiogram and stenting procedure
- Blood test
- Heart tracings (ECGs)
- Ultrasound scan of the heart
- Pictures taken from inside the artery (IVUS, OCT)
- Measurements of blood flow and pressure from inside the artery (IMR)

After discharge from the hospital:
- 1 to 2 follow-up consultations with the cardiology team at the outpatient clinic.

What is additional in this research study?

For this research study, participants will have standard care procedures. There may also be some additional procedures (as listed below); some of these may be repeated during the course of the study. There may also be repeat hospital visits **or** follow up telephone calls. A list of study time-points is below. Visits to hospital which are for the purpose of the research study ("research visits") are planned over the next 6 months. After that there will be yearly follow-up sessions until 10 years after the procedure. This follow up plan gives us a unique opportunity to keep track of your recovery from the initial treatment.

List of study time-points:

a. After the stenting treatment until discharge from the hospital
b. 1 month after stenting treatment
c. 6 months after stenting treatment
d. Yearly after stenting treatment for up to 10 years

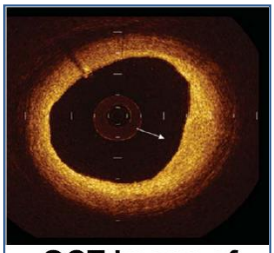
Investigations related to the study will be scheduled at **EACH** of the listed time points. The total number of investigations performed at each time point will be dependent on your consent. When there is scheduled return visit to the hospital for the purpose of this study, we will reimburse you with travel costs. The following section provides a description of the investigations performed at each time point. **The study team will indicate which research procedures you are likely to have as part of your participation in this study using the tick boxes below**. At each time point, you will be informed by the clinical/research team which procedures are carried out for research and which are part of standard care.

List of investigations at each time point:

□ **Data collection**
- We will collect clinical data from your procedure and following research/clinical investigations so we can monitor your progress after the initial angioplasty/stenting procedure.

□ Quality of Life and Patient Reported Outcomes Measures
- You may also be asked to fill in short and simple questionnaires about how you feel about your health, treatment and quality of life.

- **Blood sample collection (5 minutes)**:
  - We will take blood (approx. 25ml or just over a tablespoon) to look at trends over time of biochemical "markers" related to heart artery disease. Blood will be collected in the following ways, depending on the stage of the study:
    - From the needle/catheter inserted for the purpose of the angioplasty procedure.
    - From an extra, small needle/cannula (under local anesthetics) in the vein of either the groin or elbow or from the vein in the arm
  - There would be a maximum of 19 blood sample times in total, of which 5 would be during the angioplasty/stent procedure itself.

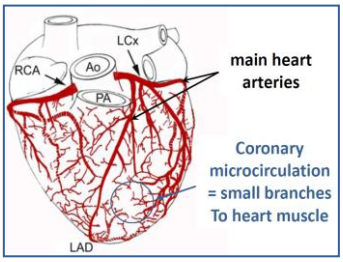


OCT image of heart artery

- **Pictures taken from within the heart artery (intravascular imaging, approx. 5-10 minutes):**
  - We now use special, tiny cameras which are guided through the artery to take pictures from the inside. These internal pictures give us a huge amount of information about the diseased artery.
  - There are different types of cameras available, including Optical Coherence Tomography (OCT) and intravascular ultrasound (IVUS). These imaging techniques are used in routine clinical practice and do not cause harm or discomfort to the patient.
  - <u>These pictures are only taken during the angiogram/angioplasty/stenting treatment</u> (<u>**These are not taken at each of the yearly follow up hospital visits**</u>).
  - Participants may receive up to three extra investigations in the study (in addition to number of scans in a typical clinical setting, as above).

- **Use of protection devices (PDs, 5-10 minutes)**:
  - Several types of PDs are used in routine clinical practice to remove and discard any 'debris' material/clot from the coronary artery during the angioplasty procedure. <u>Therefore PDs will only be used during the angioplasty/stenting procedure as required (**These are not performed at each of the yearly follow up hospital visits**).</u>
  - This material contains a lot of useful biological information about the "hot spot" within the blocked artery. So we will keep and analyse this material.

