Research information for the patient participating in medical-scientific research

Research on the treatment of uterine fibroids

"MYCHOICE: The MYoma treatment Comparison study: High intensity image guided fOcused ultrasound versus standard (minimally) Invasive fibroid care - a (Cost) Effectiveness analysis"

Introduction

Dear Madam,

We are asking you to participate in a medical scientific study.
Participation is voluntary. However, your written permission is required in order to participate. You are receiving this letter because you are diagnosed with one or more fibroids (also known as myomas), and you intend to undergo treatment for them in the near future. For this reason, your medical specialist has informed you about this study. Before you decide whether you want to participate in this study, you will receive an explanation of what the study entails. Please read this information carefully and ask the researcher if you have any questions. You can also ask the independent expert, mentioned at the end of this letter, for additional information. Of course, you can also talk about it with your partner, friends or family. Further information about participating in medical research can be found on the website www.government.nl/topics/medical-research.

1. General information

This study is coordinated from Isala Hospital in Zwolle and is being conducted by physicians and researchers at several Dutch hospitals. At least 240 subjects are expected to participate in this study. The medical ethics review committee of Isala has approved this study.

2. Purpose of this study

In this study, we compare the effects of four fibroid treatments. One of these treatments is the new MR-HIFU treatment (using sound waves to heat the fibroid, operating without cutting). The other treatments are uterine surgery (removal of the entire uterus in the operating room, also known as hysterectomy), fibroid surgery (removal of only the fibroid in the operating room, also known as myomectomy) and embolization (interrupting the blood supply to the fibroid).
The purpose of this study is to find out whether MR-HIFU works as well as the existing treatments and could be included in the package of reimbursed healthcare. In this way, the treatment could be made available to all women with a fibroid who could and would like to undergo it.

3. Background of the study

In the past, it was common for women with symptoms of a fibroid to have uterine surgery. This is generally an effective but rather large operation, and pregnancy is not possible after the uterus is removed. For these reasons, among others, alternative treatments were considered. With both fibroid surgery and embolization, the uterus is preserved and the recovery time is often somewhat shorter (several weeks). The disadvantage of these two treatments is that there is a chance that the fibroid will grow back, which may require another treatment and the recovery will take several weeks. Recently, a new way of treating fibroids has been added with a so-called MR-HIFU device. MR-HIFU is an abbreviation of MRI-guided High Intensity Focused Ultrasound. With this device it is possible to use sound waves to very specifically heat parts of the fibroid so that they die, causing the fibroid to shrink. This is currently the only treatment where surgery is performed without cutting. In addition, the advantage of the MR-HIFU treatment is that you can go home on the day of treatment and generally resume your own activities after three days. Unfortunately, there has not yet been enough research comparing the new MR-HIFU treatment directly with existing treatments. Therefore, it is not clear whether the treatment is just as good. By just as good, we mean just as much symptom improvement and increase in quality of life.

More information about MR-HIFU treatment can be found in **Appendix D** and in the digital patient brochure.

4. What participating entitles

If you are willing to participate in this study, you will complete a questionnaire at five time points. This will be once before treatment and 3, 6, 12 and 24 months after treatment.

Treatment

In this study, you will not be able to fully choose which treatment you undergo. Before you can definitely take part in the study, you will first have to undergo a screening MRI scan to see if your fibroid is treatable with the MR-HIFU treatment. If this is not the case, you will not be able to participate in the study. If you are found to be suitable, you will be assigned to one of two groups. In the first group you will undergo the MR-HIFU treatment. If you are in the second group, you will be given the choice between embolization, fibroid surgery or uterine surgery in consultation with your gynecologist.

Visits and measurements

For this study, we will collect data from your medical file and ask you to complete a questionnaire several times. This questionnaire will be sent to you via an email link. If you prefer to complete the questionnaire by telephone or on paper at home and return it to us, this is also possible. The questionnaire will be slightly different at each time point. Completing the questionnaire will take about 25 to 30 minutes each time. The questionnaire contains questions about the effect of the treatment, how you experienced the treatment and what your recovery was like after the treatment.
After your treatment, you will be called by your doctor after 1 to 2 weeks and invited to the gynecology outpatient clinic after 6 to 12 weeks. This is part of the standard care after treatment for a fibroid.

In **Appendix C** you will find an overview of the examination in the form of a schedule.

5. What is expected of you

In order for the study to proceed smoothly and for your own safety, it is important that you keep the following appointments.

