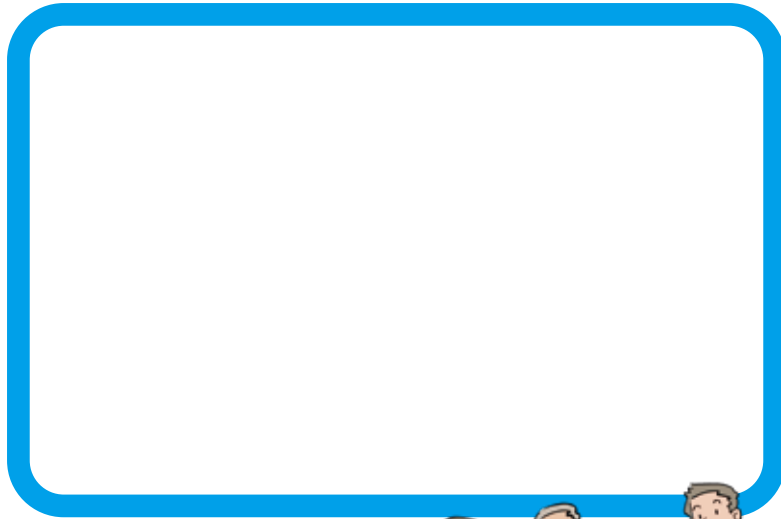


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Supervisor: Dr. Haruhiko Kijima, Professor of Neurosurgery,
Osaka University Graduate School of Medicine

For those suffering from
essential tremor or Parkinson's disease
with hand tremor symptoms

MRgFUS

MR guided Focused Ultrasound





Introduction

"I can't write because my hands are shaking..."

"I can't hold chopsticks or a cup properly while eating..."

"I feel embarrassed when others see me trembling..."

Tremors cause involuntary, uncontrollable shaking. It is a commonly experienced symptom. In addition to tremors caused by normal physiological conditions such as cold or anxiety, there are also tremors caused by diseases. The two most common examples are essential tremor and Parkinson's disease.

Essential tremor is a neurologic disorder, and its only symptoms are tremors of the limbs, head, or voice. It is not a life-threatening disorder, but it can affect a quality of life and social activities.

Parkinson's disease causes motor symptoms such as tremors, slowness of movement, muscle stiffness, and postural instability due to a decrease in dopamine.

MR guided focused ultrasound surgery (FUS) is a treatment that combines magnetic resonance imaging (MRI) and ultrasound without surgical incisions. For more information about treatment or if you have any questions, please consult your physician.



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Types of Tremors

Tremor is a commonly experienced symptom.

While some tremors are normal physiological conditions triggered by nervousness in public or coldness, others are caused by neurologic disorders or diseases. If the tremor is caused by diseases, symptoms can be improved by treatment.

■ Physiological tremor

The most common type of tremor is normal tremor, which is called physiologic tremor. It often occurs when people get nervous in public or when feel cold and does not require treatment.

■ Excessive secretion of thyroid hormones causes symptoms such as tremors, palpitations, shortness of breath, and excessive sweating. Graves' disease is a typical example.

■ Alcohol dependence

This is a mental disorder in which a person loses control over their drinking behavior and becomes mentally and physically dependent on alcohol. In addition to tremors, symptoms include increased sweating, palpitations, sleep disturbances, and anxiety.

Essential tremor and Parkinson's disease

Essential tremor and Parkinson's disease are two of the major neurologic disorders that cause tremors. While essential tremor causes only tremors, Parkinson's disease is characterized by symptoms other than tremors, such as slow movements, muscle stiffness (muscle rigidity), and postural instability (impaired postural control). The characteristic of Parkinson's disease is that tremor occurs while the patient stays still (at rest), whereas essential tremor occurs when moving or maintaining their posture, such as handwriting or holding chopsticks or cups.

Characteristics of essential tremor and Parkinson's disease tremor

	Essential Tremor	Parkinson's disease
The age at which the disease is most likely to occur	Most common in middle-aged and older adults but can occur in younger people	Most common in middle-aged and older adults
Areas where tremor occurs	Hands (fingertips and arms), head (side to side shaking), and voice	Hands, feet, head
Family history	Occasionally (Also called familial tremor)	Occasionally
Tremor characteristics	Trembling when attempting to move or in certain postures (fast tremor)	Trembling at rest (slow tremor)
Symptoms other than tremors	Gait issues	Slow movements, muscle stiffness, unstable posture
Handwriting	Handwriting and eating becomes difficult because the shaking in hands impairs their fine motor skills.	Handwriting becomes progressively smaller (Micrographia)
Eating		Movement is slow, but tremor is not noticeable at the first stage.
Disease progression	Progresses gradually over time	Progresses gradually.

What is essential tremor?

