



The **O**perating **R**oom of the Future.



ExAblate[®]OR

**Image guided Robotic Acoustic Surgery using
MR guided Focused Ultrasound technology**

ExAblate OR is a non-invasive Operating Room:

- ✓ Non-invasive outpatient procedure
- ✓ Real-time treatment outcome monitoring and control
- ✓ Minimizes complications, adverse events and recovery time
- ✓ High treatment conformity, sparing non-targeted tissue
- ✓ Non-ionizing radiation
- ✓ Single platform for multiple indications
- ✓ Single session treatment

InSightec[®]



Personalized surgery for optimal results

The ExAblate OR system integrates two well established technologies, focused ultrasound and magnetic resonance imaging, to non-invasively ablate targeted tissue within the body while sparing the surrounding tissue. Healthcare providers can now offer their patients personalized surgery with ExAblate OR to achieve optimal treatment results in an outpatient procedure.

The system uses multi-parametric MR imaging for:

- Tumor visualization and imaging in three orientations to provide precise and accurate identification of pathology
- Treatment planning and beam path visualization to assure safe treatment
- MR thermometry to provide continuous real-time temperature feedback on treatment outcome
- Complete control and monitoring of the treatment by the physician



Physician controls and monitors treatment in real-time

The ExAblate OR system delivers personalized treatment through:

- **Multi-parametric MR imaging** – enabling precise targeting
- **3D automatic planner**** – planning a conformal treatment envelope while taking into account Limited Energy Density Region (LEDR) to protect sensitive areas and organs
- **Optimal beam path visualization** – to assure conformity and control
- **Real-time temperature feedback and control** – MR thermometry shows the temperature changes during treatment in both the target and surrounding tissues to verify treatment outcome and safety
- **Maximized treatment rate** – utilizing variable length sonication (single burst of focused ultrasound energy), Enhanced Sonication and variable frequency acoustic transmission

** All of these applications have or will require a full FDA Investigation Device Exemption for clinical trials in the United States. Not all applications are approved in all regions. Please consult your local representatives and read the product labeling specific for your region to determine approved indications for use.*

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What is personalized surgery with ExAblate OR?

MR thermometry enables measurement of energy deposition in the target tissue and displays the reaction of the tissue to the acoustic energy in real-time. Based on this input, the physician can adjust the treatment parameters and achieve optimal control of the treatment outcome. This closed loop feedback allows tailoring the treatment to the specific patient while taking into account variations in tissue response and anatomical differences.

System configuration

The system allows treatment of multiple indications utilizing a single common table with application specific cradles. ExAblate OR offers both commercially approved and research treatment options for a variety of clinical indications. *

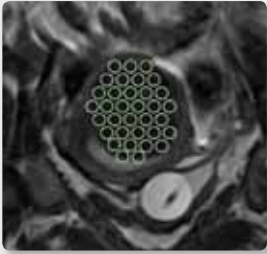
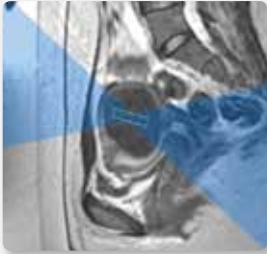
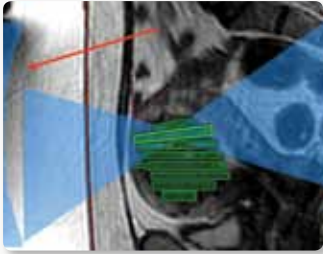
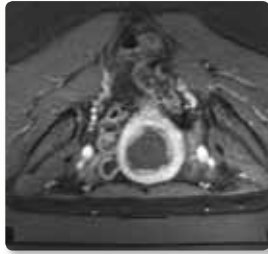


Non-invasive, outpatient operating room

ExAblate features

Complete control over treatment

The physician controls the treatment from the operator console. Adjustments are made during treatment based on treatment outcome monitoring, patient comfort and patient movement. Treatment time varies according to the indication being treated and the volume of the tumor.

