Participant Information for Medical Research Study

Safety and feasibility of the use of cryoablation in patients with brain tumors

A study on the safety and feasibility of cryoablation in patients with brain tumors.

Erasmus MC, Department of Neurosurgery

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Introduction

This information letter is to invite you to participate in a medical research study. Participation is voluntary. You are receiving this letter because you are scheduled to undergo surgery for a brain tumor. Your treating physician has suggested that you consider taking part in this study and has already provided you with some information about it.

This document explains the purpose of the study, what participation entails, and the potential benefits and drawbacks. It contains a lot of information. Please take the time to read it carefully and decide whether you would like to participate. If you decide to participate, you can complete the consent form found in Appendix C.

Ask your questions

You can make your decision based on the information provided in this letter. In addition, we encourage you to:

- Ask questions to the researcher who provided you with this information.
- Discuss this study with your partner, family, or friends.
- Ask questions to the independent expert. For contact details, see Appendix A.
- Read the information available at www.rijksoverheid.nl/mensenonderzoek.

1. General information

The Department of Neurosurgery at Erasmus MC has initiated this study. Throughout this document, Erasmus MC will be referred to as the "sponsor." The neurosurgeon will conduct the study at Erasmus MC.

The study is not funded by commercial entities. However, at the request of the researchers, a company (Boston Scientific Corporation) has agreed to provide their medical device on loan for the duration of the study. They will also donate a specific number of needles required to carry out the research.

Participants in medical research studies are often referred to as “subjects.” Both patients and healthy individuals can serve as subjects.

For this study, 30 participants with brain tumors are needed. The medical ethics review committee of Erasmus MC has approved this research.

2. What is the purpose of the study?

The purpose of this study is to determine whether cryoablation in patients with brain tumors (including gliomas, meningiomas, or brain metastases) is safer and easier compared to the standard surgical removal of brain tumors during an operation.

3. What is the background of the study?

There are many different types of brain tumors, with the most common being gliomas, meningiomas, and brain metastases. Depending on various factors, such as the type, size, and location of the tumor, symptoms, and the patient's overall health, the primary treatment for brain tumors is usually surgical removal, often followed by radiotherapy and/or chemotherapy if needed.

However, surgical removal of brain tumors is often associated with lengthy procedures, significant blood loss, and relatively high complication rates compared to surgeries for tumors in other parts of the body. This underscores the urgent need for developing new, minimally invasive techniques for the treatment of brain tumors.

Cryoablation involves treating a tumor by freezing it. While the use of cryoablation for brain tumors is still limited, this technique is already widely applied for tumors in other organs, often with better outcomes compared to conventional therapies. Cryoablation offers precise destruction of the tumor, is minimally invasive, and allows the freezing process within the tumor to be monitored through various imaging techniques, reducing the likelihood of complications.

Additionally, cryoablation may have a potential immunological effect on certain (malignant) brain tumors, encouraging the body to eliminate any remaining tumor cells. Therefore, cryoablation could represent a valuable advancement in the treatment of brain tumors.

4. How is the study conducted?

If you participate in the study, your pre- and postoperative care will be the same as that of patients who do not participate. The study itself will be conducted during your scheduled brain tumor surgery. We do not expect your surgery to take longer as a result of the study.

Step 1: Are You Eligible to Participate?
First, we will determine if you are eligible to participate. A total of 30 participants with various types of brain tumors will take part in this study. To determine your eligibility, a preoperative MRI scan will be assessed to confirm the presence of a clear brain tumor. If you are eligible, an informational discussion about the study will follow.

Step 2: The Treatment
If you decide to participate, you will receive the same pre- and postoperative care as patients who do not participate. Both groups—participants and non-participants—will undergo surgery aimed at removing as much tumor tissue as possible.

However, if you participate in the study, the tumor tissue will be frozen one or two times before being removed. Freezing the tumor ensures that most of the tumor cells will die. The tumor will be frozen by

inserting one or more needles into the tumor under ultrasound and/or CT guidance. These needles are connected to the cryoablation device, which freezes the tumor using cold argon gas. If the surgeon decides to use CT scans, several scans of the head will be taken intraoperatively in the operating room.

Although cryoablation adds more steps to the procedure, we expect the total surgery time to be shorter than standard surgery alone. Since the tumor will already have died before removal, it is anticipated that it will not bleed, allowing for faster removal.

Step 3: Tests and Measurements
Participating in this study does not require you to make additional hospital visits beyond those needed for your treatment.

