Participant Information Sheet/Consent Form

Norfolk & Norwich University Hospital NHS Foundation Trust

Short Title	The Melanoma Margins Trial (MelMarT)
Title	A Phase III, Multi-centre Randomised Control Trial Investigating 1cm v 2cm Wide Excision Margins for Primary Cutaneous Melanoma
Protocol Number	ANZMTG 03.12
Project Sponsor	Australia and New Zealand Melanoma Trials Group
Coordinating Principal Investigator/ Principal Investigator	***Marc Moncrieff***

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project, called the **Mel**anoma **Mar**gins **T**rial (MelMarT). We are asking you if you would be prepared to take part because you have been diagnosed with a form of skin cancer called melanoma. Melanoma is a type of skin cancer that develops from melanocytes (pigment cells). The study aims to further medical knowledge and may improve future treatment of melanoma. The research project will investigate how much skin is necessary to remove around the melanoma when you have your wider excision surgery. Currently, doctors do not know how much skin is necessary to take away from around a melanoma to reduce the chances of it coming back and guidelines in different countries vary in their recommendations. This study will investigate if reducing the excision margin to 1cm is as good at reducing the risk of your melanoma returning as a 2cm excision margin. The study will involve ongoing follow up visits for 10 years after the surgery; however it is normal to be checked every year for 10 years once you have had the surgery to remove a melanoma.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the research. **Please read this information carefully.** It is important to ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend, or your local doctor.

Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether or not you take part. If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

- Understand what you have read
- Consent to take part in the research project
- Consent to have the tests and treatments that are described
- Consent to the use of your personal and health information as described.

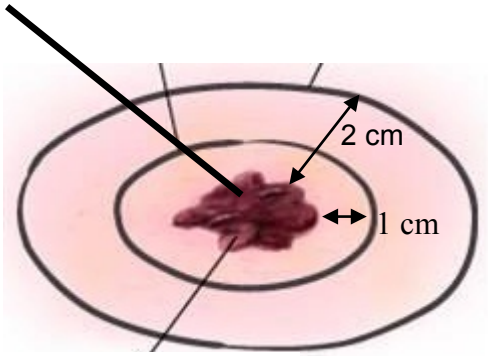
You will be given a copy of this Participant Information and Consent Form to keep.

2 What is the purpose of this research?

The purpose of this study is to investigate if reducing the current standard 2cm excision margin to 1cm is safe and whether it may change the risk of your melanoma coming back. There is currently no good evidence to prove or disprove a 1cm margin is as safe as a 2cm margin and a clinical trial is the only way to investigate the safety of a 1cm margin and its possible benefits.

The standard treatment for people with early melanoma is to remove it using surgery. This usually happens in 2 stages (described in Diagram 1 below).

Step 1: *The lesion is removed to confirm what it is (called a biopsy). This usually removes all of the lesion and leaves behind a scar*



Primary melanoma lesion

Step 2: *Once the lesion has been confirmed as melanoma, your doctor will discuss the MelMarT trial and if you consent and are randomised on to the trial, you will undergo a wider excision procedure. A wide margin of the skin surrounding the lesion is excised (either 1 cm or 2cm from the border of the lesion or from your biopsy scar).*

Diagram 1: Describes the surgical excisions when a melanoma is removed.

In the first stage, a doctor, usually a dermatologist or skin specialist, removes some of the growth in order to evaluate the tissue and make a diagnosis. A pathologist examines the growth to confirm that it is a melanoma and to see if the entire tumour has been removed. You have already had this stage performed and it is most likely that there is only a scar left at the original site of your melanoma. The second stage, known as a "wider excision", involves removing an extra "safety margin" of healthy skin surrounding the original melanoma site to ensure that any remaining scattered melanoma tumour cells are removed that may have been left behind after the first operation. This is done to reduce the chance of your melanoma returning. Depending on the country you are living in, current guidelines recommend a safety margin of between 1 and 3cm of healthy skin all around your melanoma is removed.

