Fundamental Study on Cancer Therapy by Blocking Newborn Blood Vessels Using a High-Frequency Rotating Magnetic Field (Wed-Mo-Po3.04-06)

Sato Lab

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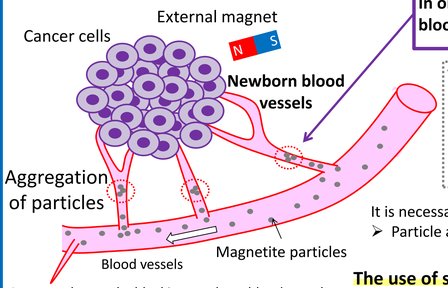
Proposed Cancer Therapy



A cancer therapy by blocking newborn blood vessels using magnetic force control and magnetite particles

In order to prevent nutrient supply to the cancer, blood vessels are blocked with magnetic aggregation.

Therapeutic embolization
- Method to necrose the cancer by blocking blood vessels around cancer tissue with embolic substance such as microgel
- High skills to introduce embolic material during angiography is required

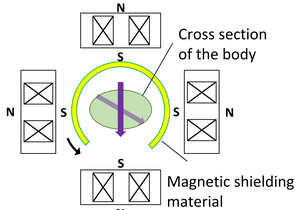
It is necessary to accumulate particles only in newborn blood vessels
➢ Particle accumulation in normal vessels causes blood clots

The use of superconducting magnets is essential in order to apply this treatment to deep cancer in the body

Procedure of the treatment	I. Catheter Injection	II. Particle Accumulation	III. Particle Aggregation	IV. Sustain of the blockage
Control of particle dispersion and aggregation	10 μm Normal blood vessels	20 μm Newborn blood vessels	20 μm Newborn blood vessels	20 μm Newborn blood vessels; Irreversible aggregation (1 week)
Control of magnetic field	-	Rotating magnetic field (RMF)	Uniform magnetic field	Removal of magnetic field

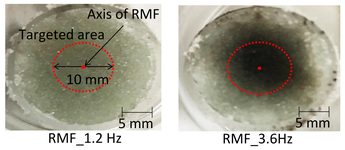
An application method of the high-frequency RMF

An application method of the RMF using four superconducting solenoidal magnets and a magnetic shielding material



The RMF is applied by the leakage magnetic field from the slit by rotating the shielding material

Previous research -Particle accumulation by the RMF-



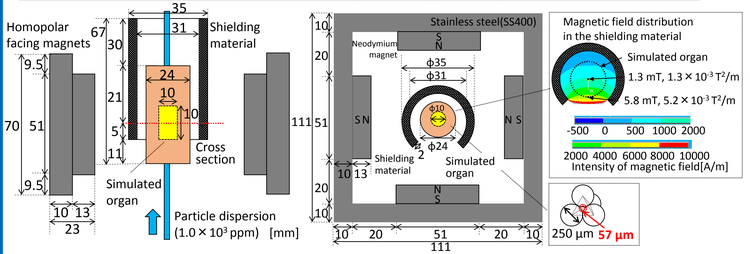
Magnetite particles are accumulated selectively on-axis of high frequency RMF*1

A method to apply a high-frequency RMF using superconducting magnets is necessary

Purpose of the research **Design of a high-frequency RMF that can locally accumulate particles within a spherical range with a diameter of 10 mm, 300 mm away from the magnet surface**

Experimental Method

Purpose・・・ **Investigation about the influence of the RMF frequency on the accumulation range of magnetite particles**

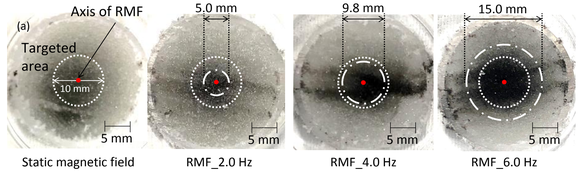


1. A simulated organ was prepared by filling a syringe with glass beads, simulating blood vessel group
2. Magnetite particles were dispersed (2.0 μm, 1000 ppm)in a gelatin solution (25℃, 4.2 mPa・s)
3. Particle suspension was introduced to the simulated organ under the RMF (1 mm/s)
4. After flowing 50 mL of the dispersion, simulated organ was solidified.
5. The simulated organ was divided into 6 sections, and the amount of iron oxide contained in each section was measured

The experiment was conducted with the frequency of RMF as 0, 2.0, 4.0, 6.0 Hz

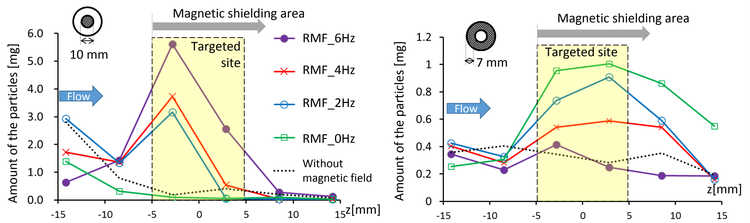
Experimental Results

◆Accumulation range on the cross section of the simulated organ by the RMF



✓Under a static magnetic field, particles are also accumulated outside the targeted area
✓The accumulation range is extended as the increase in the frequency of the RMF

The possibility of controlling the accumulation range by adjusting the frequency of the RMF



