

MR-Guided Focused Ultrasound* in Fibroid Treatment – Results of the 4th Radiological-Gynecological Expert Meeting

Magnetresonanz-geführter fokussierter Ultraschall* zur Myombehandlung – Ergebnisse des 4. radiologisch-gynäkologischen Expertentreffens

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ABSTRACT

Magnetic Resonance-guided focused ultrasound (MRgFUS; Syn.: HIFU = high intensity focused ultrasound) is a safe and effective thermoablative technique to treat fibroid-related symptoms. The evidence is limited due to a lack of randomized trials. The indication for treatment by MRgFUS are symptomatic uterine fibroids. This consensus paper covers criteria to measure success, contraindications, side effects and complications of MRgFUS treatment. The role of MRgFUS in the setting of family planning is part of this publication.

Key Points:

- MRgFUS therapy should be based on a clear understanding of the aim of treatment and the wish of the patient.
- Success of MRgFUS/HIFU treatment should be judged by the degree of improvement (alleviation) or disappearance of fibroid-related symptoms.
- The indication for treatment by means of MRgFUS/HIFU is based on a gynecological examination incl. ultrasound performed by a specialist. Necessary prerequisite for MRgFUS/HIFU treatment is a contrast-enhanced MRI of the pelvis.
- A number of more than 5 fibroids (leiomyomata) limits the success of MRgFUS/HIFU therapy; the indication to treat fibroids exceeding 10 cm in diameter should be reviewed critically.
- A recommendation for the treatment of fibroids by MRgFUS to patients who seek to conceive cannot be given based on the current state of knowledge.

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ZUSAMMENFASSUNG

Der Magnetresonanz-geführte fokussierte Ultraschall (MRgFUS; Syn.: HIFU = hochintensiver fokussierter Ultraschall) ist ein sicheres und effektives thermoablatives Verfahren zur Behandlung myombedingter Beschwerden. Die Datenlage zum MRgFUS ist aufgrund des Fehlens

* To be differentiated from non-MR-guided focused ultrasound.

** For the consensus meeting participants listed in alphabetical order at the end of the article.

randomisierter Studien limitiert. Indikation für eine Behandlung mit MRgFUS ist ein symptomatischer Uterus myomatosis. Das Konsensuspapier behandelt Erfolgskriterien, Kontraindikationen, Nebenwirkungen und Komplikationen

der MRgFUS-Behandlung. Eingegangen wird auch auf die Anwendung von MRgFUS im Rahmen der Kinderwunschbehandlung.

Introduction

Fibroid treatment using MR-guided focused ultrasound (MRgFUS; syn.: HIFU = high-intensity focused ultrasound) is a thermoablative procedure in which the tissue to be treated is heated by focused ultrasound in single small volume increments (sonifications, syn: sonications) under constant MRI monitoring until complete denaturation of the planned fibroid volume is achieved. Upon completion of thermoablation, imaging shows an absence of contrast enhancement in the treated tissue (NPV = non-perfused volume).

The MRgFUS procedure is performed transabdominally, is organ-preserving and noninvasive and can be performed on an outpatient basis.

This treatment method is provided by only a few specialized facilities.

The goal of MRgFUS therapy is to reduce or eliminate fibroid-related symptoms in affected women. Shrinking of a fibroid can be achieved with ultrasound treatment. Complete remission of the fibroid should not be expected and is not the goal of treatment.

The disciplines of gynecology and radiology agree that the indication for the treatment of uterine fibroids should be determined by a gynecologist following examination and counseling of the patient. Comprehensive patient counseling regarding the treatment options for symptomatic uterine fibroids encompasses not only medication-based and surgical options, but also non-surgical therapy options including uterine artery embolization (UAE) and MRgFUS. The decision for or against an alternative therapy should be made under consideration of the patient's wishes and with knowledge of other treatment options, their chances of success, limitations, typical side effects and possible complications (informed decision).

In Germany, Austria and Switzerland, MRgFUS represents a treatment option for patients with fibroid-related symptoms and allows further treatment individualization for uterine fibroids.

Aim of the consensus meeting

The intention of this fourth consensus meeting was to evaluate and categorize MRgFUS in the fibroid treatment spectrum. The 16 participants of the radiological-gynecological expert meeting came to a consensus following thorough discussion with evaluation of the current literature^{***} and their own experiences.

The panel of experts was aware that this was an assessment of the possibilities and limitations of a radiological treatment method held in conjunction with gynecology specialists who do not

perform the procedure themselves but have expertise and experience with the diagnosis and medication-based and surgical treatment of disorders of female reproductive organs.

The expert group comprised of 7 radiologists and 9 gynecologists that met on January 12, 2019 in Berlin for the fourth radiological-gynecological consensus meeting regarding MRgFUS treatment included participants from Germany and Switzerland.

After a discussion, the group agreed in consensus upon the following recommendations. The consensus paper is supported by the gynecologists and radiologists listed at the end of the article. The paper reflects the current state of knowledge.

However, the data regarding MRgFUS is limited due to a lack of randomized studies.

Structural requirements for performing MRgFUS treatment

MRgFUS should only be performed at medical facilities with the necessary expertise and experience regarding MRgFUS therapy. This also includes non-surgical and surgical management of side effects and complications. Moreover, there should be options for initiating post-interventional pain management.

Examinations required prior to MRgFUS therapy

Treatment decisions are based on a gynecological examination incl. ultrasound performed by a specialist. An MRI scan with contrast ideally in prone position must be acquired for planning purposes. The contrast-enhanced image is used to assess whether and to what degree the fibroid is perfused.