Summary
If you decide to participate in the study, your tumor will be frozen once or twice before removal. This will take place during your surgery. Otherwise, your treatment will be identical to that of patients who are not participating in this study.

5. What agreements will we make with you?

To ensure the study runs smoothly, we will make the following agreements with you:

- You will attend all scheduled appointments.
- You will contact the researcher in the following situations:
    - You are admitted to a hospital or receive hospital treatment.
    - You experience sudden health problems.
    - You decide to withdraw from the study.
    - Your phone number, address, or email address changes.

To report health problems, you can contact your treating physician during office hours. Outside office hours (evenings, nights, weekends, or holidays), you can contact the on-call physician for the department. Contact details are provided in Appendix A.

6. What Side Effects, Adverse Effects, or Discomforts Could You Experience?

The procedure being studied may have side effects. It is expected that the possible side effects, complications, or adverse effects of cryoablation will be similar to those of standard brain tumor surgery. Like regular brain surgery, cryoablation may result in the following adverse effects, although these complications are rare:

- Bleeding
- Infection
- Paralysis in an arm and/or leg
- Epilepsy (seizures)

- Speech problems
- Death

The procedure being studied may also have side effects that are currently unknown.

What Are the Potential Discomforts From Measurements During the Study?

To freeze the tumor, one or more needles will be inserted into the tumor during surgery. This will be performed under ultrasound and/or CT guidance. Ultrasound is a radiation-free imaging technique and is not harmful to your health. However, CT scans involve exposure to radiation. If intraoperative CT scans are used, you will be exposed to this radiation. It is expected that the study will not pose any additional risks to your health.

7. What are the benefits and risks of participating in the study?

Participating in this study can have both benefits and drawbacks. Below is an overview to help you make an informed decision. Think about these carefully and discuss them with others.

Participating in this study will not cure your condition or reduce your symptoms. However, your participation will contribute to the search for better treatments for brain tumors and help researchers gain more insight into these treatments.

Potential Benefits of Cryoablation:

- Provides precise and safe destruction of the tumor.
- Is generally minimally invasive.
- The formation of ice within the tumor can be monitored using imaging techniques, reducing the risk of complications.
- May have a potential immunological effect for some (malignant) brain tumors, encouraging the body to eliminate remaining tumor cells.
- The total duration of surgery is expected to be shorter.
- Blood loss during surgery is expected to be reduced.

Participating in the study may involve the following risks or drawbacks:

- You may experience side effects or adverse effects from cryoablation.
- The surgery will include additional steps compared to standard procedures.
- The effects of cryoablation on the brain are not yet fully understood.
- You must adhere to the study requirements and commitments.

If You Decide Not to Participate

The choice to participate is entirely up to you. Participation is voluntary. If you choose not to participate, you will receive the standard treatment for your brain tumor. Your doctor can provide you with more information about the available treatment options, including their advantages and disadvantages.

If You Change Your Mind

If you decide to participate but later wish to withdraw, you can do so at any time. You do not need to provide a reason for withdrawing. If you decide to stop participating, we ask that you first contact the researcher. Stopping your participation will not affect your treatment or follow-up care in any way. For contact details, see Appendix A.

8. When does the study end?

The researcher will inform you if new information becomes available that is important for you to know. You will then be asked whether you wish to continue participating.

The study will end for you in the following situations:

- All procedures outlined in the schedule have been completed.
- The overall study has been concluded.
- You become pregnant.
- You choose to withdraw from the study before the cryoablation surgery. If you decide to stop, notify the researcher immediately. You are not required to provide a reason. In this case, you will receive the standard treatment for your condition.
- The researcher determines it is better for you to stop participating.
- It becomes apparent during surgery that cryoablation is not feasible.
- One of the following entities decides to terminate the study:
    - Erasmus MC
    - The government
    - The medical ethics committee overseeing the study

What happens If you withdraw from the study?

If you withdraw from the study, the researchers will retain the data and biological material collected up to that point. However, if you prefer that your biological material be destroyed, you can notify the researcher, and this will be arranged.

The entire study will conclude three months after the last patient has undergone cryoablation surgery.

9. What happens after the study?

Will you receive the results of the study?

After the study is completed, you can – if you wish – receive an overview of the results. Please note that these results will be described in general terms, on a group level. You will not receive any personal results from the study. Any findings that are personally relevant to you will be discussed with you by the researcher. Unexpected findings will be shared with your general practitioner and your medical specialist.

10. What do we do with your data and biological material?

By participating in the study, you also give consent for your data and biological material to be collected, used, and stored.