The agreements are that you:

- Keep appointments for visits;
- Complete the questionnaire sent to you.

It is important that you contact the investigator:

- If you are hospitalized or treated;
- If you suddenly develop health problems;
- If you no longer want to participate in the study;
- If your contact information changes.

Pregnancy

Women who are pregnant, cannot participate in this study. This is because fibroid treatment can have consequences for an unborn child. It is not known which consequences.

If your treatment is MR-HIFU, fibroid surgery or embolization, you may become pregnant one year after treatment. Should you become pregnant after one of the treatments, please contact your treating gynecologist. Together with him or her you can discuss where the check-ups for your pregnancy will take place.

6. Possible side effects and other adverse effects

Every treatment has possible adverse effects or can lead to side effects. You can discuss the possible adverse effects and side effects of the treatments in this study with your gynecologist or find them in the patient leaflets of the specific treatments.

7. Possible advantages and disadvantages.

It is important that you carefully weigh the possible advantages and disadvantages before you decide to participate.

An advantage of participating in this study may be that you can make a valuable contribution to gaining more knowledge about MR-HIFU treatment for fibroids.

Disadvantages of participating in the study may include:

- That you will spend time filling out the questionnaire;
- It is important that you keep certain appointments.

8. If you don't want to participate or want to stop

You decide whether to participate in the study. Participation is voluntary.
If you do not wish to participate, you can be treated for your fibroid via the existing treatments. Since the MR-HIFU treatment is not reimbursed, it is not possible to undergo this treatment outside of the study. Your gynecologist can tell you more about the treatment options available and their pros and cons.

If you participate in the study, you can always change your mind and stop anyway, even during the study. You do not have to say why you want to stop. However, you should report this to the researcher immediately. If you have already received the treatment, you will be asked to attend the usual check-ups scheduled for your own safety.

If there is new information about the study that is important to you, the investigator will let you know. You will then be asked if you wish to continue participating.

9. End of the study

Your participation in the study stops when

- All questionnaires as described under section 4 have been completed;
- You choose to stop;
- You become pregnant before undergoing treatment for your fibroid;
- The investigator feels it would be better for you to stop;
- Your hospital, the government or the reviewing medical ethics committee, decides to stop the study.

The entire study ends when all participants are finished. This will likely be in 2026.
After all the data have been processed, the researcher will inform you of the main results of the study. This will happen about 1 to 4 years after your participation.

10. Use and retention of your data

For this study, your personal data will be collected and stored. This includes data such as your name, address, date of birth and data about your health. The collection, use and storage of your data is necessary to answer the questions asked in this study and to publish the results. We ask for your permission to use your data.

Confidentiality of your data

To protect your privacy, your data will be coded. Your name and other data that can directly identify you are omitted. Only the key to the code can be used to trace you back to the data. The key to the code remains safely stored at the local research institution. The data sent to the sponsor will contain

only the code, but not your name or other data that can identify you. Reports and publications about the research also do not trace the data back to you.

Accessing your data for review

Some individuals may be able to access all of your data at the research site. Also to the data without a code. This is necessary to be able to check whether the research has been carried out properly and reliably. Persons who can access your data for control purposes are: the committee monitoring the safety of the study, a monitor working for the hospital and national supervisory authorities, for example, the Health Care Inspectorate. They will keep your data confidential. We ask you to give us your permission to see them.

Data retention period

Your data must be kept for 15 years at the research site.

Retention and use of data for other research

Your data may also be important for other scientific research in the field of fibroids after this study has ended. For this purpose, your data will be kept for 15 years. You can indicate on the consent form whether or not you agree to this. If you do not agree, you can still participate in the current study.

Information about unexpected findings

During this study, something may be found by chance that is not important to the study, but is important to you. If this is important to your health, you will be informed by the specialist. You can then discuss with your doctor or specialist what should be done. You also give your permission for this.

Withdrawing consent

You can always withdraw your permission for the use of your personal data. This applies to this study and also to the storage and use for future research. The research data that has been collected up until the moment you withdraw your permission will still be used in the research.

More information about your rights when processing data

For general information about your rights when processing your personal data, please consult the website of the Authority for the Protection of Personal Data or the hospital's website.
If you have any questions about your rights, please contact the person responsible for processing your personal data. See **Appendix A** for contact details and website.

