Body and Bone Applications of Magnetic Resonance Image-Guided Focused Ultrasound Treatment

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Learning objectives

Magnetic resonance imaging-guided focused Ultrasound (MRgFUS) treatment is a recently developed noninvasive treatment method that integrates FUS and MRI system. MRI can provide the imaging information and real-time thermometry for target definition, treatment planning, and closed-loop feedback of energy deposition. With the successful treatment results of uterine leiomyomas, it is expanding application fields.

we propose to attend this objectives:

1. To understand basic knowledge of Magnetic Resonance Guided Focused Ultrasound Treatment.
2. To describe the clinical advantages of Magnetic Resonance Guided Focused Ultrasound Treatment over the conventional treatments
3. To demonstrate the body and bone applications of Magnetic Resonance Guided Focused Ultrasound treatment, especially regarding to the uterine leiomyoma, prostate cancer, metastatic bone disease.
Background

Magnetic Resonance Guided Focused Ultrasound is a new treatment modality combining the MR imaging and focused ultrasound. It is a non-invasive approach, which is coped with current treatment trend. The best advantages of it over the other modalities are that target site is monitored with MR. MR Technique can provide the exact three dimensional anatomic information and real-time temperature monitoring, which is mandatory for safety and efficacy in these kinds of treatment modalities. With the successful treatment results of uterine leiomyoma, it now extends the application fields, especially oncologic diseases.

1. **Basic principles for MRgFUS**

In the past decades, minimally invasive treatment methods have been introduced. Among them, high-intensity focused ultrasound (HIFU) or focused ultrasound (FUS) became recognized as a noninvasive extracorporeal thermal ablation method and has been tested for the ablative treatment of benign lesions and malignancies. In FUS therapy delivery systems, piezoelectric transducers generate acoustic energy. The frequency between 200 kHz and 4 Mhz is used depending on the application.

If live tissue is heated beyond the threshold for protein denaturation (57-60°C) for a few seconds, coagulation necrosis occurs. Lower temperatures can also kill tissues if the exposure time is lengthened (exponential relationship). The ideal treatment is a selectively killing the tumor cell with appropriate margin, while sparing the neighboring normal tissue as much as possible. To achieve this goal in thermal ablations, spatial and temporal monitoring of temperature distribution within the targeted tumor volume is mandatory. MRI can provide the MR thermometry, so optimal energy delivery with MRgFUS can be monitored and controlled in real time.

MRI has clear advantages over other imaging modalities for guiding and monitoring FUS ablation:

- MRI provides high-resolution imaging in any orientation for planning treatment and evaluating treatment effects owing to its superb soft tissue contrast. In contrast, ultrasound (US) imaging is inferior to MRI for ability to clearly define tumor margins and may limit application of HIFU technology.
- MRI is the only currently available technique to non-invasively create quantitative thermal map. Without these essential features that MRI possesses, US-guided HIFU will have a relatively narrow application area and, in most cases, will not be competitive with surgery.
**MRgFUS consists of** operator console and docking table/interchangeable cradle system, allows multiple applications. FUS device is fully integrated into the MR system and cradle. Subject is placed on the MRI table/cradle and moved into the MRI scanner.

**The treatment process of MRgFUS (Fig. 1)**

- begins with radiologist acquiring a set of MR images, identifying target volume of tissue to be treated, and drawing treatment margin.
- The therapy planning software computes the type and number of sonications required to treat defined region.
- MR images taken during the actual sonications provide quality diagnostic image of target tissue and a quantitative, real-time temperature map overlay, to confirm therapeutic effect of the treatment.
- The focus is then automatically moved electronically or mechanically to succeeding treatment point and the process is repeated until entire volume has been treated.
- MR imaging permits safe targeting of the energy, provides 3D anatomical information for exact tumor localization and visualizes the beam path to avoid surrounding tissue, nerves, scars and other organs.
- MRgFUS involves real time and continuous MR thermal feedback, and determines whether the energy was directed correctly and the appropriate amount delivered. Thermal ablation also enables immediate evaluation of the treatment response and allows repeated treatments.
- At the end of the treatment, the results are evaluated by the non-perfused regions on T1-weighted contrast enhanced images. These areas are summed to create a volume, termed-non-perfused volume (NPV)

2. **Advantages of MRgFUS over the other treatments**

As more people wish to improve their quality of life and generally avoid invasive procedures, the demand for alternative treatments has increased during the last decade. The conventional treatments accompany the higher morbidity and mortality.