- **Measurement of blood flow characteristics aka "IMR" (20-30 mins)**:
  - The picture shows the main heart arteries and smaller branches of arteries bringing blood into the muscles.
  - By passing a special catheter wire down the main heart arteries, we are able to measure the blood flow characteristics and function in these small heart vessel branches. Study participants may receive up to three extra measurements.
  - <u>These measurements *will require a repeat angiography,* 48 hours, 1 month and 6 months after your first (clinical) angiography (**These are not taken at each of the yearly follow up hospital visits**).</u>



- **Prolonged infusion of adenosine (12 hours)**
  - Adenosine is a naturally occurring compound used in routine clinical practice to increase blood flow. It works by opening the small arteries of the heart. You will have been given this drug already either to treat or measure the effects from the heart attack.
  - We know that after a heart attack the small arteries of the heart muscle may not work well and this may cause further damage to the heart muscle. Since adenosine increases the blood flow to the heart, we would like to understand how a longer infusion of adenosine affects the tests we do on the heart.
  - If you agree, we would continue the adenosine that you have already received at half the dose for 12 hours following your heart attack and measure the effects on blood flow the next day using the IMR technique as described above.
  - <u>The infusion of adenosine will only be given after your heart attack treatment **(The adenosine infusion is not given during any of your follow-up appointments).**</u>

- **Ultrasound scan (20-30 mins)**

- This involves the operator applying a small amount of lubricating gel and a small probe to the skin to obtain pictures of the organ(s) lying beneath. This could be your heart, or blood vessels in your arm or neck.
- Participants in the study may receive up to 15 ultrasounds in this study of which some will be needed for clinical reasons.

Magnetic resonance imaging (MRI) of the heart (maximum 75 mins)

- A MRI scanner looks like a Polo Mint (see picture), the hole inside measuring about 60 cm wide. It uses the magnetic properties of different body organ components to obtain highly detailed pictures. It does not involve any radiation, but may require an injection of a small dose of special dye to make scan images clearer.
- MRI scan of the heart is now widely used in clinical setting for assessing various aspects of heart muscle function.
- In some of imaging sessions, we look the effects of the additional oxygen on the images. The oxygen is commonly used to help breathing and has no colour or perceivable smell. You will be asked to wear an oxygen mask or breathe through a mouthpiece during the MRI imaging session. Beyond assessing the effect of the oxygen on the images, we will ask your opinion whether the oxygen improves your comfort in holding your breath.
- During a scan, you will be asked to lie still on your back while your heart is scanned. You will be asked to breathe in and out and hold your breath for several seconds for some of the scans. You will be in constant communication with the operators. You cannot have a MRI scan if you have:

- A permanent pacemaker
- Metal clips in blood vessels of the brain
- An injury to the eye involving fragments of metal
- Shrapnel injuries
- Other metal/electronic implants affected by the magnetic field
- Back pain, unable to lie flat

- The study investigator will confirm your suitability for the scan.
- If you have suspected metal in your eye we will ask if you to have an x-ray of the eye
- Participants may receive up to 4 MRI scans in this study, which are additional to standard care.

ECG

- ECG (electrocardiography) is used to measures the electric impulses of the heart and is performed as part of your standard clinical care. We may ask you to wear a special portable ECG machine called a Holter monitor. The Holter monitor records electrical signals from the heart via a series of electrodes attached to the chest, these electrodes are connected to a small piece of equipment that can be attached to your belt or hung around the neck. The Holter monitor will keep a continuous log of the heart's electrical activity throughout the recording period. We may ask you to wear the Holter monitoring for a maximum duration of three days at time points 2-4.

Follow-up schedule

- We will contact you once a year for the next 10 years. This gives the researchers the opportunity to monitor your progress after the initial angioplasty treatment.
- These yearly check-ups may involve a phone call, or a return visit to the hospital for other investigations to detect the changes observed over a period of time.
- We may send short and simple Quality of Life and Patient Reported Outcomes Measures questionnaires to you via the post, at the study time points listed, if it is not convenient for you to return to the hospital.
- We may also follow your progress by using national health registries, existing cardiovascular databases or by contacting your GP, if appropriate.

Please be assured that you can withdraw from the study at any stage. Your decision to take part in the study during your initial treatment does not mean you have to take part in all study time points.

Are there any side effects/risks of participating?
Please be reassured that all these investigations are proven and safe techniques used by clinicians. We give details of side effects associated with each technique below:

Blood sample collection
Some people find having a cannula inserted uncomfortable and there can be bruising at the site of needle entry.

Pictures taken from within the heart artery (OCT/IVUS)
Both angioplasty/stent and OCT/IVUS involve the placing of very fine guide wires down the arteries using X−Rays (radiation) to position the wires, balloons and stents correctly. But in the case of OCT/IVUS, the actual images are then taken from inside the artery using ultrasound only. So although the correct positioning of the OCT/IVUS apparatus may involve a brief additional exposure to radiation, this is very low in proportion to the entire dose required for angioplasty/stent and is not a significant risk to you.