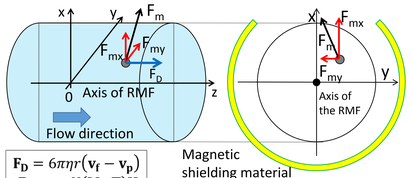
The distribution of accumulated particles in the flow direction (left: within the targeted area, right: outside the targeted area)

✓ The RMF with higher frequency can accumulate particles more efficiency
✓ More particles are guided to the outside under the low frequency RMF
✓ There are more particles in the targeted area than outside the targeted area

Magnetite particles guided to the outside, is likely to flow downstream by the drag force

A calculation method of particle trajectory under RMF-

Purpose・・・**The reason why the magnetite particles are less likely to be guided to the outside of simulated organ under the high-frequency RMF are discussed**

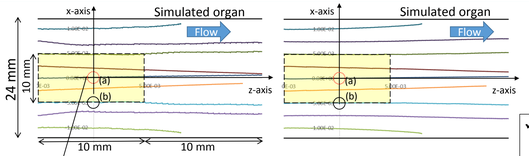


$$\mathbf{F_D} = 6\pi\eta r(\mathbf{v_f} - \mathbf{v_p})$$
$$\mathbf{F_m} = \mu_0 V(\mathbf{M}\cdot\nabla)\mathbf{H}$$

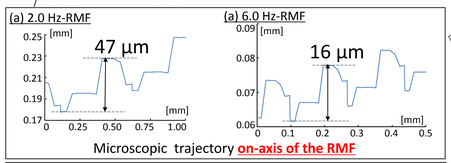
Calculation conditions of particle trajectory	
Particle density	5170 kg/m³
Particle diameter	30.0 μm
Saturation magnetization	0.55 Wb/m²
Viscosity coefficient of 3.8 wt% gelatin solution	4.2 mPa・s
Density of fluid	1.0 × 10³ kg/m³
Rotational frequency of RMF	2.0, 4.0, 6.0 Hz
Vacuum permeability	1.257 × 10⁻⁶ m・kg/(s²・A²)

✓ For considering the time-dependence of the magnetic field, magnetic field was calculated when the shielding material was rotated every 30 degrees. Based on these 12 magnetic field distributions, the magnetic force considering the time change was calculated. (Ansys 10.0, Cybernet System, Japan)
✓ The existence of glass beads are neglected in order to simplify the calculation system, and calculated the particle trajectory when simulated blood flowed into the syringe at a uniform flow rate of 1.0 mm/s.

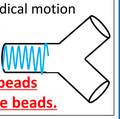
Discussion -Comparison by frequency difference-



✓The particles existing outside of the targeted site are guided to the outside of the simulated organ

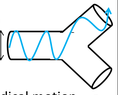


✓ Each particle **on-axis of the RMF** repeats periodical motion with constant amplitude (< width of flow path)



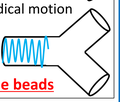
The particles adhere to the surface of glass beads or continue the periodical motion among the beads.

✓ Under the 2.0 Hz RMF, a particle is likely to be guided to the outside and flow downstream (Amplitude 120 μm > Width of flow path 57 μm)



The particles are not accumulated

✓ Under the 6.0 Hz RMF, a particle repeat periodical motion (Amplitude 36 μm < Width of flow path 57 μm)



The particles adhere to the surface or continue the periodical motion among the beads

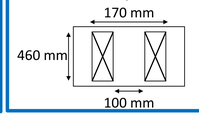
Under the high frequency RMF
✓ **The particles near the target boundary are hardly guided to the outside of the simulated organ**
✓ **The particles are likely to continue the periodical motion along the wall surface of the flow path**

Discussion for Practical Application

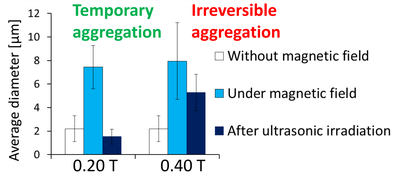
	Particle diameter	Magnetic field product for particle accumulation by RMF
Experimental condition	30 μm	1.34×10⁻³ T²/m
Practical condition	**5.0 μm**	**0.29 T²/m**

Magnetic field product of 0.29 T²/m should be applied to the part about **300 mm away** from the magnet surface

Superconducting solenoidal magnet was designed



Superconducting material	Nb_3Sn
Central magnetic field	5.0 T
Magnetic field on axis of RMF	0.21 T



Particle size of propionic acid-modified magnetite particles*2

By applying a magnetic field over 0.40 T, the particles form irreversible aggregation. These irreversible aggregation can keep the blockage even after the removal of magnetic field, which correspond to the final stage of the treatment.

*1:Makoto KIRIMURA, Yoko AKIYAMA, "Fundamental Study on Cancer Therapy by Blocking Newborn Blood Vessels Using a Rotating Magnetic Field", Journal of Physics: Conference Series (in press)
*2:Makoto KIRIMURA, Yoko AKIYAMA, Shigehiro NISHIJIMA, "Fundamental Study on Cancer Therapy by Blocking Newborn Blood Vessels by Magnetic Force Control", Progress in Superconductivity and Cryogenics, vol. 20, No.2, pp.11-15(2018)

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