Registration of the study

Information about this study is also included in an overview of medical scientific research, namely in the CCMO register (https://www.toetsingonline.nl/) and in the Netherlands Trial Register (www.trialregister.nl). These do not contain any data that can be traced back to you. After finishing this study, the website may show a summary of the results. You can find this study using study number NL74716.075.20

11. Insurance for participants

Insurance has been provided for everyone participating in this study. The insurance covers damage caused by the research. Not all damages are covered. In **Appendix B** you will find more information about the insurance and the exceptions. It also states to whom you can report damage.

12. Informing general practitioner and treating specialist

We will always send your general practitioner and treating specialist a message to let them know you are participating in the study. This is for your own safety. If you do not like this, you cannot participate in this study. You cannot participate in the study if you do not have a general practitioner.

13. No compensation for participating

There are no additional costs associated with participating in this study, even if you undergo MR-HIFU treatment. However, you can expect to pay for care costs that are part of the deductible, such as the gynecologist's appointment at the outpatient clinic. The travel expenses you incur because you have to travel to another hospital for the MR-HIFU treatment will be reimbursed up to a maximum of 50 euros in total.

14. Questions?

If you have any questions, please contact the investigator. For independent advice about participating in this study, please see the independent physician. He knows a lot about the study, but has nothing to do with this study. If you have any complaints about the study, you can discuss them with the researcher or your treating physician. If you prefer not to, you can contact the Isala complaints officer. All details can be found in **Appendix A**.

15. Signing informed consent

When you have had sufficient time to think about it, you will be asked to decide whether to participate in this study. If you give your consent, we will ask you to confirm it in writing on the accompanying consent form. Your written consent indicates that you have understood the information and agree to participate in the study.

Both you and the researcher will receive a signed version of this consent form.
Thank you for your consideration.

16. Appendices

A. Contact information
B. Insurance information
C. Overview study design
D. Additional information treatment
E. Informed consent

Appendix A: contact details for hospital Isala Zwolle

Principal Investigator:

M.F. Boomsma, radiologist

m.f.boomsma@isala.nl

088-6247202

Executive investigator:

D.J. Slotman

mychoice@isala.nl

088-6242243

Independent physician:

E.C.J. Phernambucq, radiotherapist

e.phernambucq@isala.nl

088-6246181

Complaints:

Isala complaints secretariat

088-6244727

Data Protection Officer of the institution:

Liesbeth Boekel

e.w.boekel@isala.nl

088-6247955

For more information about your rights:

Isala Hospitals

088-6245000

Dokter van Heesweg 2

8025 AB Zwolle

https://www.isala.nl/praktische-informatie/rechten-plichten-en-klachten/

Appendix B: Insurance information

Isala Hospital has taken out insurance for everyone who participates in this study. The insurance covers damages resulting from participation in the study. This applies to damage during the study or within four years of the end of your participation in the study. You must have reported any damage to the insurer within those four years.

The insurance does not cover all damages. At the bottom of this text you will find a short description of the damages that are not covered. These provisions are in the 'Decree on compulsory insurance in medical scientific research with humans 2015'. This decree can be found in the government's Law Database (https://wetten.overheid.nl).

In case of damage, please contact the insurer directly. In addition, in case of damage, you are requested to contact the principal investigator as soon as possible at:
m.f.boomsma@isala.nl
088-6247202

The insurer of the study is: Stichting Holding Isala Klinieken
Name: VLC & Partners B.V
Address: Postbox 1999, 5200 BZ ‘s HERTOGENBOSCH
Phone number: 073-6924762
E-mail: claims.zakelijk@vlc-partners.nl
Insurance number: PH2007879
Contact person: VLC & Partners B.V. t.a.v. de heer R. van Harten