Use of Protection Devices (PDs)
As with OCT/IVUS, the correct guidance and positioning of the PDs in the vessels may involve a brief additional exposure to X-ray radiation; this is very low in proportion to the entire dose required for angioplasty/stent and is not a significant risk to you. The use of PDs is sometimes associated with temporary angina-like symptoms during the procedure.

Measurement of blood flow characteristics in the heart muscle
This means **up to** three heart angiography procedures which are additional to your standard care:

- Angiogram is associated with a small risk of bleeding and there can be bruising at the access site.
- There is additional exposure to X-ray radiation required for the angiogram each time but is unlikely to lead to any long term effect.
- In order to do an accurate measurement we need to increase the blood flow to your arteries using adenosine. Potential side effects of adenosine are described below. You can tell us to stop the procedure if you feel any discomfort.

Radiation exposure related to the study procedures
Some of the study procedures (OCT/IVUS/IMR) and x-ray of the eye (if required) will incur a small amount of additional radiation exposure. The radiation exposure involved with performing an angiogram and an x-ray of the eye for the purpose of the research is about the same as you would experience from taking a transatlantic flight from United States to London. This is about 10 times less than the exposure required for the procedure required to treat your heart attack. There is minimal risk of long term health effects caused by the addition exposure related to the study.

MRI scans of the heart
MRI is very safe and there are no known significant side effects from the types of scanner that we use. The scan is noisy and we provide headphones to protect your ears. The scan also involves lying flat in a slightly confined space; a small number of people find this claustrophobic. If you are a woman who is pregnant, breast-feeding or who may become pregnant during the study period, you should not take part. If you have suspected metal in your eye we may offer you an x-ray of the eye. An orbital x-ray will involve a small additional radiation exposure as detailed above. A small injection of a special dye called Gadolinium (GAD) is used for the MRI scan. GAD is routinely used in MRI scanning and has a good safety profile. Known side effects are rare and include general feeling of warmth/cool, dizziness, nausea, headache, rash, itching, vomiting, or irritation of the throat. These side effects are reversible upon stopping the infusion. GAD itself is NOT being tested as a treatment in the study. You may also be given medications like adenosine in order to evaluate your heart function fully. Potential side effects of adenosine are described below. If you have any current or previous injury to the lungs, chronic obstructive pulmonary disease (COPD), neuromuscular disorders, morbid obesity or musculoskeletal disorders you may not be given oxygen during the scan. There are no known side

effects or risks of giving oxygen in appropriately selected patients. You can tell us to stop the procedure if you feel any discomfort; we will give you an alarm trigger to hold which can stop the scan at any time.

Administration of adenosine:
Adenosine is a naturally occurring compound and it is used in routine clinical practice. Prolonged infusions of adenosine in heart attack patients have been used before and did not cause any major side effects in the short or long term. Common side effects of adenosine include light headedness, nausea, shortness of breath or chest tightness. Almost all our patients tolerate adenosine without problems but as it is a very short lasting medication the side effects pass quickly when the drug is stopped and any unpleasant symptoms will usually last less than two minutes. You can tell us to stop the procedure if you feel any discomfort.

You may be given adenosine:

1) **as part of the angiogram to measure blood flow characteristics of the heart muscle**
2) **during the MRI scan**
3) **during prolonged infusion of adenosine**

What are the possible benefits?
There is no immediate benefit for you as an individual taking part in this study. We hope that by studying people with your condition using these investigations, we may be able to improve understanding of this condition and help to inform management of future patients.

What happens when the research study stops?
Your participation in the study would end. Copies of any publications connected to this study are available on request from the OXAMI investigators.

If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

PART 2

What if relevant new information becomes available?
Sometimes we (the study investigators) get new information about the procedures being studied. If this happens, we will discuss with you whether you should continue in the study. If there is sufficient evidence to suggest you may be harmed from participating in this study, the study could be stopped.

Unexpected findings during the study
In the event of any unexpected findings which come to light as part of the research procedures in this study, a designated clinical specialist will discuss the implications with you and may arrange for further investigations as necessary. However, it is important to note that this research is not for diagnostic purposes, and is not a substitute for a clinical appointment. So if we find anything unusual, it would be appropriate for us to notify your GP so that they can arrange on-going clinical care for you. But we would only do this after we and the specialist had discussed your options and gained your permission.

What will happen if I don't want to carry on with the study?
You are free to withdraw from the study at any time. If you wish, we can then just make use of the information we already have about you. Alternatively, we can ensure if your samples and information are used for future research it is entirely anonymously, or we can destroy any identifiable samples or information we hold about you. Even if you are not able to take part in every aspect of the study, the information we collected from you will still be extremely useful to the overall scientific value of the study.

