Fundamental Study on Cancer Therapy by Blocking Newborn Blood Vessels Using a Rotating Magnetic Field

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Abstract. In this study, we examined a novel cancer therapy by blocking newborn blood vessels with ferromagnetic particles. In this treatment, we try to necrose cancer by accumulating and aggregating the ferromagnetic particles inside the newborn blood vessels. Practically, this method needs to accumulate the particles in the deep part of the body, so the use of superconducting solenoidal magnets is essential. In addition, a design of magnetic field for accumulating the particles selectively in newborn blood vessels is necessary. We designed a rotating magnetic field that can locally accumulate the particles within a spherical range of 10 mm in diameter, 200 mm away from a source of magnetic field. According to the result of experiment and particle trajectory calculation, it was found that the accumulation range of the ferromagnetic particles can be controlled by the rotation frequency of the rotating magnetic field.

1. Introduction
In order to improve the quality of life of patients, some cancer treatments with low side effects and less invasiveness have been studied in recent years. One of them is therapeutic embolization which treats cancer by blocking blood vessels around cancer with microgel[1]. This therapy is expected as a less invasive method with low side effects. In order to treat the diseased part selectively, a skill to guide a catheter to the vicinity of the cancer tissue during angiography is necessary. By the difficulty and the high-risk level of this treatment, the current applications are limited to specific organs such as the liver[2]. To solve this problem, we consider a novel cancer therapy by blocking newborn blood vessels by magnetic force control with multiple superconducting solenoidal magnets. In this therapy, as shown in Figure 1, ferromagnetic particles administered inside the body are accumulated at the target site by the magnetic field control from the outside of the body. After that, blockages of newborn blood vessels are formed around the cancer cells by aggregation of the particles that prevent cancer growth and metastasis.

Figure 2 shows the flow of the therapy we propose. First, the ferromagnetic particles are administered from blood vessels upstream of the cancer tissue with a microcatheter. Next, the administered ferromagnetic particles are accumulated in the newborn blood vessels by the magnetic field control. Thereafter, the particles are aggregated by a uniform magnetic field to block the newborn blood vessel. As a final step, the blockage should be maintained until the cancer tissue is necrosed after removing the magnetic field.
Figure 1. A cancer therapy by blocking newborn blood vessels.

Figure 2. Four-step flow of this therapy.

2. Purpose of this study
In the second stage of this treatment in Figure 2, the particle accumulation in the blood vessels outside the target site causes blood clots. Therefore, in order to apply this therapy to deep cancer in the body, it is necessary to accumulate the ferromagnetic particles only in newborn blood vessels existing deep inside the body.

In our previous research, we simulated ferromagnetic particles trajectories under a rotating magnetic field (RMF) around a human body on the axis containing the target site\(^3\). In the blood vessel on-axis of the RMF, stable magnetic force acts on the particle in a direction toward the outside of the blood vessel, so the particles show a circular movement along the wall surface of the blood vessel. On the other hand, since a stable magnetic force does not act on the particle in the blood vessel off-axis of the RMF, the particles flow out downstream when the magnetic force temporarily becomes small. As a result, the ferromagnetic particles selectively accumulate on-axis of the RMF\(^3\). However, the particle accumulation is confirmed only in a simple experiment simulating two blood vessels parallel to the rotation axis of the magnetic field. Thus, the particle accumulation in a more complicated vascular system is necessary for practical use.

We considered an application of this treatment to pancreatic cancer as an example of cancer that develops deep inside a body. The pancreas is about 200 mm from the body surface and the size of the cancer is about 10 mm at the initial stage\(^4\). Accordingly, we designed the RMF that can locally accumulate the particles within a spherical range of 10 mm in diameter, 200 mm away from a source of magnetic field. Compared with the previous studies\(^2\), we simulated more complicated vasculature closer to practical use. Also, we focused on the frequency of the RMF which is expected to greatly affect the particle accumulation to investigate the relationship between the frequency of the RMF and the accumulation range of the particles.
3. Experiment

3.1. Particle accumulation in simulated organ

In order to investigate the accumulation range of the particles under the RMF as shown in Figure 3, a simulated organ was prepared by filling a syringe (inner diameter: 22 mm) with glass beads (particle diameter: 250 μm). When a fluid flows through this syringe, the flow path (about 57 μm) is formed among the glass beads. Since the size is almost the same as the inner diameter of capillary blood vessels and newborn blood vessels, it can be said that they simulate those blood vessels. In the simulated organ, 10 mL simulated blood in which magnetite particles (particle diameter: 0.10 μm, Fe₃O₄, Mitsui Mining, Japan) were dispersed in 500 ppm flowed in 120 sec. at a constant flow rate of 1.0 mm/s. In the meantime, the RMF was applied to accumulate the particles. After that, the distributions of the particles in the flow direction and in the cross-section perpendicular to the flow were investigated.