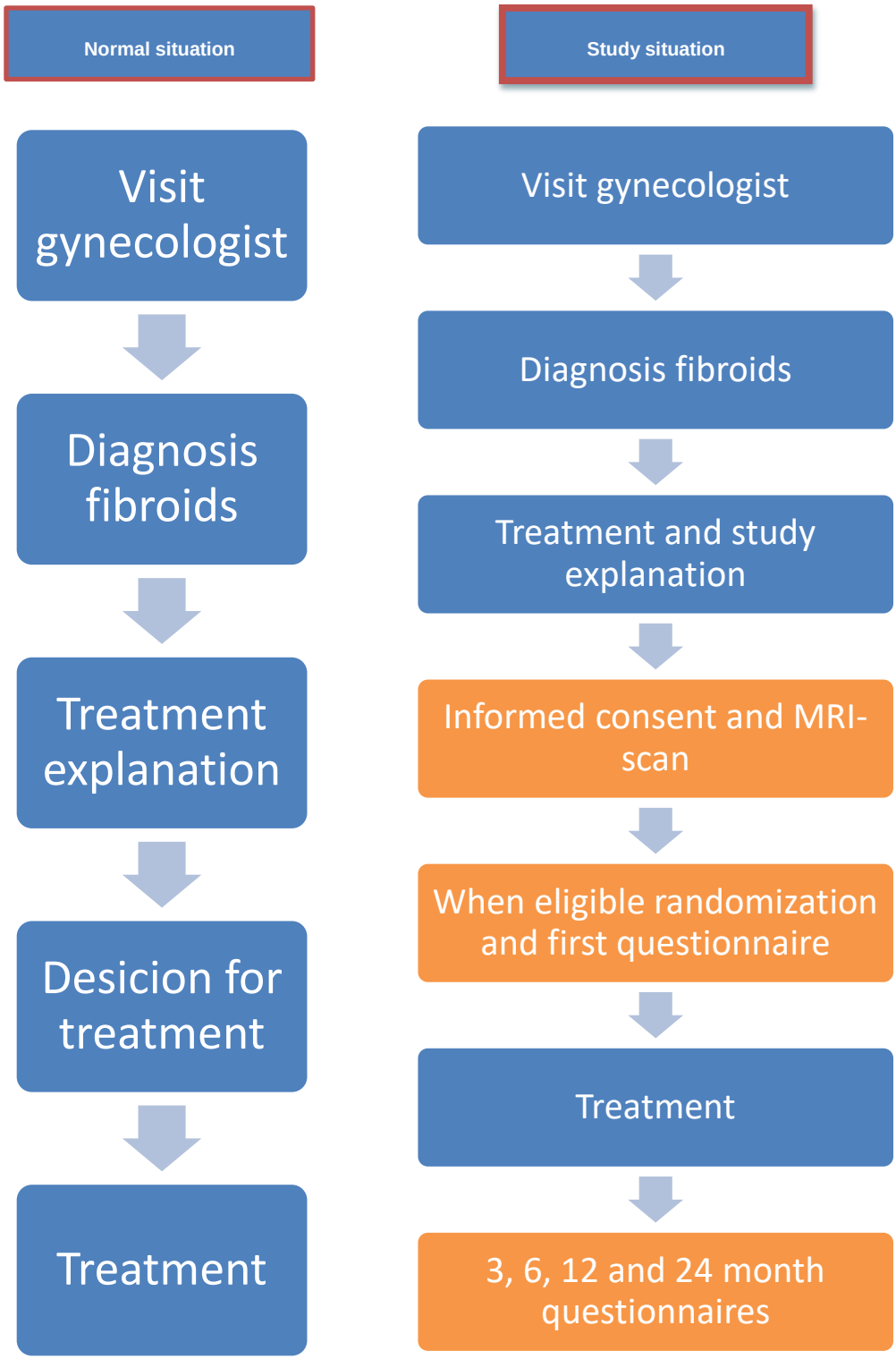
The insurance provides coverage of € 650,000 per subject and € 5,000,000 for the entire study and € 7,500,000 per year for all studies from the same sponsor.

The insurance does not cover the following damages:

- Damage caused by a risk about which you have been informed in the written information. This does not apply if the risk occurs more seriously than was anticipated or if the risk was very unlikely;
- Damage to your health that would also have occurred if you had not taken part in the study;
- Damage as a result of not (fully) complying with directions or instructions;
- Damage to your offspring as a result of a negative effect of the research on you or your offspring;
- Damage as a result of research into existing treatment methods.

Appendix C - Overview of research design

The diagram below shows what the route looks like in the normal situation and if you participate in this study. The orange blocks indicate an abnormal situation.



Appendix D - Additional Information MR-HIFU treatment

MR-HIFU is a treatment that combines an MRI scan with an ultrasound. MR-HIFU is short for Magnetic Resonance guided High Intensity Focused Ultrasound. It is a new treatment for women who suffer from fibroids. More than 30,000 women worldwide have already been treated. MR-HIFU is a non-invasive treatment, meaning that surgery is performed without cutting.

Preparation

The evening before the treatment, it is important that you depilate the skin of your lower abdomen. In addition, it is important to be sober for an MR-HIFU procedure:

- You may eat and drink normally up to 6 hours before the procedure;
- You may only drink clear liquids up to 2 hours before the procedure.

Clear liquids are water, tea, black coffee, lemonade, apple juice, sports drinks, but no dairy products.