Shaking, medically called 'tremor', is a condition in which a part of the body involuntarily moves rhythmically. 'Essential' as a medical term means that "the cause is not clear." Although it may sound unfamiliar, "essential tremor" is reported to be present in 4% of people over the age of 40 and in 5-14% over the age of 65.

(Source: Japan Neurotherapy Society, "Standard Neurotherapy: Essential Tremor")

Treatment of essential tremor begins with pharmacotherapy, and if it is not sufficiently effective, surgery may be considered.

Complications and side effects are also taken into consideration when treatment is selected.



General Treatment of Essential Tremor

Pharmacotherapy

Pharmacotherapy is commonly used to treat mild and moderate essential tremor.

■ β blocker

Pharmacotherapy is commonly used to treat mild and moderate essential tremor. The beta-blocker Arotinolol suppresses tremor by acting on the sympathetic nervous system and is covered by insurance.



Surgery

Surgery is considered when medication is not sufficiently effective or when medication side effects are too severe.

■ Radiofrequency coagulation (RF)

This treatment reduces the symptoms of tremor by thermally coagulating the nerve circuits in the thalamus of the brain to break down the abnormal nerve signals that cause tremor. A small hole is made in the skull and a thermocoagulation needle is inserted to heat and coagulate the treatment site with radiofrequency waves.

■ Deep Brain Stimulation (DBS)

This is a treatment to reduce the symptoms of tremor by sending electrical signals to the neural pathways in the thalamus of the brain to interrupt the abnormal nerve signals that cause a tremor. A small hole is made in the skull to implant a stimulating electrode, and a pacemaker-like stimulator is implanted in the chest.

What is Parkinson's disease?

It is a neurological disease of unknown cause in which dopamine neurons in the substantia nigra of the midbrain decrease and produce less dopamine, making it difficult to smoothly control body movements.

The main motor symptoms of Parkinson's disease are tremor, slow movement, muscle stiffness, and postural instability.

It is characterized by a resting tremor, which occurs when the patient is sitting with hands on knees.

The number of patients is said to be about 160,000 in Japan, or 1 to 1.5 per 1,000 people, but the disease is more common among the elderly, with a reported incidence of approximately 1 per 100 people over the age of 60.

(Source: Ministry of Health, Labor and Welfare, 2017 Patient Survey in Japan)

The basic treatment for Parkinson's disease is pharmacotherapy, but surgery is considered when medication is not sufficiently effective.

Treatment is selected in consideration of complications and side effects.



General Treatment of Parkinson's Disease

Pharmacotherapy

Dopamine, which has decreased due to a decrease in dopamine neurons, is replaced with a drug called L-dopa. To enhance the effects of dopamine, it is common to use concomitant medications that act on non-dopaminergic nerves, such as inhibitors that prevent L-dopa from being converted to dopamine or broken down before reaching the brain.



Surgery

Surgery is considered when medication is not effective or when the duration in which medicine works becomes shorter.

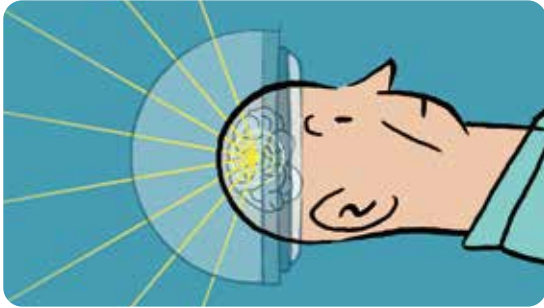
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What is MR guided focused ultrasound surgery (FUS)?



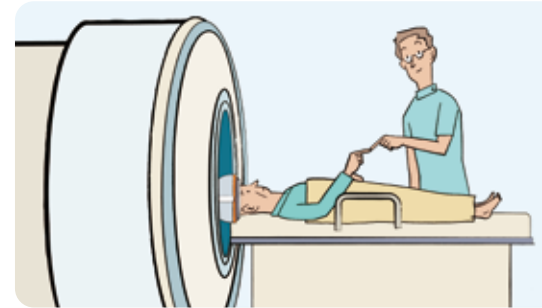
The patient's head is fixed in a treatment helmet containing over 1000 transmitters of ultrasound energy. The ultrasound waves are focused on the ventral intermediate nucleus of the thalamus, an area through which the faulty brain signals causing tremor pass, for thermal coagulation.

Ultrasound penetrates the skull, eliminating the need to drill (perforate) the skull as in conventional surgical therapy. Therefore, the risk of bleeding and infection is considered low.

MRI (magnetic resonance imaging) is used in conjunction with the treatment, so that the exact treatment site and temperature can be determined during the treatment. During treatment, the patient and physician interact with each other to ensure safety and efficacy.