Planning	Treatment	Beam shaping	Evaluation
			
Pre-treatment 3D multi-parametric imaging enables precise tumor targeting	Real-time feedback and beam path visualization for controlled treatment	Ability to shape the beam to overcome obstacles and for greater treatment volume**	Post-treatment contrast imaging enables precise assessment of treatment outcome

3D automatic planner**

The ExAblate OR 3D automatic planner is designed to generate the highest level of conformity with the reference volume. On completion of the treatment, contrast enhanced images help evaluate the non-perfused volume (NPV), shown to be the best predictor of tissue necrosis, and a measure of treatment success.¹

Non-perfused volume (NPV) is the volume of tissue which following ablation, does not get enhanced after injection of contrast material.



ExAblate OR table with enhanced ergonomics for patients and physicians

Enhanced ergonomics for patients and physicians**

The improved table is designed to include enhanced features for patient comfort and to facilitate table handling via automatic docking.

Five axis robotic transducer**

The ExAblate phased array transducer is positioned by a robotic system and can be steered to move laterally, up-down and tilt in superior-inferior, left-right directions.

The five axis robotic system enables optimal positioning of the transducer thereby reducing energy density at the beam path. Data accumulated (outside the USA) shows that this feature supports treatment in proximity to non-targeted sensitive areas to achieve greater treatment volume.

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Bone Metastases

ExAblate may provide non-ionizing, localized pain relief by thermally ablating the nerves on the periosteum.

Each sonication is capable of ablating a large area along the bone surface. Since the thermal conduction of the bone is relatively low, the focused ultrasound beam affects mainly the area on the bone that is covered by the beam. During a bone treatment, the system is configured so that the targeted bone will be heated in a uniform way.

During each sonication, the heat absorbed by the bone is capable of ablating the pain receptors in the periosteum resulting in pain relief. Patients are under sedation during this non-ionizing outpatient treatment. Bone treatments generally require 10 to 40 sonications and last one to two hours.

Single session, pain reduction within days

Over two hundred patients with painful bone metastases have been treated using ExAblate system.

Phase I and II clinical studies have shown that pain scores were reduced from an average of 5.9 to 3.8 within three days after treatment and further reduced to 1.8 at thirty days follow-up. Pain relief was maintained for at least three months. 72% of the patients experienced significant pain relief and 50% experienced complete pain relief.^{2,3,4}

An ongoing phase III clinical study for FDA approval is currently being conducted.

Patients with osteolytic as well as osteoblastic lesions can be treated, regardless of the primary cancer.

Enhanced accessibility and improved patient comfort

ExAblate offers two systems for pain management:

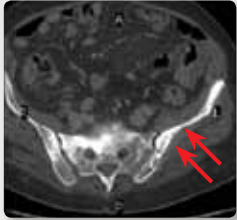
- A robotic transducer system within the cradle (similar to the uterine fibroid configuration)
- Portable conformal bone transducer system which enables access to multiple anatomical locations. MR tracking coils are used to keep track of its positioning and chilled degassed water is circulated within a semi-permeable membrane to provide acoustic coupling and to cool the skin during treatment.



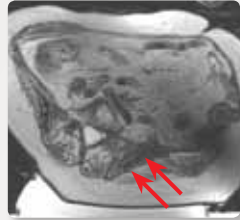
Patient being treated with conformal bone transducer

Bone Metastases

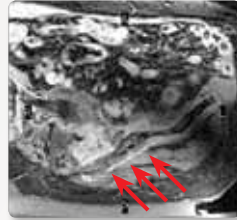
Case review A



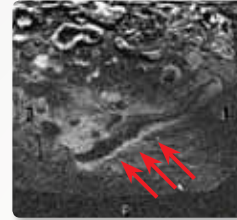
CT image



Axial T2w planning image



Post-treatment contrast enhanced images showing non-enhanced area of the targeted bone, surrounded by soft tissue edema



Post-treatment contrast enhanced subtraction images showing non-enhanced area of the targeted bone, surrounded by soft tissue edema

Female patient with primary breast cancer

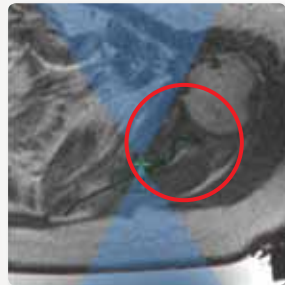
Osteoblastic bone lesion in the left iliac bone