We store the following data:

- Your name
- Your gender
- Your address
- Your date of birth
- Health-related information
- (Medical) data collected during the study

What biological material do we store?
We collect, use, and store tissue samples (biopsy) from the tumor. Additionally, we may also use material collected during treatment.

We may also request information from your general practitioner about your health.

Why do we collect, use, and store your data and biological material?
We collect, use, and store your data and biological material to answer the research questions and to publish the results. Data and/or biological material may be used by the sponsor and companies assisting the sponsor in conducting the study, analyzing research data, and performing measurements on the biological material.

How do we protect your privacy?
To protect your privacy, we assign a code to your data and biological material. We only use this code on your data and biological material. The key to this code is stored securely at Erasmus MC. When processing your data and biological material, we only use the code. In reports and publications about the study, it will not be possible to identify you.

Who can view your data?
Some individuals may access your name and other personal details without the code. These may be data specifically collected for this study or information from your medical record. These individuals are responsible for ensuring that the study is conducted properly and reliably. These individuals may include:

Members of the committee overseeing the safety of the study

A monitor hired by the researchers or a monitor working for the sponsor
These individuals are required to keep your data confidential. We will ask for your consent for these individuals to access your data. The Health and Youth Care Inspectorate may access your data without your consent.

How long do we store your data and biological material?
We store your data for 20 years with the sponsor.
Your biological material is stored at the hospital and kept for 20 years to allow further tests related to this study to be conducted. Once this is no longer necessary, your biological material will be destroyed.

Can we use your data and biological material for other research?
Your collected data and any remaining biological material may also be relevant for other scientific research related to your condition and/or treatment methods. Your data and biological material will be stored for 20 years at the hospital for this purpose. In the consent form, you indicate whether you agree to this. If you do not give consent, you can still participate in the study and will receive the same care.

What happens if unexpected findings occur?
During the study, we may accidentally discover something that is not directly related to the study but could be important for your health. The researcher will then contact your general practitioner and medical specialist. You will discuss with your doctor or specialist what actions need to be taken. The costs will be covered by your health insurance. You give consent through the form for your doctor or specialist to be informed.

Can you withdraw your consent for the use of your data?
You can withdraw your consent for the use of your data at any time. Just inform the researcher. This applies to both the current study and any future research. However, if data has already been collected for the study, the researchers may still use this data. As for your biological material, the researchers will destroy it after you withdraw your consent. If any measurements have already been made with your biological material, the researcher may continue to use the results.

Would you like more information about your privacy?

- If you would like to learn more about your rights regarding personal data processing, visit www.autoriteitpersoonsgegevens.nl.
- If you have any questions about your rights or a complaint regarding the processing of your personal data, contact the person responsible for processing your data for this study:
    - Prof. Dr. A.J.P.E. Vincent. See Appendix A for contact details and website.
- If you have complaints about the processing of your personal data, we recommend discussing them with the research team first. You can also contact the Data Protection Officer at Erasmus MC, or file a complaint with the Dutch Data Protection Authority.

Where can you find more information about the study?
More information about the study can be found on the following website(s): www.ClinicalTrials.gov. After the study, the website may provide a summary of the results. You can find the study by searching for 'Safety and feasibility of the use of cryoablation in patients with brain tumors.

11. Will you receive compensation for participating in the study?

The treatment for the study will not cost you anything. You will not receive any compensation for participating in this study. However, you will be reimbursed for your additional travel expenses.

12. Are you insured during the study?

Insurance has been arranged for everyone participating in this study. The insurance covers damage caused by the study, but not all types of damage. More information about the insurance and its exclusions can be found in Appendix B. It also explains how to report any damage.

13. We will inform your general practitioner

The researcher will send a letter to your general practitioner to inform them that you are participating in the study. This is for your own safety

14. Do you have any questions?

If you have any questions about the study, you can ask the research team or your treating physician. If you want advice from someone with no vested interest in the study, you can contact the independent expert listed in Appendix A. They are knowledgeable about the study but are not involved in conducting it. If you have a complaint, please discuss it with the researcher or the physician treating you. If you prefer not to do so, you can contact the complaints officer/complaints committee at Erasmus MC. Appendix A provides details on how to reach them.

15. How do you give consent for the study?

You can take some time to think about the study. Then, you tell the researcher whether you understand the information and whether you want to participate or not. If you wish to participate, you will fill out the consent form provided with this information letter. Both you and the researcher will receive a signed copy of the consent form.

Thank you for your time.