- As MRgFUS use the extracorporeal ultrasound as an energy source, there are no risks related with invasive procedures, such as bleeding, infection.
- As an example of uterine leiomyoma which is commercially treated with MRgFUS, outpatient clinic-based MRgFUS can be done in single session and general anesthesia is not required. Therefore the recovery period is very short and rapid return to normal activity is possible within 1-3 days.
- There is no radiation exposure with MRgFUS, so no long term radiation hazards.
- Because of the lack of tissue toxicity, MRgFUS can be repeated multiple times, if necessary.
3. **Body applications**

The evidence for the effectiveness of the uterine leiomyoma procedure, which is the first commercialized application for MRgFUS, was the starting point of expansion to the other indications that are currently under clinical investigation. These include pain palliation of bone metastases, breast cancer, prostate cancer, liver tumors and brain growth and other central nervous system diseases. Among them, we had clinical experiences with uterine leiomyoma, bone metastasis, prostate cancer. MRgFUS with pain palliation of bone metastasis and prostate cancer were done in a clinical trails sponsored by InSightec company (Haifa, Israel).

### 3.1 Uterine leiomyoma

**Uterine leiomyomas (UL)**

- the most common gynecological problem experienced by women
- clinical significance in 20-40% of women of childbearing age
- classified according to their location; Intramural, submucosal, and subserosal
- The most common clinical symptoms are menorrhagia (30%), pelvic pain with or without dysmenorrhea or pressure symptoms (34%), infertility (27%), and recurrent pregnancy loss (3%).
- Other symptoms include anemia (consequent on heavy menstrual bleeding), urinary incontinence, and sexual dysfunction.

There are several options for treatment of symptomatic UL: invasive/semi-invasive procedures (hysterectomy, uterine arterial embolization) and medical therapy (hormonal therapy). The women want to preserve their uterus, although they will not be a future pregnant, and health related quality of life (HRQoL) has become the important issue in treatment of UL.

**MRgFUS**

- alternative as a non-invasive, safe, and effective treatment
- can avoids the need for anaesthesia and be performed with outpatient clinic base
- preserves the uterus and ovaries for further pregnancies
- short recovery time and allows faster return to normal activities
- fewer adverse effects than current alternative treatments

**For successful treatment of MRgFUS in UL**, we need to select an appropriate candidate. The considering factors during screening include the location, size, number, distance from sacral bone surface, obstacles to the ultrasound beam path, vascularity,
abdominal wall scar, possibility of malignancy. Symptom improvement after MRgFUS is closely related with the non-perfused volume (NPV) after treatment (Fig. 3, 4). The reported good indication for MRgFUS is UL with the hypo-intense signal intensity in T2-weighted MRI. The intensity of the MR signal of the uterus may be associated with the degree of blood flow and the fluid content of the tissue. MR hypo-intensity of UL means the less vascularity and fluid content of tissue, so there is a positive correlation between the ability to ablate the tissue by MRgFUS and the hypo-intensity and homogeneity of the fibroid on MR. On a recent report, the long term success rate was 69%.

3.2 Prostate cancer

With the increased prostate cancer awareness and screening, the incidence of prostate cancer has rapidly increased in recent period. In 2011, prostate cancer was the most frequent cancer in men in US (29%) and the second leading cause of cancer death in American men (11%). In Korea, prostate cancer is the most rapidly increasing cancer in men and 5th most frequent cancer in Korean man. However, most prostate cancers currently diagnosed fall into the low-risk category with minimal risk of disease progression.

Traditional treatment of men diagnosed with localized low risk prostate cancer

- radical prostatectomy and whole-gland radiation therapy (external beam or brachytherapy), although clinically effective, give rise to significant morbidity, including incontinence, impotence and rectal injury,
- active surveillance has the risk of disease progression involving significant burden to the patient and health care systems, as well as long-term psychological pressure. It has been shown that about 90% of the patients under active surveillance will eventually undergo some kind of radical treatment.
- The desire to achieve adequate tumor control while avoiding unnecessary treatment related complications has driven research into minimally invasive focal procedures designed to eliminate the aggressive portions of the tumor without affecting surrounding critical structures.

