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Summary

- Magnetic resonance imaging-guided focused ultrasound (MRI-FUS) is a minimally invasive alternative to surgical and less invasive treatments for uterine fibroids.

- Early results from small sample studies indicate that the procedure may provide short-term symptom relief with advantages such as shorter recovery time. Few occurrences of major adverse events are reported.

- Little information is available on the costs or comparisons with other treatments.

- Long-term studies of larger patient groups are needed to provide further reliable evidence on the safety of this procedure, as well as its clinical and cost-effectiveness.

The Technology

MRI-FUS is a minimally invasive treatment in which thermal ablation is used to reduce the size of uterine fibroids. During the procedure, focused ultrasound waves penetrate the anterior abdominal wall and heat the targeted fibroid tissue. The local temperature reaches 55°C to 90°C for a few seconds, causing cell death (necrosis) at the focal points. The necrotic tissues are later absorbed by the body. MRI monitoring is used during the procedure to minimize the risk of injuring adjacent tissue and organs; and to detect the changes in temperature at the treated tissue. While no surgical incision is required, the procedure can take several hours. Patients are usually discharged after one hour of observation and typically resume normal activities within one or two days.

The ExAblate® 2000 system (InSightec Ltd., Israel) is a device that is used to ablate tissue with focused ultrasound under the guidance of an MRI scanner (Signa 1.5T MRI system, GE Healthcare, Waukesha WI US).

Regulatory Status

The ExAblate® 2000 system received US Food and Drug Administration (FDA) marketing approval in October 2004. The device is intended to treat women who have completed child bearing or who do not intend to become pregnant. The ExAblate 2000 received CE (Conformité Européene) recognition for European marketing in 2002. The ExAblate 2000 system is not licensed by Health Canada for marketing in Canada, though a system was used in clinical trials for breast cancer, breast fibroadenoma and uterine fibroids, at the Saint-Luc hospital in Montréal (Rob Newman, InSightec – North America, Dallas: personal communication, 2005 Mar 4). The technology is available in seven US health centres.

Patient Group

Uterine fibroids, also known as uterine leiomyomas, are benign tumours of the uterus that occur in 20% to 50% of women >30 years old. Although most women with uterine fibroids are asymptomatic, the condition may cause heavy menstrual bleeding, resulting in anemia, pelvic discomfort and reproductive dysfunction – including infertility.

MRI-FUS treatment may be an option for women who would like to achieve symptom relief without undergoing surgery. This treatment is not intended for women whose uterus is >24-week gestation size; who may wish to become pregnant in the future; or who cannot...
have MRI (such as those with metallic implants or pacemakers).\textsuperscript{11,12} Depending on their location, some fibroids, such as those near the bladder or bowel walls; or submucosal fibroids may be unsuitable for MRI-FUS treatment.\textsuperscript{7}

**Current Practice**

A hysterectomy is the standard, permanent treatment for women who have symptomatic uterine fibroids and who do not want to retain their uterus. Myomectomy, another surgical treatment for fibroids, involves the removal of individual fibroids, while leaving the uterus in place. Several less invasive treatments are available to treat the symptoms of pressure or heavy bleeding, including uterine fibroid embolization (UFE), endometrial ablation and drug therapy.\textsuperscript{1,10,13-15}

**The Evidence**

No systematic reviews or randomized controlled trials that compared MRI-FUS to uterus-sparing alternatives for patients with symptomatic fibroids, were identified. The available evidence of the benefit and harm associated with MRI-FUS comes from one prospective cohort study and five case series. The cohort study was described in the manufacturer’s information booklet,\textsuperscript{11} while the results for patients treated with MRI-FUS were reported in a journal article.\textsuperscript{16} Four case series were published as abstracts or conference proceedings;\textsuperscript{17-21} one was published as a journal article.\textsuperscript{3} Patients with a uterus size <20 weeks gestation or fibroid size <10 cm were eligible to be enrolled in the case series. The number of study participants ranged from nine to 55. The case series described decreased fibroid volume after the procedure and improved fibroid-related symptoms in most of the patients. The patients were followed <6 months after the procedure.

A prospective cohort study compared 109 patients in the ExAblate treatment group to 83 patients in the hysterectomy group.\textsuperscript{11} Patients in both groups reported a better health-related quality of life (QoL) and satisfaction with the treatment outcomes. In the ExAblate group, 77 out of 99 patients achieved significant symptom relief (defined as a >10-point reduction in the Symptom Severity Score subscale of the Uterine Fibroid Symptom Quality of Life (UFS-QOL) questionnaire). The mean (± SD) volume of fibroids decreased from 334.4±240.4 cm\(^3\) at baseline to 295.4±256.4 cm\(^3\). Symptom improvement from baseline was maintained in 38.5% (42/109) of patients 12 months post-treatment. Although both groups showed significant QoL improvement three months and six months after the treatment compared with baseline, the ExAblate group reported better outcomes in the first three months compared with the hysterectomy group, while the latter reported better outcomes than the ExAblate group three months post-treatment.