MR guided focused ultrasound therapy is a treatment for the symptomatic relief of hand tremor caused by essential tremor or Parkinson's disease. It does not treat the underlying cause of the disease.

Characteristics of MR guided focused ultrasound therapy



➤ No radiation exposure

➤ No drilling or implantation of devices results in less stress on the body

➤ The treatment is guided in real-time by MRI, providing correct position and temperature monitoring.

➤ During the treatment, the physician interacts with the patient to check the ultrasound exposure and determine its effectiveness.

Treatment process

1 Examination before treatment



- A CT scan is performed to assess the skull.
- The brain is imaged with an MRI.



- Before treatment, the physician combines CT and MRI images to determine the location of thermal coagulation.
- The physician decides whether the treatment can be performed.

2 Preparation for treatment (before entering the treatment room)

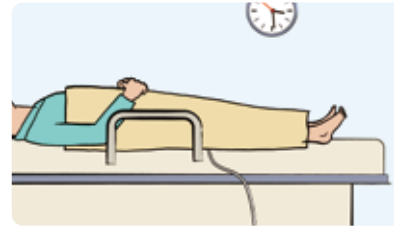


- Shave off hair.



- A metal frame, called a "headframe" is attached to the head to hold it in place and prevent it from shifting position during treatment.

3 Preparation for treatment (in the treatment room)



- Move to the treatment room and lie face up on the treatment bed. Treatment usually takes 3-4 hours.

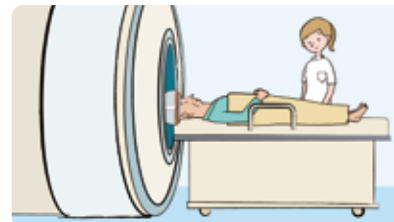


- Connect the head frame to the treatment helmet and secure it so that the head does not move.

4 Treatment begins



- Patient holds a switch in the opposite hand from the treatment side in case he/she feels sick or uncomfortable.

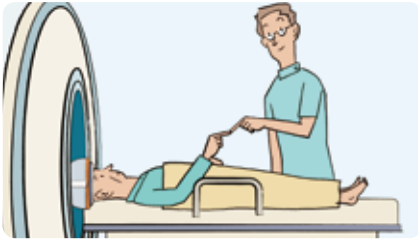


- Patient goes into the MRI. Treatment is performed while the patient is awake.



- A more precise MRI image of the brain is taken over a period of 30 minutes to one hour to confirm the target.

5 Under treatment



- The physician checks for various reactions during treatment. For this reason, treatment is performed without anesthesia while the patient is awake.



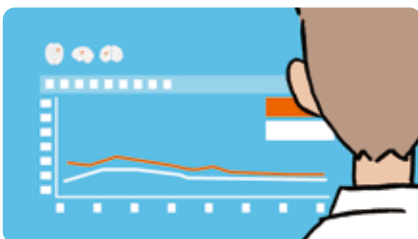
- Patient is required to respond to various movement requests from the physician.



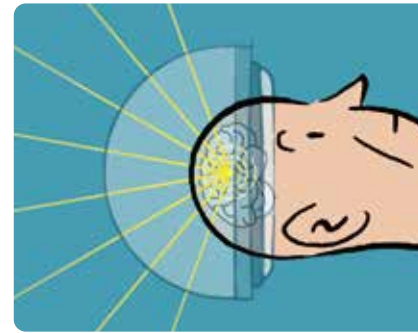
- Various tests will be repeated. Please inform your physician of any symptoms of tremors or sensory abnormalities.



- The physician continuously checks for improvement in tremors and side effects.
- The final determination is made for the optimal treatment site of thermal coagulation.

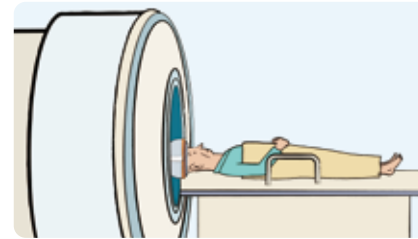


- Gradually increase the temperature of coagulation while conducting trials to check the state of coagulation.



- Ultrasound waves (yellow line in the left figure) emitted from the treatment helmet are focused on a single targeted site (a few millimeters in its size), and the targeted site is then thermally coagulated (like a boiled egg) by raising its temperature to 54-60°C.

6 Completion of treatment



- After the entire treatment process is complete, the head frame is removed and another MRI is performed to confirm the results of the treatment.