Courtesy of LATO-S. Raffaele Giglio Hospital, Cefalù, Italy

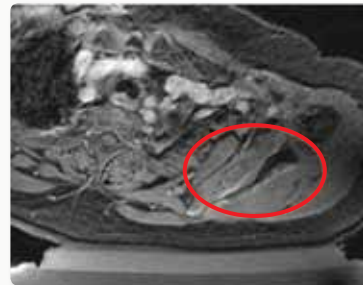
Case review B



CT image of targeted bone lesion in the left scapula



Axial T2w MR image with planned sonication

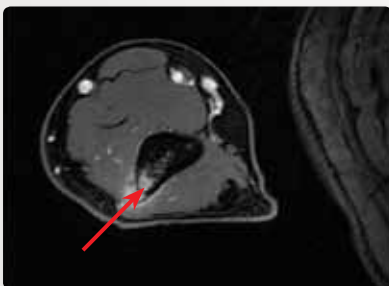


Axial T1w FatSat contrast-enhanced MR image shows non-enhanced areas at the targeted bone surrounded by soft tissue edema

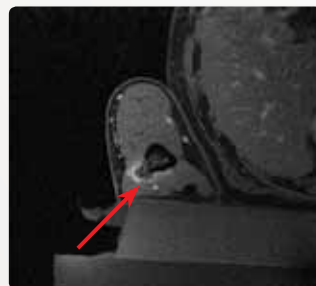
52 year old patient with primary breast cancer

Courtesy of Bundang CHA Hospital, Korea

Case review C



T1w FatSat MR image with contrast shows the enhancement of the lesion before the treatment



Immediately post-treatment T1w FatSat contrast-enhanced image shows non-enhanced area at the location of the lesion

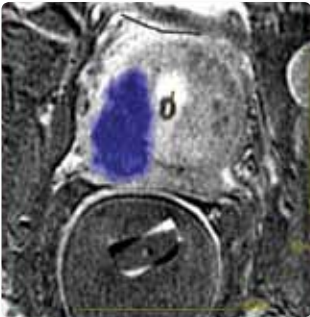
61 year old male patient with primary lung cancer tumor

Courtesy of Petrov Institute of Oncology, St. Petersburg, Russia

ExAblate is being investigated for the treatment of early stage, low risk prostate cancer. The ExAblate OR prostate module is an endorectal device designed for non-invasive thermal ablation of prostate tumors using high intensity focused ultrasound under real-time MR imaging monitoring and control. Current treatment options for prostate cancer include prostatectomy (surgical removal of the prostate gland), radiation therapy, brachytherapy (implantation of radioactive seeds), and cryotherapy. Ultrasound guided high intensity focused ultrasound (HIFU) has also been used, outside the USA, to treat prostate cancer. The potential advantages of MR guidance over ultrasound guidance are improved imaging of the prostate and surrounding critical structures and real-time measurement of thermal energy deposition allowing better control of the treatment.

Current treatment alternatives are accompanied by relatively high levels of adverse events which significantly impact the quality of life of prostate cancer patients. The most common are incontinence and impotence. Due to the introduction of PSA screening tests, prostate cancer is diagnosed at an earlier age thereby increasing the necessity for a treatment option that minimizes adverse events. The ExAblate prostate system has been designed to provide effective treatments while minimizing the debilitating side-effects caused by damage to functional areas of the prostate and neurovascular bundles, thus the treatment is expected to enable patients to return to normal life within a day or two while maintaining their quality of life. Feasibility trials (outside the USA) which started in 2010 continue to show initial promising results.

Case review



NPV with dose overlay acquired by MR thermometry showing correlation between thermal dose and non-perfused volume

71 year old patient who had no adverse effects after treatment

Courtesy of Petrov Institute of Oncology, St Petersburg, Russia



Prostate module

**Caution – Will require FDA
investigational device exemption**

ExAblate is being investigated (outside of the USA) for the treatment of liver tumors. This is a prevalent disease with limited treatments available. Surgical resection is an option for only a small percent of patients and local ablative techniques such as microwave, laser, cryotherapy and radiofrequency ablation treat another relatively small group of patients and require penetration of the liver capsule which may cause adverse events.