![Figure 3. The experimental setup of particle accumulation in the simulated organ by using the RMF.](image)

As simulated blood, a 3.8 wt% gelatin solution was used to simulate the viscosity of blood. The temperature and viscosity of the solution were 293 K and 4.2 mPa·s. A superconducting magnet is necessary for the actual treatment, but as basic research in the small scale, a cylindrical neodymium magnet (φ30 mm × 15 mm, a surface maximum magnetic flux density: 0.50 T) was used. Table 1 summarizes the magnetic field strength applied to the simulated organ. The center of the syringe was set to the central axis of the RMF, and the rotational radius of the RMF was set to 25 mm. The experiments were conducted at the rotation frequencies of 1.2 Hz, 2.4 Hz and 3.6 Hz.

| The upper side of the organ | 2.3 × 10⁻¹ mT |
|-----------------------------|----------------|
| On the central axis of the RMF | 5.0 × 10⁻¹ mT |
| The lower side of the organ | 1.0 × 10² mT |

After the experiment, the simulated organ was cooled and solidified at 268 K. The solidified simulated organ was divided into 10 sections (4.8 mm in the width) and a cross-section was observed by an optical microscope to make the images of the distribution of the cross-section perpendicular to the flow direction. Furthermore, in order to quantify the distribution of the particles in the flow direction, after dissolving each section with 8 mol/L hydrochloric acid and diluting them by distilled water, the concentration of iron ion was measured with ICP-AES (ICPS-7500, SHIMADZU, Japan) and converted into the concentration of the particles.

3.2. Particle trajectory in the simulated organ under the RMF

To investigate the accumulation by the RMF, we calculated the trajectories of the ferromagnetic particles flowing into the simulated organ under the RMF.
The forces acting on a particle in the simulated organ are magnetic force by the RMF and drag force by the blood flow. First, a method of calculating the magnetic force when the RMF is applied to the ferromagnetic particle, is described in Figure 4. Here, the plane including a rotation axis of the RMF and the initial central axis of a magnet is defined as S1, and the plane including the rotation axis and the central axis of the magnet after t [sec] is defined as S0.

Figure 4. Magnetic force acting on the particle under the RMF.

Firstly, we consider the plane S0 as a reference. Assuming that the rotation axis of the RMF is x-axis and the central axis of the magnet is y-axis, the magnetic forces $F_{mx}$ and $F_{my}$ acting in the respective directions are given by the following equations.

$$F_{mx} = \mu_0 V \left( m_x \frac{\partial H_x}{\partial x} + m_y \frac{\partial H_y}{\partial y} \right) \cdots \cdots \text{(eq. 1)}$$

$$F_{my} = \mu_0 V \left( m_y \frac{\partial H_y}{\partial y} + m_x \frac{\partial H_x}{\partial x} \right) \cdots \cdots \text{(eq. 2)}$$

Here, $\mu_0$ is the permeability in vacuum [m⋅kg/(s²⋅A²)], $V$ is the volume [m³] of the particle, $m_x$ and $m_y$ are the magnetization [Wb/m²] of the particle, and $H_x$ and $H_y$ are the magnetic field strength [A/m] in each direction.

Next, assuming that the plane S1 is x’-y’ plane and the direction perpendicular to the plane of the drawing is z’ axis as shown in Figure 4, the magnetic forces $F’_{mx}$, $F’_{my}$ and $F’_{mz}$ are expressed by the projection of $F_{mx}$ and $F_{my}$ on the plane S1. So the magnetic forces $F’_{mx}$, $F’_{my}$ and $F’_{mz}$ are given by the following equations when the rotation frequency is $f$ [Hz].