Evidence from previous research suggests that a 1cm excision is enough to reduce a patient's risk of the melanoma coming back in the same area; however a trial is needed to prove this theory. Other advantages of a reduced surgical margin include:

- A smaller margin could mean less surgery which means a smaller scar and potentially less scar tissue.
- A smaller margin could mean that extra surgery to repair the wound, such as a skin graft or other reconstruction, is no longer necessary.
- A smaller margin could reduce the time it takes for patients to recover from their surgery, possibly resulting in a reduced stay in hospital post operatively. Less time in hospital may make it easier for patients to return to their normal routine as well as being more affordable overall.
- Reducing the pain that patients may feel immediately after their operation and in the longer term.
- Using a smaller margin may reduce the length of time it takes surgeons to perform the surgery, allowing them to see more patients in a day and increasing the availability of the surgeons so they can treat more people.

- This study will also look at the costs and effects of having surgery for both patients and the health system. In addition, this study will look at the financial impact of melanoma on patients' households. By finding out if patients and their families are suffering from financial hardship, this information will help policy makers to address out-of-pocket costs for melanoma patients.

3. What does participation in this research involve?

You will be participating in a randomised controlled clinical trial. Sometimes we do not know which treatment is best for treating a condition. To find out we need to compare different treatments. We put people into groups and give each group a different treatment. The results are compared to see if one is better. To try to make sure the groups are the same, each participant is put into a group by chance (random). In this way, we will be able to compare the results of the different margins and therefore determine which is the more effective in melanoma. This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way and avoids study doctors or participants jumping to wrong conclusions. Randomisation means that you are put into a group by chance. Neither you nor your doctor can choose the group you will be in. In this study you will have a 50% chance of receiving 1cm or 2cm margin, much like if you flipped a coin.

Screening: You will be asked to read though this form and be given the chance to ask questions and to sign to say you have understood. This process is known as informed consent. Once you have provided your informed consent, you will be asked to:

- Undergo a complete physical exam (Your physician will examine you and record your height, weight etc).
- Review your medical history with your treating physician.
- Have a photograph taken of the site of your primary melanoma lesion.
- Complete quality of life questionnaires (known as the FACT-M and EQ-5D-5L questionnaires). These questionnaires ask you how you feel about your treatment, disease and how it affects you and your daily life.
- Complete a pain assessment questionnaire (known as the PainDetect questionnaire).
- The questionnaires will take no longer than 30 minutes to complete in total and are multiple choice.

Treatment: You will be assigned to receive either a:

- 1cm Wider Excision of your primary melanoma lesion
- 2cm Wider Excision of your primary melanoma lesion

At the same time you will have a special test called a Sentinel Lymph Node Biopsy (SLNB). This is a staging procedure and your physician will discuss this with you further. Every patient will be offered this because it is a routine part of treatment and information about the SLNB result will also be collected by the trial team.

There are no costs associated with participating in this research project, nor will you be paid. All medication, tests and medical care required as part of the research project will be provided to you free of charge.

If you decide to participate in this research project, the study doctor will inform your local doctor.

What do I have to do?

For this trial you will be asked to attend regular visits with a doctor involved in this research. These visits are normal for patients with your condition; are recommended by your doctor and align with the national treatment guidelines.

MelMarT Study Visit schedule:

During the first Year (Year 1): You will attend the first study visit (called the baseline visit) and subsequently at visits performed at 3, 6 and 12 months (called follow up visits).

During Years 2 to 10: Regular follow up visits will be performed, as part of the trial, once per year for up to 10 years; however it is normal to be checked at least every year for 10 years once you have had the surgery to remove a melanoma. There is no reason why you should not see your doctor more frequently if you need to. These follow-up visits are normal for patients with your condition; are recommended by your doctor and align with the national treatment guidelines.

At all of these visits you will be asked to have a physical examination to check that your melanoma has not returned and to see if your health and skin has changed. At some of these visits, you will also be asked to fill out the same Quality Of Life questionnaires you completed at the start of the trial.

Also, if you decide to participate in the MelMarT trial, your study doctor will inform your local doctor.

X-Rays and Imaging: If, as part of your standard care, your physician would like you to have any of the following (including but not limited to), we would also like to ask for copies of the reports and images:

- X-Rays
- Computed Tomography Scans (CT)
- Magnetic resonance imaging (MRI)
- Positron emission tomography (PET)
- Ultrasound

It is not required as part of this study that you have any of the above procedures, we only wish to collect copies if they form part of your routine care.

4. Other relevant information about the research project

This research is an international study with many doctors coming together to share their findings. This research has been initiated by the lead study doctor, Dr Marc Moncrieff who is based at the Norfolk & Norwich University Hospital, in Norwich, England. This research is being conducted by the Australia and New Zealand Melanoma Trials Group (ANZMTG) in collaboration with Norwich Clinical Trials Unit, United Kingdom. ANZMTG does not make any profit from its work. It exists to further knowledge about melanoma, and works with doctors in other countries, including those based in Norwich.