As a condition of the US FDA regulatory approval, InSightec Ltd. is required to continue a three-year follow-up study of the 109 patients from the pivotal study; and to study an additional 250 patients – including a cohort of African-American women who have a higher incidence of fibroids and who were underrepresented in the initial trial.\textsuperscript{6}

According to the cohort and case series studies, the ablated volume by MRI-FUS was not considerable, but the relief of fibroid-related symptoms was significant. The number of fibroids that were treated in one session was limited to four. The limitations of the studies include no control group; short-term follow-up; absence of full reporting; a small number of patients being involved in most studies; and all studies being sponsored by the manufacturer. There might be an overlap between studies in the reports on some patients. In the prospective cohort study, hysterectomy was an inappropriate comparator because of the significant differences between the two treatment modalities. In addition, patients in the hysterectomy group reported more comorbid conditions such as diabetes, hypertension and anemia, as compared with the ExAblate group. The difference in treatment effects between the two groups should be interpreted cautiously. Uterine fibroid embolization (UFE) would be more suitable as a comparator,
because of the similarity in the targeted patient population (women with symptomatic fibroids who prefer a less invasive treatment); and relevant outcome measures (e.g., shrinkage of fibroids and symptom relief). No comparative trials of MRI-FUS and UFE have been published.

**Adverse Effects**

The adverse events that were most commonly reported during the procedure and within 10 days post-treatment were pain or discomfort; and urinary tract and gastrointestinal symptoms. Cases of transient nerve damage were also recorded. Compared to patients treated with MRI-FUS, those treated with hysterectomy experienced more adverse events, such as fever and infection; and had more disability days (19.2 days versus 1.2 days in the ExAblate group). Twelve months post-treatment, 21% (23/109) of the patients treated with MRI-FUS had a recurrence of symptoms and underwent a second MRI-FUS treatment or alternative treatments, such as hysterectomy. No device-related deaths, life-threatening injuries, permanent injuries or device-related emergency interventions occurred during the 12-month follow-up period. Skin burns during the treatment and nerve stimulation or injury causing leg pain or tingling were reported. Injuries to other structures or organs are possible if the effect of the focused ultrasound therapy extends beyond the target area. Data regarding the impact of MRI-FUS on future pregnancy are lacking – particularly data on the possible risk of uterine rupture. In patients who receive MRI-FUS therapy and other conservative treatments for fibroids, fibroid recurrence is possible.

**Cost**

The MRI-FUS system costs US$2.5 million when the use of a MRI scanner is included. Other costs include the presence of a radiologist who is required during treatment. The cost of one treatment with MRI-FUS might be cheaper than that of a hysterectomy because of shorter hospital stays and fewer procedure complications. Treatment with MRI-FUS is a long process (the procedure may take several hours); and it requires the collaboration of a gynecologist and a radiologist. There is no evidence regarding the cost-effectiveness of this treatment relative to other modalities.

**Concurrent Developments**

Diagnostic ultrasound is a potential alternative to MRI for guidance during the procedure. This may reduce the cost, making the treatment more readily available to smaller health care centres or outpatient clinics. Ultrasound guidance cannot detect local temperature changes and has poorer resolution. MRI-FUS is also being investigated for the treatment of patients with benign and cancerous breast and other tumours.

**Rate of Technology Diffusion**

As the effect of MRI-FUS on fertility is unknown, the technology has only been used in pre- or peri-menopausal women who do not desire a future pregnancy. Given the high prevalence of uterine fibroids and the non-invasive nature of this treatment, wide acceptance by women with symptomatic fibroids might be expected – if its ability to maintain fertility can be shown.

**Implementation Issues**

MRI-FUS provides a minimally invasive opportunity to treat symptomatic fibroids in an outpatient setting. It offers potential advantages over surgical treatments, such as shorter recovery time and fewer complications. Multiple treatments may be required. Some patients will ultimately require a hysterectomy because of the fibroid regrowth and symptom recurrence. The application of MRI-FUS is in an early phase. The cost-benefit for treatment with MRI-FUS is unknown. Studies of the long-term effectiveness of MRI-FUS for the treatment of uterine fibroids in a larger study group; and in comparative studies with other uterine-sparing methods, such as ultrasound-guided-FUS and uterine fibroid embolization, are needed.
References


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