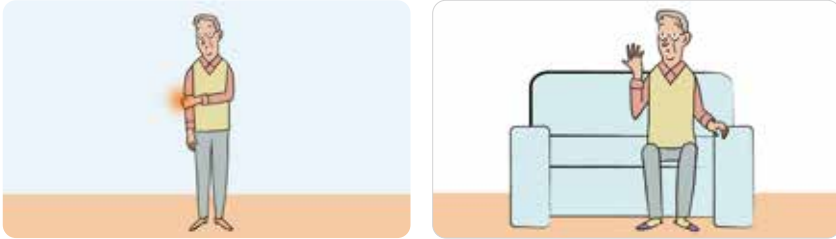
- After treatment is completed, the patient returns to the hospital room. Please consult with your physician regarding the length of your hospital stay.

7 After discharge from hospital



- The patient will receive periodic outpatient consultations. Please consult with your physician regarding schedule.

Risks and side effects associated with treatment



- In rare cases, muscle weakness or extreme sensitivity of the fingertips may occur.
- Temporary gait instability may occur.
- There may be temporary difficulty in gaining strength after treatment.
- If symptoms recur, please consult with your physician before further treatment.

When treatment is not available

- If you cannot stay in the MRI for an extended period of time.
- Inability to respond to physician's questions during treatment.
- Treatment may not be possible depending on the results of various tests.

Please discuss in advance with your physician the treatment plan, method, and reasons why you may not be able to receive it.



Frequently Asked Questions

Q

Will I feel heat or pain while being irradiated with ultrasound?

A

Heat or pain may be felt temporarily. The patient can stop the ultrasound at any time by pressing the button in his/her hand.

Q

Can ultrasound affect other parts of the brain?

A

In treatment, about 1,000 ultrasound waves are focused on a single point, but each ultrasound wave is weak by itself.

Q

When can I start to feel a reduction in tremor?

A

During treatment, the physician will use various tests to confirm ideal location for reduction of tremor and minimizing side effects. Results of the treatment are seen immediately after treatment.

Tremor Self-Check Sheet

After using this tremor self-check sheet, if you notice any tremor symptoms, or if you have any concerns about tremors in your daily life, please consult your doctor or a neurologist at a hospital.

1. Tremor symptoms check

- ☐ My hand trembles when writing. [Yes • No]
- ☐ My hands tremble when holding a spoon or a cup while eating or drinking. [Yes • No]
- ☐ My hands tremble at rest. [Yes • No]
- ☐ My hands tremble while walking. [Yes • No]
- ☐ My head and neck tremble occasionally. [Yes • No]
- ☐ My voice shakes when talking. [Yes • No]
- ☐ I have family members or relatives with tremor symptoms. [Yes • No]

2. Handwriting check

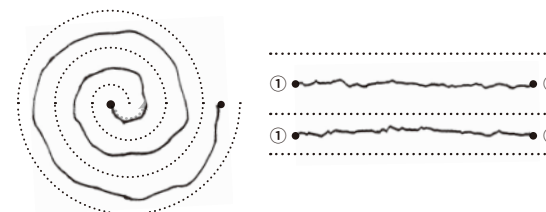
Please write the phrase "It's a beautiful day today."

3. Line drawing check: Draw a spiral line and straight lines.

【Line drawing instructions】

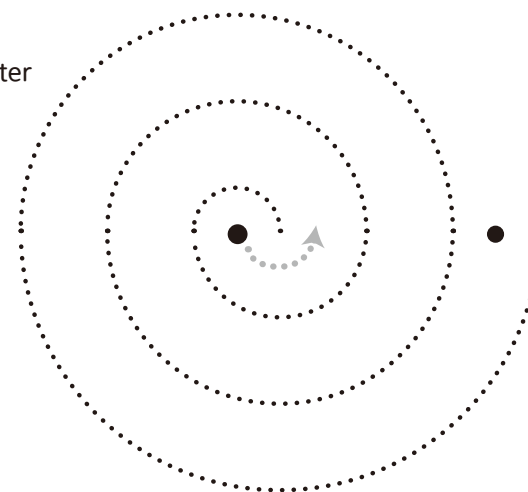
For both spiral and straight lines, try to connect the two dots as smoothly as possible without touching the dotted lines. Do not let your elbow or wrist touch the paper or desk when drawing.

【Example】



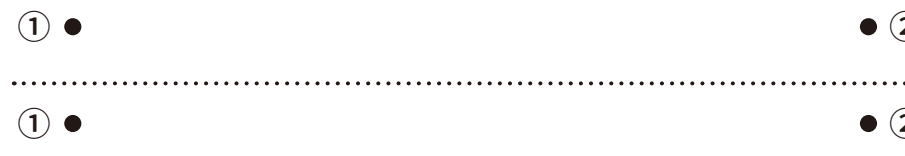
☐ Spiral line:

Draw from the center outward.



☐ Straight lines:

Draw from ① to ② with your right hand, and from ② to ① with your left hand.



Supervised by Dr. Noriaki Hattori, Professor, Department of Rehabilitation Medicine, Faculty of Medicine, Academic Assembly, University of Toyama