Prostate system consists of endocavitary (endorectal) probe devise. Equipped active cooling system maintains the temperature around 10°C of rectum and protects it from thermal injury (Fig. 4). The real time thermal monitoring and multiplanar anatomic information regarding to prostate provided by MRI allow the effective treatments of tumor and the critical structures, such as neurovascular bundle and sphincter, etc., preservation.
Our early clinical experience with two cases showed MRgFUS treatment for prostate cancer can be performed safely with preserving the potency and continence (Fig. 5) until 6 months and 3 months. Further follow up is remained to determine the oncologic outcome.

3.3 Metastatic bone tumor

Bone is the third most common organ involved by metastatic disease behind lung and liver. Current treatments for patients with bone metastases are primarily palliative and include localized therapies (radiation and surgery), systemic therapies (chemotherapy, hormonal therapy, radiopharmaceutical, and bisphosphonates although the primary goal of the use of these therapies are often to address the disease itself), and analgesics (opioids and nonsteroidal anti-inflammatory drugs). Treatment with external beam radiation therapy (EBRT) is the standard of care for patients with localized bone pain, and results in the palliation of pain for many of these patients. Twenty to 30% of patients treated with radiation therapy do not experience pain relief. Re-treatment rates are generally reported in the range of 10-25%.

Contrast to conventional bone treatment system, which is installed in a table/cradle system, the recently developed Conformal System integrates new features that were developed for the bone application. The system to be used in this study utilizes new software, a conformal transducer and patient interface that increases coupling by using a cooled porous membrane that in turn enhances safety (Fig. 6). These new features enable the patients to assume a position that is most comfortable for them as they will avoid lying on a painful body site, thereby decreasing pain experienced during treatment, compared with treatments performed with the original fixed position in table system. Our early clinical experience showed MRgFUS with conformal bone system is effective for pain palliation in patients with bone metastasis (Fig. 7, 8). Most of the patients showed pain reduction more than 2 VAS score on 3 days after treatment. Two patients with breast cancer showed complete or near complete response on 90 days.
**Fig. 1:** MRgFUS has a real time closed loop system. MR imaging permits safe targeting of the energy, provides 3D anatomical information for exact tumour localisation and visualises the beam path to avoid surrounding tissue, nerves, scars and other organs. MRgFUS involves real time and continuous MR thermal feedback, and determines whether the energy was directed correctly and the appropriate amount delivered. At the end of the treatment, the results are evaluated by the non-perfused regions on T1-weighted contrast enhanced images.

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Fig. 2: MRI of (a) T2-weighted image on pretreatment and (b) contrast enhanced T1-weighted image on immediate posttreatment. Low signal intensity of uterine leiomyoma is noted, which is good indicator of successful result, on pretreatment MRI. Contrast enhanced MRI shows non-perfused area/volume of ablated leiomyoma (arrows), which mean a coagulation necrosis due to thermal ablations by MRgFUS.

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**Fig. 3:** MRI of (a) pretreatment and (b) 12 months after treatment in a 38-years old woman complaining severe menorrhagia and bulk related symptoms. The size of leiomyoma shows decrease and the patient's symptom is almost relieved.

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Fig. 4: The (a) frontal and (b) profile view of endocavitary/endorectal transducer of prostate system. (c) After enveloped with disposable rubber, internal circulating system with cool water lowers the temperature of contacted rectum to protect it from a thermal injury.

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**Fig. 5:** MRI of (a) calculating thermal dose and (b) contrast enhanced T1-weighted image immediate posttreatment in prostate cancer. The area with blue color means the calculated volumetric accumulation of thermal dose which can make the ablated tissue coagulation necrosis. This area is well corresponded with the non-perfused area on contrast enhanced T1-weighted image.

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**Fig. 6:** Transducer of conformal bone system
Fig. 7: MRI of (a) pretreatment and (b) 90 days after treatment in patient with metastasis to left iliac bone. The size of the enhancing mass on left iliac bone has been decreased, especially short diameter. CT of (c) pretreatment and (d) 90 days after treatment. There is new bone formation (arrows) at treated area after 90 days.
**Fig. 8**: VAS score on 90 days after treatment was reduced in the most patients.

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Imaging findings OR Procedure details

A 1.5 or 3 tesla MRI can be used for MRgFUS. Protocol included pretreatment axial, sagittal, and coronal T2 spin echo acquisition and posttreatment sagittal T2 spin echo with axial, sagittal, and coronal T1 gradient echo acquisition after gadolinium injection.
Conclusion

As a non-invasive treatment modality, Magnetic Resonance Guided Focused Ultrasound Treatment seems to be a promising treatment option for various diseases.
References


