

## YOUR JOURNEY THROUGH THE TRIAL

### Stage 1: Initial invitation

During your appointment at the outpatient clinic the Orthopaedic Consultant decided you might be suitable for the trial and described the treatment options to you. You were given the Patient Information Leaflet to take home.

### Stage 2: Informed consent

You attend an appointment at the Research Clinic with the study coordinator who describes the trial to you and answers any queries you have. You also have an opportunity to speak to the Orthopaedic Consultant again if you wish. If you decide to participate in the trial and give written consent you will have a blood test and you will also need to complete a questionnaire.

### Stage 3: Confirmation of eligibility

About 1-2 weeks later you receive a letter confirming you are eligible for the study and letting you know the approximate date of your operation. If there is a problem with your blood test results then the surgeon will telephone you.

### Stage 4: Pre-randomisation assessment

You attend the clinic prior to your operation where a physiotherapist will talk to you to find out how you are affected by your knee condition. You will also be asked to spend about 30 minutes filling in some questionnaires about your knee condition and will receive a diary to take home.

### Stage 5: Treatment allocation

The study coordinator will let you know which treatment you were randomly allocated to receive.

### Stage 6: Your operation

You have your knee operation. If you are having the cell grafting option you have a second operation about 3-6 weeks later.

You follow the recommended rehabilitation programme for your treatment.

### Stage 7: Follow-up over ten years

After your operation you attend the usual follow-up clinics and see the surgeon as appropriate. A physiotherapist will assess your progress and will ask you to fill in the study questionnaires. These clinic visits will be at 2-3 months, 6 months and 12 months after your operation.

After Stage 7 you will be contacted annually to complete the questionnaires for the trial and at 3, 5 and 10 years after your operation you will attend the Research Clinic to be assessed by the physiotherapist.



**AUTOLOGOUS CHONDROCYTE  
TRANSPLANTATION / IMPLANTATION VERSUS  
EXISTING TREATMENTS**

## Patient Information Leaflet

**For individuals invited to take part in the trial**



## **Cartilage repair by autologous chondrocyte implantation (CARTILAGE CELL GRAFTING)**

ISRCTN 48911177

### **INTRODUCTION**

*You have been invited to take part in a research study. 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 others if you wish. If there is anything that is not clear or if you would like more information, please ask us. Take as much time as you need to decide whether or not you wish to take part.*

### **PURPOSE OF THE STUDY**

Defects in the cartilage which covers the bones of the knee, do not heal by themselves. A new technique to treat this, called autologous chondrocyte transplantation, (also known as cartilage cell grafting), was developed in Sweden and has been used on a number of patients in the UK and US. This has given good results in many patients but has not yet been tried and tested in a formal trial.

### **WHY HAVE I BEEN INVITED?**

You have been invited to take part in the trial because you have a defect in the cartilage in your knee that is still causing you symptoms even though you have already had surgical treatment for it. Six hundred patients will be invited to take part in this trial in the UK and others in the rest of Europe.

### **DO I HAVE TO TAKE PART?**

*It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. You would still be free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or not to take part, will in no way affect the standard of care you receive.*

### **WHO FUNDS THE STUDY?**

The Medical Research Council is funding the research costs of the study. None of the doctors looking after you will be paid for including you in the study.

The North Staffordshire Multicentre Research Ethics Committee has approved this study.

*Thank you for reading this.*

*You will be given a copy of this INFORMATION LEAFLET and if you agree to take part, a copy of the signed consent form to keep.*

### **CONTACT FOR FURTHER INFORMATION**

Local Coordinator

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or  
Local Principal Investigator

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or  
Chief Investigator  
Professor James Richardson  
Robert Jones and Agnes Hunt Orthopaedic and District  
Hospital NHS Trust  
Tel: Janet Morris (sec) 01691 404386

or  
Heather Smith (Trial Manager)  
Robert Jones and Agnes Hunt Orthopaedic and District  
Hospital NHS Trust  
Tel: 01691 404142

## **RISKS AND BENEFIT**

If you are allocated to the cartilage cell grafting group this involves a 2-stage procedure, so you will have two operations under general anaesthetic. In addition to the normal risks of knee surgery there is a small risk that you may experience an allergic reaction to a substance used in the cell transplantation. However, this reaction is very rare. We hope that whichever treatment you have will help you. However, this cannot be guaranteed. The information we get from this study may help us to recommend the best course of action for patients like you in the future.

As with other research trials of this kind, should taking part in this research project harm you, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms would be available to you.

## **CONFIDENTIALITY**

We will notify your GP that you are participating in the trial.

All information that is collected about you during the course of the research will be entered into the ACTIVE Trial database by study staff and kept strictly confidential. We will need to access your hospital records so that we can collect information on any subsequent surgery or treatment you have on the same knee.

If you have the cell grafting treatment your cells will only be used for your treatment, they will not be stored and used for any other purpose.

## **WHAT HAPPENS TO THE RESULTS?**

The results will be regularly reviewed by an independent Data Monitoring and Ethics Committee. The Committee can stop the study if it is clear that any group of patients is being disadvantaged. At the end of the study the results will be published. You will not be identified in any way.