$$F’_{mx} = F_{mx} \cdots \cdots \text{(eq. 3)}$$

$$F’_{my} = F_{my} \cos(2\pi ft) \cdots \cdots \text{(eq. 4)}$$

$$F’_{mz} = F_{my} \sin(2\pi ft) \cdots \cdots \text{(eq. 5)}$$

In other words, the magnetic force $F’_{m}$ acting on the particle after $t$ seconds from the start of the application of the RMF can be expressed by (eq. 6) by assuming the unit vectors of x’, y’ and z’-axis are $\hat{i}$, $\hat{j}$ and $\hat{k}$, respectively.

$$F’_{m} = \hat{i}F’_{mx} + \hat{j}F’_{my} + \hat{k}F’_{mz} \cdots \cdots \text{(eq. 6)}$$

Next, a drag force $F_D$ acting on the particle by the blood flow was considered. The drag force is calculated by (eq. 7) using the viscosity coefficient $\eta$ [Pa⋅s], the fluid velocity $v_f$ [m/s], and the particle velocity $v_p$ [m/s].

$$F_D = 6\pi \eta (v_f - v_p) \cdots \cdots \text{(eq. 7)}$$
By substituting the magnetic force $F_m$ and the drag force $F_D$ calculated by (eq. 1) to (eq. 7) into the equation of motion (eq. 8), the particle trajectory was calculated by solving it by time evolution using Runge-Kutta method.

$$a = (F_m + F_D)/m \quad \cdot \cdot \cdot$$  (eq. 8)

However, we didn't consider the existence of glass beads in order to simplify the calculation, and considered the particle trajectory when simulated blood flowed into the syringe at a uniform flow rate of 1.0 mm/s. The diameter of the particle is supposed to be 5.0 μm which is the secondary diameter after application of the magnetic field, and other necessary values for this calculation are summarized in Table 2. Magnetic field distribution and flow velocity distribution were analyzed by finite element method using ANSYS 10.0 (Cybernet system, Japan).

### Table 2. Calculation conditions of the particle trajectory.

| Property                              | Value               |
|---------------------------------------|---------------------|
| Particle density                      | 5170 kg/m$^3$      |
| Particle size                         | 5.0 μm              |
| The saturation magnetization (measured value) | 0.55 Wb/m$^2$              |
| Viscosity coefficient of gelatin solution (3.8 wt%, 298 K) | 4.2 mPa·s        |
| Density of fluid                      | $1.0 \times 10^3$ kg/m$^3$ |
| Rotation frequency of the RMF         | 1.2, 3.6 Hz         |
| Vacuum permeability                   | $1.257 \times 10^{-6}$ m·kg/(s$^2$·A$^2$) |

### 4. Results

Figure 5 and Figure 6 show the amount of the magnetite particles accumulated per unit volume in the flow direction under the static magnetic field and the RMF. Comparison between Figure 5 and Figure 6 show that the accumulation range of the particles is more narrowed by using the RMF. This is because the particles tend to accumulate at both ends of a magnet by the large magnetic field gradient under the static magnetic field. Furthermore, it can be seen from Figure 6 that the accumulation range of the particles became narrower with an increase in the rotation frequency. This suggests the possibility of more precise particle accumulation in the flow direction by using the RMF with high frequency.

![Figure 5](image5.png)  
**Figure 5.** Accumulation in the flow direction (Static magnetic field).

![Figure 6](image6.png)  
**Figure 6.** Accumulation in the flow direction (RMF).

Figure 7 shows photographs of the cross-section on the central axis of the magnet after the application of a static magnetic field and the RMF. From the comparison of Figure 7(a) and (b), it can be seen that by utilizing the RMF, the accumulated particles are distributed not only on the installation side of the magnetic field source but also on the entire cross-section. By comparing Figure 7(b)-(d), the particles
are accumulated in a part close to the axis of the RMF, and the accumulation range is also extended as the increase in the frequency of the RMF.

**Figure 7.** Accumulation of particles in the simulated organ by the RMF (a) static magnet field (magnetic field source at the bottom) (b) 1.2 Hz (c) 2.4 Hz (d) 3.6 Hz.

5. Discussions

In this part, three results are discussed by using the particle trajectory calculation. We considered a reason why the RMF can make the accumulation range narrower in the flow direction compared with the static magnetic field, the reason why the particles are accumulated on-axis of the RMF on the plane perpendicular to the flow direction, and the reason why the accumulation range is wider by using the RMF with high frequency.