The first phase (pilot study) of this trial involves patients from a select number of hospitals. During this first phase, 400 people will take part in this study to determine if the project is feasible. The second phase (full study) will involve more countries and may include patients from the following countries:

- United Kingdom (UK)
- Australia and New Zealand
- United States of America
- Sweden
- Netherlands
- Brazil
- Poland
- Italy
- Canada

All data gathered at any stage will help us make the right conclusions when it comes to the final analysis. If you consent to participate in the first phase; we will also use your data in the full study without needing to complete another form.

A total of 10,000 people will take part in the second phase (full) study. This is a large trial which is why so many different countries, doctors, hospitals and people with melanoma are involved. Recruitment will take place over 5 years and those included will be followed up for a maximum of 10 years. Therefore the study will take 15 years to complete.

5. Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage. Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you, or your relationship with your institute [Norfolk & Norwich University Hospital NHS Foundation Trust].

If you decide to discontinue the study treatment, please notify a member of the research team beforehand. You will be asked to attend follow-up visits to allow collection of information regarding your health status. Alternatively, the investigator/sponsor will request your permission to access your medical records for collection of follow-up information for research and analysis.

6. What are the alternatives to participation?

Surgery is considered standard of care treatment for people with this diagnosis however surgery can be performed outside the trial setting. This would mean you would undergo the standard 2 cm wide excision margin, or as determined by the treatment guidelines in your country. If you decide not to be part of the study you will be treated and followed up as per your local standard care guidelines. In most cases this is a 2cm surgical wide excision procedure. You will be followed up in the same way as you would if you were part of the study.

Participation in this study is voluntary. If you choose not to participate in this study, you and your doctor can discuss and agree on the most appropriate treatment for your illness.
Whatever your decision, it will not affect your relationship with the staff caring for you. If you wish to withdraw from the study once it has started, you can do so at any time. You do not have to give a reason.

7. What are the possible benefits of taking part?

The results of the study may not directly benefit you. If you are allocated to the group receiving the 2cm excision then you will receive no direct benefit as this is the same as standard procedure. However you will contribute to research and the results may benefit those in the future with melanoma. Possible benefits if you are allocated to the 1cm margin include:

- Having less surgery to remove the primary melanoma lesion
- A smaller scar
- Less pain at the site of your surgery
- Reduced chance of requiring a skin graft to repair removed skin, which means a less complex procedure
- A shorter hospital stay post operatively
- A reduced time for recovery. This may have an implication on costs for yourself, your family, industry and the health system. We will ask you about the costs associated with your disease in order that we can help inform policy makers about the costs associated with treating melanoma.

8. What are the possible risks and disadvantages of taking part?

Surgery may cause side effects and all patients on the trial will undergo a wide excision. So irrespective of what treatment arm you are allocated to (1 or 2 cm excision margin) you may experience none, some or all of the effects listed below, and they may be mild, moderate or severe. If you have any of these side effects, or are worried about them, talk with your study doctor. Your study doctor will be looking out for side effects throughout the whole trial.

Common Side Effects:

- Having a tissue sample taken may cause some discomfort, bruising, minor infection or bleeding (short term)
- Pain at surgical site (short and long term)
- Scarring at the surgical site (long term)

Rare Side Effects:

- Reduced mobility in some locations on the body (face, hands areas surrounding joints etc) (short and long term)
- Infection at the surgical site (short term)
- Minor Bleeding (short term)
- Swelling at the site of surgery or in a limb (called lymphoedema) (long term)
- Reopening of the wound (short term)
- Tingling or numbness relating to damage to nerves (short and long term)

Many side effects disappear shortly after the end of treatment. However, sometimes side effects can be serious, long lasting, or permanent. Your study doctor will discuss the best way of managing any side effects with you. There may be other side effects that the researchers do not expect or do not know about and that may be serious. Please tell your study doctor immediately if you experience any new or unusual symptoms.