## **WHAT HAPPENS IF I DO DECIDE TO TAKE PART?**

Sometimes because we do not know which way of treating patients is best, we need to make comparisons. If you do decide to take part you will be put into one of two groups. One group will have the new cartilage cell grafting treatment and the other group will receive the most appropriate alternative treatment. The groups will be allocated by computer, i.e. by random chance. You have a 50:50 chance as to which group you will be in. You will have a full assessment of your knee and be asked to complete questionnaires about your knee function, how it affects your quality of life and about previous treatments.

If you are allocated to the **cartilage cell grafting group**, you will have a 2-stage operation. Both operations will be carried out under general anaesthetic. The first operation (Stage 1) is keyhole surgery during which the defect is cleaned and a small sample of healthy cartilage is taken from the knee. That sample is taken to the laboratory for the cells to be grown. This process is called cell-culture. The cells are grown in a medium containing your own blood. This is why we will need to take 100ml of your blood (about half a cupful) before the first operation. After 3 to 5 weeks, there should be sufficient cells to transplant back into the cartilage defect in your knee.

At the second operation, (Stage 2) the knee is opened and a patch is stitched over the defect. The patch will either be periosteum (the membrane which covers the surface of your bones) or it will be a synthetic material. There will be a 50:50 chance as to which type of patch you will have. If the patch is to be periosteum, the usual procedure is for this to be removed from your shin through a small additional incision just below your knee. Sometimes the periosteum thickens and a further operation may be required to reduce the thickening once the cells have regenerated. A newer procedure, in use for 5 years, is a synthetic patch made from pig collagen. An advantage is that an additional incision is not required and you will not have the possible discomfort in your shin. However there has not yet been long-term follow up of this new type of patch in comparison with periosteum.

The cells grown in the laboratory are then injected into the defect behind the patch and the knee closed with sutures.

If you are allocated to the **alternative treatment group**, your surgeon will discuss the treatments with you. These are debridement, microfracture/drilling or mosaicplasty. They are all different methods carried out under general anaesthetic and have been in use for 5-15 years. Your surgeon will explain them in full and together you can decide which of them is best for you.

### **BLOOD TESTING**

All patients who have cell treatments in the UK such as cartilage cell grafting must have a blood test to show that they are HIV, hepatitis B, hepatitis C, syphilis and human lymphotropic virus (HTLV I & II) negative. If you enter this study we will not know in advance which treatment will be allocated, so all patients who agree to take part will first have a blood test. For this about 7ml (about 2 teaspoons) of your blood will be needed. If you have a positive result you will not be able to take part in the study as you will not be able to have cell cartilage grafting. Since 1994 the Association of British Insurers has stated that a negative HIV test does not affect an insurance application. However, if you test positive for HIV your ability to take out life insurance or a mortgage will be affected. Counselling will be available to you before and after the test if you wish.

### **WHEN WILL I KNOW WHAT GROUP I WILL BE IN?**

When you have decided to participate and have signed a consent form you will be registered for the trial. You may be randomised at this stage and you will be informed which treatment group you will be in. If there is expected to be a delay in treatment longer than 6 months, the group you are in will be allocated nearer the time and you will be told as soon as this happens.

### **HOW LONG WILL I BE IN HOSPITAL?**

Debridement, microfracture/drilling or cartilage grafting Stage 1 are usually undertaken as a day-case procedure.

Mosaicplasty or cartilage grafting Stage 2 generally require a 2 day stay in hospital. You will use a special machine to keep the knee moving but you will not need to stay in bed all the time.

### **WHAT HAPPENS AFTER SURGERY?**

Whichever group you are in, you will have the standard physiotherapy and rehabilitation programme that is best for the treatment you received. After you are discharged you will not be required to attend any further physiotherapy but you will be expected to do your best to follow the exercise programme you have been given. Generally crutches are

needed initially and this may vary from 1 week to 2 months depending on the treatment received. Rehabilitation following the cartilage grafting treatment is likely to be slower than the other treatments because the cells need time to generate repair tissue. You should avoid driving for 7 weeks but how long you are off work will depend on the nature of your employment. If your work is very strenuous, this may be several months. If you wish to resume high contact sports such as rugby, the recommended rehabilitation period is approximately 12 months but the surgeon will advise you on this before you decide whether to take part in the trial. All patients, whichever treatment they receive, will be given a follow-up appointment 2 or 3 months after surgery and again at 6 months and at 1 year after surgery. This will give your surgeon a chance to see how you are progressing. On each occasion you will be asked to complete some questionnaires. You will also have your knee function measured by a person who does not know which treatment you have had, and it is important that you do not tell them and that you wear a stocking (which will be provided) to cover both your knees (so that person cannot be influenced by the knowledge of which treatment you have had).

Because we want to compare the long-term outcome of the treatments we will ask you to return to the clinic 3 years, 5 years and 10 years later. This will also alert the surgeon to any problems you may have, whichever treatment you received. We also ask that you agree to let us contact you by post, phone or e-mail on one occasion each year for 10 years so we can check on your progress. Although this sounds like a long time, your cooperation is vital to the success of the trial so it is very important that we can remain in contact with you. If you have difficulty getting to the hospital for a follow-up visit at the proper time, the assessor may be able to arrange to visit you at home.

You will not be asked to take any special medication except that which is normally necessary for your surgery and after you are discharged you are able to take any other medication that is prescribed or recommended for you. You are not prevented from having any further treatment on your knee if your condition warrants this whichever group you are in.

A schedule of your journey through the trial is presented on the back page of this leaflet.