First, the reason why the RMF can reduce the accumulation range of the particles in the flow direction is considered. Figure 8 and Figure 9 show the particle trajectories under a static magnetic field and under the RMF with 1.2 Hz, respectively. From Figure 8, it is shown that the particles flowing in the simulated organ are guided only to the magnet side. On the other hand, in Figure 9, the particles near the side surface of the simulated organ were guided in the outward direction. Furthermore, focusing on the particle introduced from the point closest to the side in Figure 8, the particle is guided to the side surface at 23 mm upstream from the magnetic field source under the static magnetic field. Besides, in Figure 9 the particle is guided on the side surface at 15 mm upstream under the RMF. These results indicate that the accumulation range under the static magnetic field extends to the upstream side. That is, the accumulation range in the flow direction is widened under the static magnetic field because the particles are guided on the further upstream on the side of the simulated organ.

**Figure 8.** Particle trajectories in the simulated organ under a static magnetic field.

**Figure 9.** Particle trajectories in the simulated organ under the RMF (3.6 Hz).

Next, the reason why the particles are accumulated on-axis of the RMF on the plane perpendicular to the flow direction is considered. Figure 10 shows the particle trajectories under the RMF with the frequencies of 1.2 Hz and 3.6 Hz. It indicates that the macroscopic particle trajectories hardly changed by the difference of the frequencies, and the particles existing near the side were guided to the outside of the simulated organ. However, the lower diagram in Figure 10 showing the microscopic particle
trajectory in the RMF, indicates that the particles on-axis of the RMF periodically move with constant amplitude. Though the particle which is on-axis of the RMF also seems to flow out to the downstream in these Figureures, some particles are considered to show the cyclic motion along the inner wall surface of the glass beads in the actual experiment with the simulated organ\cite{5}. In this case, these particles hardly flow downstream since the drag force becomes small near the inner wall surface of the beads. That is, the reason why the particles are accumulated on-axis of the RMF is the cyclic motion of the particles along the surface of the flow path, that makes the particles hardly flow out to the downstream.

\begin{figure}[h]
\centering
\includegraphics[width=0.8\textwidth]{figure10.png}
\caption{Particle trajectory on-axis of the RMF above the magnetic field source (a) 1.2 Hz, (b) 3.6 Hz.}
\end{figure}

Finally, the reason why the accumulation range of the particles becomes wider by using the RMF with higher frequency was considered. Figure 11 shows the microscopic particle trajectories off-axis of the RMF. It can be seen that the amplitude motion occurs at about 180 μm in the cross-section above the magnetic field under the RMF of 1.2 Hz, whereas the amplitude is 45 μm at 3.6 Hz. In the experiments with simulated organ, glass beads form flow path in the inner diameter about 57 μm. These results show that the particles under the RMF of 1.2 Hz have a larger amplitude than the gap of the glass beads. It indicates the possibility that the particles are gradually guided to the outside of the simulated organ at the branch of the flow path. At the same time, the particle flows out gradually to the downstream. On the other hand, under the RMF of 3.6 Hz, the amplitude matches the size of the gap of 57 μm. It indicates that it is easy to continue the periodical motion along the inner wall between the beads staying on the cross-section above the magnetic field source. Combined with this consideration and the discussion on Figure 10, the reason why the accumulation range becomes wider by using the RMF with higher frequency is that the particles near the target boundary are hardly guided to the outside of the simulated organ, and that the particles are likely to show cyclic motion along the wall surface of the flow path between the glass beads.

From above consideration, with respect to particle accumulation by the RMF, when the amplitude of cyclic motion becomes smaller than about 57 μm of flow path width, the particles tend to accumulate. Whereas when the amplitude becomes larger than about 57 μm, the particles tend to be guided to the outside of the simulated organ. Based on this, at the cases of 1.2, 2.4 and 3.6 [Hz], the diameters of the accumulation range in the cross-section are calculated to be 1.2 [mm], 9.2 [mm] and 14.2 [mm], respectively. Also, by comparing the result with Figure 7 showing the results of the experiments with the simulated organ, it can be seen that the sizes of the range almost agree. This suggests that the accumulation range of the particles in the simulated organ is determined by the magnitude relation
between the amplitude of the cyclic motion of the particle and the flow path width.