What if something goes wrong or I have a complaint?
If you wish to complain about any aspect of the way in which you have been approached or treated during the course of this study, you should contact Prof Keith Channon (Tel: 01865572783) or you may contact the University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865572221 or the head of CTRG, email heather.house@admin.ox.ac.uk. The University has arrangements in place to provide for harm arising from participation in the study for which the University is the Research Sponsor. NHS indemnity operates in respect of the clinical treatment with which you are provided.

Will my taking part in the study be kept confidential?
If you take part in the study, this will be indicated on your hospital medical records. We will also send a letter to your GP, with a copy of this patient information sheet, to inform them that you have agreed to participate in this study. Some parts of your medical records and the data collected from the study would be looked at by authorised persons from the University of Oxford, to check that the study is being carried out correctly. They may also be looked at by authorised persons from the NHS Trust. All investigators have a duty of confidentiality to you as a research participant and nothing that could reveal your identity would be disclosed outside the research site. The data collected from the study will be recorded anonymously and you would not be identifiable from this. We also ask for your permission to allow the researchers access of your medical records during the study period so that we can look up the necessary medical information.

Participation in future research
We will ask if we can contact you about future studies. This is optional i.e. you can take part in this study but decline to be contacted again. If you consent, we will keep your contact details separately from research data you have provided. Both your details and data will carry the same unique ID. This means your data is anonymised but that we can "link" details to data. In this way we can approach patients about studies relevant to their particular healthcare status. You can withdraw your consent for future contact at any time.

What will happen to any samples I give?
All samples will be retained in a secure environment for future analysis and to be stored in an anonymous format at sample storage facilities used by the University of Oxford. Samples collected during this study may be sent to other centres, including those outside the UK, for specific analysis according to the availability of specialist techniques. We will also ask for your consent for the samples

will be stored for 5 years after the end of the study period, to be used in future research as our understanding of heart function grows. We may also seek approval from a recognised ethics committee for use of the samples in future research. This future research may include genetic research (see below). Samples will be destroyed by the research team after the end of ethical approval.

Will any genetic tests be done?
It is possible that some samples will be used for genetic research. This research may be conducted by the study research team or collaborating research teams. The samples will be stored anonymously but a record of who donated the samples will be kept so that we can relate any findings to your medical history. Keeping these records ensures that if you decide to withdraw your consent, we will be able to destroy your samples. Genetic tests would involve looking at common variations in genes that affect how blood vessels work. We do not propose to test for inherited genetic diseases, or for conditions that will involve any other members of your family. There is no evidence to suggest that the results of these genetic studies are likely to have significant implications for you personally.

What will happen to the results of the research study?
We anticipate that the results will be published in a scientific journal for the benefit of the wider medical community. Social media (e.g. twitter) and a study website may also be used to inform participants about the study and its progress. However, individual patients will not be identified and your personal and clinical details will remain strictly confidential. Any scientific publications arising from the study will be available on request to all participants. You would have no legal right to a share of any profits that may arise from the research.

Collaboration and Partnership with Commercial Companies
The University of Oxford, Oxford University Hospitals Trust and the OxAMI study may work in partnership with, and receive support from, commercial companies who provide the devices and imaging technology used during your heart attack treatment and the research investigations. As part of this partnership we may make available research data to the company specifically related to the use of their device or imaging technology. All data is anonmisyed and you would not be identifiable from this.

Who is organising and funding the research?
The investigators are Prof. Keith Channon, Dr. Adrian Banning, Dr. Colin Forfar, Dr. Bernard Prendergast, Prof. Robin Choudhury, Dr. Raj Kharbanda, Dr. Charalambos Antoniades, Dr. Regent Lee, Dr. Vanessa Ferreira, and Dr. Erica Dall'Armellina. If you wish to know more about any aspect of the study, please contact Prof Keith Channon on 01865 851085 or email us at oxami@cardiov.ox.ac.uk. The research is funded by NIHR Biomedical Research Centre, Oxford.

Who has reviewed the study?
The South Central – Oxford C Research Ethics Committee has reviewed and approved the study.

Where can I find independent information about taking part in research?
You can contact local branches of the NHS Patient Advisory Liaison Service (PALS). Here is their website: http://www.pals.nhs.uk/.

Further information and contact details
Prof Keith Channon, Dept of Cardiovascular Medicine, University of Oxford, Level 2 John Radcliffe Hospital, Oxford OX3 9DU, email oxami@cardiov.ox.ac.uk