Because ExAblate delivers thermal energy to a precisely defined tumor deep in the body non-invasively, it has the potential to provide a good treatment option for many patients who suffer from primary and secondary tumors, including those who are not eligible for other treatment options and those who have limited liver reserves.

An initial cohort of patients has been successfully treated and InSightec is currently developing an abdominal system to handle respiratory motion gating and rib interference with energy delivery.

Case review



Post treatment (1 week)



Post treatment (2 months)

54 year old patient with 2 cm hepatoma

Following treatment, tumor area was non-enhanced and the sequential T2w images show that surrounding edema is shrinking

Courtesy of St. Mary's Hospital, London, UK

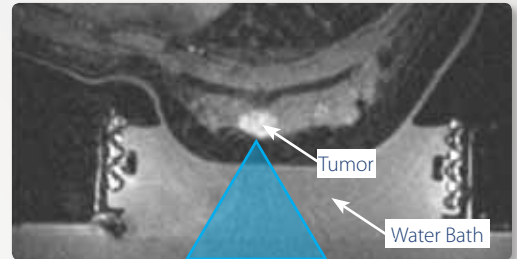
Breast cancer

Caution – Investigational Device Limited by United States Law to Investigational Use.

The ExAblate OR breast module is being investigated (outside of the USA) and is currently under FDA investigational review for the treatment of breast cancer. The desired result is total non-invasive ablation of the tumor verified by MR images.

ExAblate may offer the following potential benefits:

- Non-invasive alternative to surgical lumpectomy
- Definition of tumor boundaries by multi-parametric MR imaging
- No general anesthesia, surgery, surgical scar, or need for breast reconstruction



Breast treatment setup with projected treatment beam path

To date, over two hundred breast cancer patients have been treated in various clinical trials. In one series, patients were treated with ExAblate and then underwent a lumpectomy. Assessment of the resected specimen showed an average necrosis of 97% with 50% of the patients achieving 100% necrosis⁵. These patients then continued their treatment regimen according to the standard of care.

Case review



Pre-treatment



Post-treatment



19 months follow-up



30 months follow-up

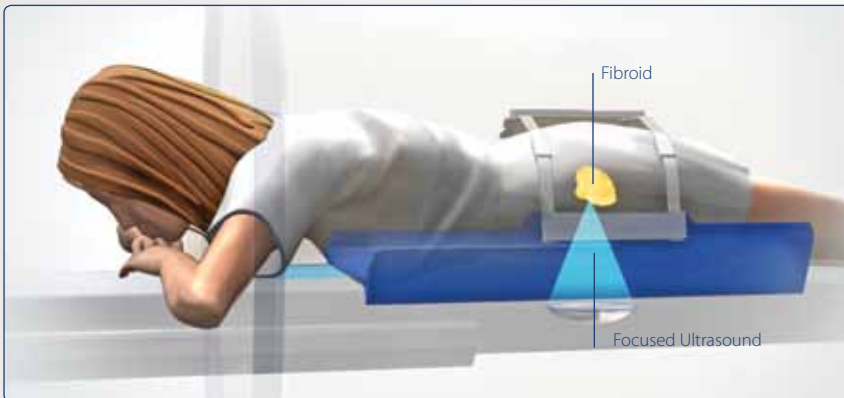
37 year old patient, right breast treated

Courtesy of Breastopia Namba Hospital, Miyazaki, Japan

Uterine fibroids

Approved for commercial use

ExAblate® OR treats symptomatic uterine fibroids. This outpatient treatment provides ablation of fibroids and offers sustained symptom relief. The system enables precise treatment monitoring; outcomes can be predicted immediately after completion of the procedure.



Focused ultrasound generates heat by focusing ultrasound waves, ablating tissue only at the focal point

More than six thousand women worldwide have opted for the ExAblate non-invasive treatment for uterine fibroids and the numbers keep growing. ExAblate expands treatment choices for women, offering:

- Uterus sparing procedure
- Consistent, predictable and immediate results
- Few to no side effects
- No hospital stay
- Quick recovery compared to alternative treatments

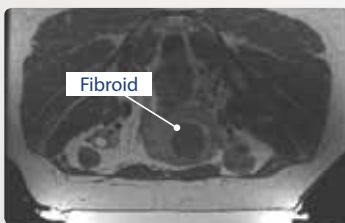
Recent advances in ExAblate technology now enable the treatment of large and vascular fibroids as well as adenomyosis** (CE approved), broadening the patient base. The ability to treat a greater volume of the fibroid is expected to result in greater clinical efficacy.