We believe that there will be no difference in the chance of the melanoma coming back between the patients that have a 2cm margin and those that have a 1cm. However it is possible that a 1cm margin is less effective and therefore you may be at an increased risk of your melanoma coming back. We do not know if this is the case and that is why we are conducting this study. There is a potential risk that the 1cm margin may not be wide enough for a small number of patients to completely remove all of the melanoma that can be seen under the microscope. The risk is very small but if this happens then you may need to have yet more surgery to ensure no melanoma has been left behind. This will be inconvenient and delay your recovery. We also believe that there is an increased risk of suffering any of the side-effects listed above for patients that have the bigger, 2cm margin, though this is standard treatment patients would normally be offered by their doctor for their melanoma. In order to manage this risk your doctor will be checking on you regularly as part of this study.

9. What if new information arises during this research project?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your study doctor will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw, your study doctor will make arrangements for your regular health care to continue.

10. Can I have other treatments during this research project?

Yes, while you are participating in this research project, you are able to continue taking any of the medications or treatments you have been taking for your condition or for other reasons.

However it is important to tell your study doctor and the study staff about any treatments or medications, including over-the-counter medications, vitamins, herbal remedies, acupuncture, or other alternative treatments. You should also tell your study doctor about any changes to these during your participation in the research project. Your study doctor should also explain to you which treatments or medications need to be stopped for the time you are involved in the research project.

11. What if I withdraw from this research project?

If you decide to withdraw from the project, please notify a member of the research team before you withdraw. If you do withdraw your consent during the research project, the study doctor and relevant study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected by the sponsor up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them before you join the research project.

12. Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons which will be reviewed by the trial management committee and your study doctor will be immediately notified of any decision to stop the trial; reasons may include:

- Feasibility and recruitment issues
- Unacceptable side effects
- The 1cm margin is shown not to be as safe as the 2cm margin

13. What happens when the research project ends?

Once you have completed the study, the study team will collate and publish the results in the medical community in journals and conference presentations. The final published results will be shared with you by your study doctor, and publicly accessible for the benefit of all patients diagnosed with melanoma, doctors, and researchers.

Furthermore, you will be followed up as per your local healthcare provider's standard of care. If your melanoma returns you will be offered the choice of the best treatment available by your treating doctor.

Part 2 How is the research project being conducted?

14. What will happen to information about me?

By signing the consent form, you consent to the study doctor and relevant research staff collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential. Your information will be non-identified and will not be linkable to yourself in any way. Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law.

Information about you may be obtained from your health records held at this and other health services for the purpose of this research. By signing the consent form you agree to the study team accessing health records if they are relevant to your participation in this research project.

Your health records and any information obtained during the research project are subject to inspection (for the purpose of verifying the procedures and the data) by the relevant regulatory authorities. By signing the Consent Form, you authorise release of, or access to, this confidential information to the relevant people working on this study, those to whom they report and the organisations over them.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission. Information about your participation in this research project may be recorded in your health records. Any information obtained for the purpose of this research project and for the future research described in Section 16 that can identify you will be treated as confidential and securely stored. It will be disclosed only with your permission, or as required by law

15. Complaints and compensation

You may have a right to take legal action to obtain compensation for any injuries or complications resulting from the study. Compensation may be available if your injury or complication is sufficiently serious and is caused by unsafe drugs or equipment, or by the negligence of one of the parties involved in the study (for example, the researcher, the hospital, or the treating doctor). By signing the consent form, you have not waived any legal or other right to seek compensation.

16. Who is organising and funding the research?

This research is being organised and funded by ANZMTG and Norfolk & Norwich University Hospital. There is a local sponsor of this study in each participating country who is also responsible for organising and funding the research in your institution. No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

17. Who has reviewed the research project?

All research in the UK involving humans is reviewed by an independent group of people called a National Research Ethics Service Committee (NRES). The ethical aspects of this research project have been approved by the NRES of East of England.

This project will be carried out according to the principles agreed at the International Conference on Harmonisation Good Clinical Practise. In *the UK* this is governed by *Research Goverance Framework.*

18. Further information and who to contact

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal study doctor, or clinical research nurse on *01603 288128* or any of the following people:

Clinical contact person

Name	*Marc Moncrieff*
Position	*Consultant Plastic Surgeon*
Telephone	*01603 288127*
Fax	*01603 288378*

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Complaints contact person

Name	*Patient Advice & Liaison Services*
Position	*Norfolk & Norwich University Hospital*
Telephone	01603 289036
Website	*http://www.nnuh.nhs.uk/dept.asp?id=83*