Prior to every MRgFUS procedure, the indication for hysteroscopy and fractionated curettage must be critically reviewed with respect to bleeding pattern and endometrium thickness and structure. Unremarkable cytological smear findings of the uterine cervix must have been obtained within the previous 12 months.

During the informed consent discussion prior to MRgFUS, the patient should be informed of the lack of preinterventional histological confirmation of the presumed uterine fibroids, as in all other organ-preserving fibroid treatment methods.

The total risk of an undetected uterine malignancy (including uterine sarcoma) in patients undergoing surgery for a presumed fibroid is specified between 0.09 % and 0.18 % in the current literature. Symptoms and imaging do not allow exclusion of a uterine sarcoma in particular.

*** The appendix contains references to selected relevant publications.

The decision for an organ-preserving medication-based, surgical, or interventional-radiological treatment option should therefore include explanation of the risks of delayed diagnosis of a sarcoma.

Indications for MRgFUS therapy

A symptomatic uterine fibroid with an anatomical position allowing safe access for MRgFUS is an indication for MRgFUS treatment. Treatment is complicated by the presence of more than five fibroids. In the case of fibroids with a diameter greater than 10 cm, the use of MRgFUS therapy should be carefully reviewed due to the large fibroid volume and the resulting long treatment time. The data regarding fibroid number and volume is unclear.

MRgFUS is used as an alternative to surgical and medication-based methods and to UAE. Treatment decisions should be based on the treatment objective and the wishes of the patient. Given technical feasibility, MRgFUS is a good option for patients desiring the least invasive treatment possible.

Success criteria for MRgFUS treatment

The goal of MRgFUS therapy is the improvement or elimination of fibroid-related symptoms. A volume reduction is desired but is considered a secondary treatment goal.

An NPV (= non-perfused volume) that is as large as possible and is positively associated with symptom control is considered a technical parameter for treatment success in focused ultrasound.

Contraindications for MRgFUS therapy

- Suspicion of malignancy (absolute)
- Pregnancy (absolute)
- Acute inflammatory process (absolute)
- Pedunculated subserosal fibroids (absolute)
- Submucosal fibroids type 0 and I (relative; absolute in case of a desire to have children)
- Insufficient acoustic window for treatment (e.g. intestine in the planned path of the ultrasound beam) (absolute)
- Uterine fibroids with more than 5 fibroids (relative)
- Uterine fibroids with a diameter greater than 10 cm (relative)
- Large scars in the acoustic window (relative)
- Fibroid positioned near the os sacrum (relative)
- General contraindications to MR contrast agents (relative)
- Postmenopausal patient (relative)
- Relative and absolute MRI contraindications

Ulipristal acetate can result in increased perfusion of fibroids; consequently the evaluation of the feasibility of MRgFUS therapy and the actual treatment can be negatively affected.

MRgFUS therapy in patients wishing to become pregnant

There is no published prospective data regarding women who wish to become pregnant and have been treated with MRgFUS/HIFU. Therefore, a recommendation on the use of MRgFUS/HIFU prior to a planned pregnancy cannot be made for women who want to conceive.

MRgFUS and pregnancy

Pregnancy after MRgFUS therapy is possible.

However, if a patient wants to become pregnant after MRgFUS/HIFU therapy, a minimum wait time of approximately 6 months between fibroid treatment with MRgFUS and conception is recommended.

Side effects/complications of MRgFUS therapy

Relevant side effects and complications during and after MRgFUS therapy are rare:

- Pain
- Skin burns
- Inflammation of subcutaneous adipose tissue and the musculature of the abdominal wall
- Paresthesia of the leg due to nerve irritation or damage
- Deep vein thrombosis (very rare)
- Bowel perforation (extremely rare)

Fibroid treatment with MRgFUS can result in increased and/or irregular bleeding in the three months after treatment as well as expulsion of (necrotic) fibroid material that is unpleasant and painful for the patient. In such cases a uterine-preserving approach with vaginal extraction and, if appropriate, in combination with hysteroscopy is usually possible. Perioperative antibiotic prophylaxis is recommended in these cases.

Follow-up after MRgFUS therapy

Post-treatment examination by a specialist is recommended after MRgFUS. Imaging procedures are useful (e.g., sonography in conjunction with Doppler sonography, MRI). If treatment is unsuccessful (no improvement in symptoms and/or increase in fibroid size) or in the case of abnormalities on imaging (increase in size of fibroid(s) or uterus), further diagnostic workup is required.

Outlook

Based upon available data and experience, a revision of recommendations for MRgFUS therapy of fibroids is planned in 2021.

The participants of the consensus meeting recommend the preparation of an interdisciplinary guideline on all aspects of the diagnosis and treatment of uterine fibroids on "uterine fibroids".

Appendix

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Participating professional societies and professional organizations:

BVF, Berufsverband der Frauenärzte [Professional Association of Gynecologists]
DeGIR, Deutsche Gesellschaft für Interventionelle Radiologie und minimal-invasive Therapie [German Society for Interventional Radiology and Minimally Invasive Therapy]
DGOG, Deutsche Gesellschaft für Gynäkologie und Geburtshilfe [German Society of Gynecology and Obstetrics]
DRG, Deutsche Röntgengesellschaft [German Radiological Society]
NOGGO, Nordostdeutsche Gesellschaft für Gynäkologische Onkologie [Northeastern German Society of Gynecological Oncology]

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Conflict of Interest

The authors declare that they have no conflict of interest.

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