**Figure 11.** Particle trajectory off-axis of the RMF above the magnetic field source (a) 1.2 Hz, (b) 3.6 Hz.

6. Study for practical application by using superconducting magnets

In this chapter, a method for a practical application of the RMF and the specification of superconducting solenoidal magnets for this method are examined. In our previous study,[4] we designed the RMF to accumulate ferromagnetic particles (particle diameter: 0.10 μm) in the deep part of the human body. In the above research, it was calculated that a superconducting solenoidal magnet A and B shown in Table 3, can apply a magnetic field product of 8.3 T²/m respectively to the position 150 mm and 50 mm away from the magnet surface. Here, the magnetic field product means a product of magnetic flux density [T] and magnetic field gradient [T/m].

In the above calculation, the patient was assumed to be a child, whose cross-section of the body was assumed to be an elliptical shape of 200 × 140 mm in long and short axis. In order to apply the RMF in the center of the body, we examined a method by periodically changing the excitation intensity of the four magnets. In this case, a pair of magnets A are arranged in front and behind, and a pair of magnets B are arranged on both sides of the body. However, it is difficult to apply the high-frequency RMF in this setting, because the maximum frequency is 8.9 × 10⁻³ Hz even in the maximum excitation speed of the superconducting magnet, 0.2 T/s.

| Superconducting solenoidal magnet A | Superconducting solenoidal magnet B |
|------------------------------------|------------------------------------|
| **Superconducting material**       | Nb₃Sn                               | Nb₃Sn                               |
| **Diameter [mm]**                  | 190                                 | 400                                 |
| **Height [mm]**                    | 200                                 | 230                                 |
| **Central magnetic field [T]**     | 5.9                                 | 4.6                                 |

To solve the problem, we propose a new method in this study. As shown in Figure 12, four superconducting solenoidal magnets are arranged around the body, and the RMF is applied by rotating a cylindrical magnetic shielding material with a slit. In this method, the RMF is applied to the body by...
the leakage magnetic field from the slit. It enables to apply the high-frequency RMF by rotating the magnetic shielding material because it is unnecessary to repeat excitation and demagnetization of the solenoidal magnets.

Based on this, we considered the superconducting solenoidal magnets which are necessary for this method. From the experiment shown in chapter 4, it was found that the magnetic field product required to accumulate the ferromagnetic particles (particle size: 5.0 μm) by the RMF was 0.15 T²/m on the rotation axis. Because this treatment is also applied to adults, we assumed that the cross-section of the body is an elliptical shape of 440 mm × 320 mm in long and short axis. Accordingly, it is necessary to apply the magnetic field product 0.15 T²/m to the position 220 mm away from the body surface. Furthermore, considering the thickness of the shielding material, it is necessary to apply the magnetic field product to the part about 300 mm away from the magnet surface. However, since the magnetic field product for this treatment is 0.15 T²/m, which is much smaller than the magnetic field product 8.3 T²/m required for our previous study, it can be achieved sufficiently by using the magnets smaller than the magnet A in Table 3.

Furthermore, in order to apply this therapy to cancer of various parts, it is necessary to accumulate the particles selectively at the target site off-axis of the RMF. By controlling the magnetic field strength of each superconducting solenoidal magnet in Figure 12, the particles can also be accumulated at the target off-axis of the RMF. In future work, we plan to design these superconducting magnets and shielding materials.

![Figure 12. Method of applying the RMF using superconducting solenoidal magnets and a magnetic shielding material](image)

7. Conclusions

In this study, we examined a novel cancer therapy by magnetic force control. The ferromagnetic particles are administered into the body, accumulated in newborn blood vessels existing around cancer, and aggregated to prevent the cancer growth and metastasis. In order to put this therapy into practical use, it is necessary to design a magnetic field to accumulate the ferromagnetic particles only in newborn blood vessels.

In the discussion, the following reasons for the three experimental results were considered by calculating the particle trajectory in the simulated organ under the RMF. Firstly, the reason why the RMF can make the accumulation range narrower in the flow direction compared with the static magnetic field was considered. Secondly, the reason why the particles are accumulated on-axis of the RMF on the
plane perpendicular to the flow direction was considered. Lastly, the reason why the accumulation range is wider by using the RMF with high frequency were considered.

For practical application, it is necessary to accumulate the particles at a deeper position than this simulation experiment. For that purpose, we use four superconducting solenoidal magnets and the cylindrical magnetic shielding material with a slit arranged around the human body. The magnetic shielding materials are rotated in order to apply the RMF to the human body. In future works, we plan to design these superconducting magnets and shielding materials.

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