16. Appendices to this information

A. Contact details
B. Information about the insurance

C. Consent form for the participant

Appendix A: Contact details

If you have any questions or complaints during the study, we ask that you contact the researcher or your treating physician.

Researchers at Erasmus MC:

Prof. Dr. A.J.P.E. Vincent – Neurosurgeon Phone number: +31 6 39428949

Mr. S. Mohammadian – Researcher Phone number: +31 6 40272220

Independent Expert
If you have doubts about participating in the study or if you have questions you would prefer not to ask the researchers, you can always contact the independent expert:
Dr. M.L.C. van Veelen – Neurosurgeon Phone number: +31 10 7035993

Complaints
If you are not satisfied with the study or the treatment, you can contact the independent complaints committee at Erasmus MC:
Phone number: +31 10 7033198

Data Protection Officer of the institution:
functionaris.gegevensbescherming@erasmusmc.nl

Rights
For more information about your rights, you can contact the person(s) responsible for processing personal data at Erasmus MC:
Phone number: +31 10 7034986

Appendix B: Information about the Insurance

The sponsor has arranged insurance for everyone participating in the study. The insurance covers any damage you incur as a result of participating in the study. This includes damage that occurs during the study or within 4 years after the end of your participation in the study. You must report any damage to the insurer within 4 years.

Have you suffered damages due to the study?

The insurer for this study is: Name of insurer: Centramed Address: Maria Montessorilaan 9, 2719 DB Zoetermeer Phone number: +31 70 3017070 Email: info@centramed.nl (Policy number: 626.107.154)

The insurance provides a maximum coverage of €650,000 per participant, with a maximum amount of €5,000,000 for the entire study. If the sponsor of this study is conducting multiple studies, a maximum amount of €7,500,000 applies per insurance year for all studies. Coverage for specific damages and costs is limited to certain amounts, which are outlined in the "Besluit verplichte verzekering bij medisch-wetenschappelijk onderzoek met mensen" (Regulation on compulsory insurance for medical-scientific research involving humans). Information about this can be found on the website of the Central Committee on Research Involving Human Subjects: www.ccmo.nl.

Note: The insurance does not cover the following types of damage:

- Damage from a risk about which we have provided information in this letter, unless the risk turned out to be greater than initially expected, or if the risk was highly unlikely.
- Health-related damage that would have occurred even if you had not participated in the study.
- Damage resulting from your failure to follow instructions or guidelines properly.
- Damage to the health of your children or grandchildren.
- Damage caused by an existing treatment method, or research into an existing treatment method.

These provisions are part of the "Besluit verplichte verzekering bij medisch-wetenschappelijk onderzoek met mensen 2015" (Regulation on compulsory insurance for medical-scientific research involving humans 2015). You can find this regulation on the government's legal website: https://wetten.overheid.nl.

Appendix C: Participant Consent Form

Related to the study on the safety and feasibility of cryoablation in patients with brain tumors.

- I have read the information letter. I was also able to ask questions, and my questions have been adequately answered. I had enough time to decide whether I want to participate.

- I understand that participation is voluntary. I also understand that I can decide at any time not to participate in the study, or to stop my participation. I do not have to explain why I wish to stop.
- I give the researcher permission to inform my general practitioner that I am participating in this study.
- I give the researcher permission to request information from my general practitioner about my health.
- I give the researcher permission to provide my general practitioner or specialist with information regarding unexpected findings from the study that are relevant to my health.
- I give the researchers permission to collect and use my data and/or biological material. The researchers will only use this to answer the research question of this study.
- I understand that, for the purpose of study monitoring, certain individuals may access all of my data. These individuals are listed in this information letter. I give these individuals permission to access my data for this monitoring.
- Please indicate below whether you agree or disagree with the following statements:

I give permission for my data to be stored and used for other research, as described in the information letter.	Yes ☐	No ☐
I give permission for my (remaining) biological material to be stored and used for other research, as described in the information letter. The biological material may be stored for up to 20 years.	Yes ☐	No ☐
I give permission to be contacted after this study to ask whether I would like to participate in a follow-up study.	Yes ☐	No ☐

- I wish to participate in this study.

Participant's name: ……..

Signature: …… Date : __ / __ / __

I declare that I have fully informed the participant about the aforementioned study.
If any information emerges during the study that could influence the participant's consent, I will inform the participant in a timely manner.

Name researcher (or representative):…….

Signature: …… Date : __ / __ / __

<If applicable>

Additional information provided by:

Name: _____

Position: _____

Signature: _____ Date: __ / __ / __

The participant will receive a complete information letter along with a signed copy of the consent form.