ExAblate technology for uterine fibroids attracts patients

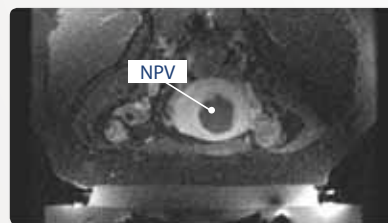
The ExAblate system has been shown to significantly increase patient interest and traffic. A leading site in Tokyo, Japan reported that the number of patients treated for uterine fibroids has increased threefold in one year. Patients who were not eligible for the ExAblate treatment were referred for other procedures such as hysterectomy and myomectomy.⁶

Case review

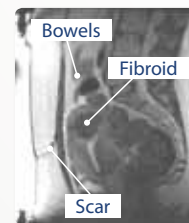
A 43 year old patient suffered from heavy menstrual bleeding, blood clots, and fluctuations in the menstrual cycle. Pre-treatment imaging showed a fibroid volume of 50cc with a significant scar in the energy beam path. The treatment took 55 minutes. The result post treatment showed 90% NPV with no adverse effects.



Axial T2w



Axial T1+c Post treatment result



Sagittal T2w

Courtesy of COGP Hospital,
Moscow, Russia

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References

1. Al Hilli MM, Stewart EA. Magnetic Resonance-Guided Focused Ultrasound Surgery, *Seminars in Reproductive Medicine*, 2010, 28(3):242-249
2. Catane R, Beck A, Inbar Y, Rabin T, Shabshin N, Hengst S, Pfeffer RM, Hanannel A, Dogadkin O, Liberman B, Kopelman D. MR-guided Focused Ultrasound Surgery (MRgFUS) for the Palliation of Pain in Patients with Bone Metastases – Preliminary Clinical Experience, *Annals of Oncology*, 2006.
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4. Gianfelice D, Gupta C, Kucharczyk W, Bret P, Havill D, Clemons M. Palliative Treatment of Painful Bone Metastases with MR Imaging-Guided Focused Ultrasound, *Radiology*, 2008.
5. Furusawa H, Namba K, Thomasen S, Akiyama F, Bendet A, Tanaka C, Yasuda Y, Nakahara H. Magnetic Resonance-Guided Focused Ultrasound Surgery of Breast Cancer: Reliability and Effectiveness, *J Am Coll Surg*, 2006, 203(1):54-63.
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Excellence Backed by Experience

InSightec® is the pioneer and global leader in MR guided focused ultrasound technology for image guided acoustic surgery.

ExAblate® 2000 system was the first system to use the MR guided focused ultrasound technology. The ExAblate 2000 system received CE mark in 2002 and the Food and Drug Administration (FDA) approval in 2004 for the treatment of symptomatic uterine fibroids. ExAblate 2000 received the European CE Mark for pain palliation of bone metastases in June 2007 and for adenomyosis in June 2010. This device has won numerous innovation awards and has been used to treat thousands of patients around the world.

ExAblate® OR is a non-invasive Operating Room. The system incorporates interchangeable cradles for each application that are interfaced with the common table. ExAblate OR offers both commercially approved and research treatment options for a multitude of clinical indications such as: uterine fibroids and adenomyosis**, breast cancer, prostate cancer, pain palliation of bone metastases and various other indications*.

ExAblate® One is designed to address women's health needs, including the treatment of uterine fibroids, adenomyosis**, and clinical research of breast cancer.*

ExAblate® Neuro** is designed for the non-invasive treatment of various brain disorders.

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About InSightec

InSightec Ltd. is a privately held company founded in 1999 and owned by Elbit Imaging, General Electric, MediTech Advisors, LLC and employees. InSightec is headquartered in Haifa, Israel with US offices in Dallas, TX. InSightec's systems are compatible with 1.5 and 3.0T GE Healthcare MRI systems (Signa and Discovery 450 and 750).

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