Treatment

Prior to the treatment, you will receive pain medication, an enema, an IV and a bladder catheter. The treatment is done under sedation. This is a combination of a sedative and possibly a strong painkiller, mainly meant to make it easier to lie still for a long period of time. You can read more about this in the patient folder on sedation.

The radiologist performs the treatment. During the treatment you lie on your stomach in an MRI scanner. The MRI table contains an ultrasound machine (Focused Ultrasound transducer), which emits high-energy sound waves (ultrasound). By focusing these sound waves into the fibroid, its temperature rises. This causes the tissue to break down without damaging the surrounding tissue around the fibroid. This allows us to treat the fibroid very precisely from the outside, without cutting into your body. The treatment changes and shrinks the fibroid and reduces your symptoms. Immediately after the treatment, we look at how the treatment went with an MRI scan. Whether MR-HIFU treatment is suitable for you depends on the goal of the treatment:

- Reduce symptoms
- Prevent growth of fibroids
- Remove fibroids

Because your uterus is not removed, there is a chance that a fibroid will grow back or a new fibroid will form in a different place in your uterus. You may then need to undergo another treatment. This could be an MR-HIFU treatment, but also a uterine surgery or embolization (interrupting the blood supply to the fibroid). You can find more information about this on the Isala website.

Benefits

- The main advantage of MR-HIFU is that the fibroid can be treated from the outside, without cutting into your body.
- You do not have to undergo anesthesia, as is the case with uterine or fibroid surgery.

- You will be approachable during the treatment. You can express how you feel.
- The procedure takes an average of three hours and recovery is less painful than other procedures such as uterine surgery or embolization.
- You may return home on the day of treatment.
- You recover faster from MR-HIFU treatment than from other fibroid treatments.

Possible risks

The risk of a complication during or after MR-HIFU treatment is small. However, there are risks associated with any treatment. Possible side effects of MR-HIFU treatment include:

- You may have muscle pain for a few days after the treatment because you have to lie still on your stomach for a long time in the MRI scan.
- Your abdomen may be sensitive or you feel cramps.
- Sometimes menstruation occurs after treatment.
- Although we use the MRI scan to precisely locate the fibroid, there is a chance (0.1%) that we heat tissue elsewhere in your abdomen. Think of the bladder, intestines or spinal nerves. You may then incur damage to these areas for which you will need additional treatment, but usually the symptoms go away on their own.
- The skin of your abdomen can also heat up too much, causing a burn. A recovery treatment with burn ointment may then be necessary. In exceptional cases, surgery may be necessary.

After the treatment

After the MR-HIFU treatment, you will be taken to the nursing ward. Here you can recover quietly. When the sedation has worn off completely and you are feeling well again, you can go home, unless there are medical reasons to keep you in the hospital for a longer period of time for observation. Because you have been given a light sedation, you will not be allowed to go home alone or drive a vehicle after the MR-HIFU treatment. Therefore, please arrange for someone to accompany you home before the treatment.

Appendix E: consent form for participant

Research on the treatment of fibroids

- I read the information form. I was also able to ask questions. My questions were adequately answered. I had enough time to decide whether to participate.
- I know that participation is voluntary. I also know that I can decide at any time not to participate or to stop the study. I do not have to give a reason for doing so.
- I consent to informing my general practitioner and the specialist treating me that I am participating in this study.
- I consent to requesting information about my fibroid from my gynecologist treating me.
- I consent to the collection and use of my data to answer the research question in this study.
- I give permission for my data to be shared with the research team at Isala Zwolle.
- I know that for the purpose of monitoring the study, some people may have access to all my data. Those people are listed in this information form. I give permission for that access by those people.
- I give permission for my general practitioner and treating specialist to be informed of unexpected findings that (may) be important to my health.
- I know that if I become pregnant before the treatment, I will not be able to undergo this treatment and will not be able to participate in this study. I know that after treatment I can become pregnant within the study under certain conditions.
- I do give consent to keep my personal data longer and to use it for future research in the field of my condition.
  □ Yes □no
- I do give permission to approach me again for follow-up research after this study.
  □ Yes □no
- I want to participate in this research.

Name participant:
Email address participant:
Signature: Date: __ / __ / __

I certify that I have fully informed this subject about the said study.

If any information becomes known during the study that could affect the subject's consent, I will inform her in a timely manner.

Name of investigator (or his/her representative):
Signature: Date: __ / __ / __

Additional information was provided by:

Name:

Position:

Signature: Date: __ / __ / __

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