

# Investigation of field free region formed by dual Halbach array for focused magnetic hyperthermia

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One of the challenges with magnetic fluid hyperthermia (MFH) is the limited control of magnetic nanoparticle (MNP) oscillations. To overcome this problem new approaches such as localization of MNP oscillations are being explored. In this study, we investigated the manipulation of field free region form by dual Halbach array displacements. We used finite element method simulation to examine gradient patterns in the workspace. Then, we created an experiment platform and took point probe measurements. As a result of the research, it was found that the field free region form can be manipulated by parametric distance changes of dual Halbach array. According to the findings, the field free region can expand and its shape can change from a point-like form to an ellipse-like surface by varying the distance between the arrays. The mapping of dual Halbach array generated gradient patterns for focused MFH was investigated for the first time in this study.

**Keywords:** cancer treatments, field free region, dual Halbach array, magnetic fluid hyperthermia, gradient pattern

## 1 Introduction

Conventional cancer treatments like ultrasound and microwave hyperthermia have relatively poor treatment outcomes and side effects. For example, in microwave hyperthermia the depth of penetration is poor and not suitable for the treatment of deep tumors. Although focusing abilities and depth of penetration are better, ultrasound therapy has the disadvantages of high energy absorption and reflection. RF probe hyperthermia has limited location sensitivity and poor access to deeply located tumors. An alternative approach to cancer treatments is magnetic fluid hyperthermia (MFH). MFH is a thermal therapy in which the temperature of cancerous cells are increased by the help of magnetic nanoparticles (MNPs). When nanoparticles MNPs are exposed to an alternating magnetic field (AMF) they cause an increase in the temperature of the tumor to which they are injected [1, 2]. This temperature 42 – 46°C can be used to destroy tumors, inhibit their growth or increase the susceptibility of tumors [3, 4]. Preclinical studies show that magnetic hyperthermia has significant potential to increase the sensitivity of cancer cells to radiation and chemotherapy or directly kill them [5, 6].

An applied AMF provides energy to change the orientation of the moments of MNPs. This moment movement that releases thermal energy is called the Nel relaxation mechanism [7] and depends on the anisotropy constant ( $K$ ) and the volume of the particle ( $V$ ). AMF can cause not only moment alignment but also the particle spin in the liquid medium. Such spin motion constitutes the Brownian mechanism, in which heating occurs in the surrounding carrier fluid. The Brownian relaxation time de-

pends on the viscosity of the solution ( $\eta$ ) and the hydrodynamic volume of the particle ( $V_H$ ), [8]. Effectively, the relaxation time is combined as these two

$$\begin{aligned}\tau_N &= \frac{\tau_0}{2} \sqrt{\pi \frac{kT}{KV}} e^{KV/kT}, \\ \tau_B &= \frac{3\eta V_H}{kT}, \\ \frac{1}{\tau} &= \frac{1}{\tau_B} + \frac{1}{\tau_N}.\end{aligned}\quad (1)$$

One of the models describing the energy loss of MNPs under the influence of AMF is the Rosensweig model, which is expressed as

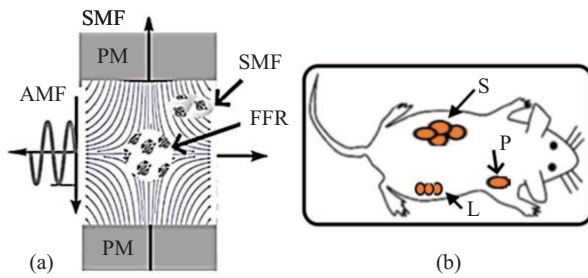
$$P = \frac{1}{2} \omega \mu_0 \chi_0 H^2 \frac{\omega \tau}{1 + \omega^2 \tau^2}, \quad (2)$$

where  $\chi_0$  is magnetic susceptibility,  $H_{ac}$  and  $f$  are amplitude and frequency of AMF and  $\omega$  is angular frequency.

This model correlates MNP energy loss with some physical properties of MNPs and AMF frequency and amplitude [8].

In practical applications of MFH, MNPs tend to move from tumor to healthy tissue over time. In an example study, the effect of dynamic viscosity ( $3 \times 10^{-5}$  Pas) on particle concentration and particle velocity distributions in healthy and tumor tissue were examined numerically [9]. Cancerous cells and healthy tissue regions are represented as concentric circles and MNP injection point is center of inner circle. It was observed that MNPs transported from tumor region to the healthy tissue over time. Because AMF is applied to the entire area, MNPs undesirably heat healthy tissue after certain time. Therefore,

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**Fig. 1.** (a) – Field free region formation by static magnetic field sources, (b) – schematic representation of test animal as target object

increasing the temperature of the tumor without damaging the healthy tissue surrounding the tumor emerges as a problem. Local focusing is necessary to ensure that heat is only increased at the target lesion site.

According to theoretical and experimental studies [10, 11] MNP behaviors under the influence of AMF can be changed with static magnetic field superposition. When static magnetic field sources are placed with two repelling poles face-to-face, this positioning creates static magnetic field free region at the center of the workspace and gradient zones at the corners, see Fig. 1(a). Thus, MNPs in the field free region can be freely oscillates while the entire region is under the influence of AMF. Conversely, the oscillations of MNPs outside the field free region is restricted or completely blocked by static magnetic field gradients.

In bioelectromagnetic applications, current-fed electromagnets [12] or permanent magnets [13] could be preferred as static magnetic field sources. Coils require power supplies and, in some cases, coolers. This makes experiment setups more complex and costly. Compared to coils, neodymium iron boron (NdFeB) magnets have higher magnetic flux density [14] and magnet-based experimental setups are less complex and relatively cost-effective compared to coil-containing setups.

Tasci *et al* [15] proposed a test setup with an static magnetic field source made of DC coils. These coils are on both sides of the AMF generating coil. The study

showed that MNP oscillations can be controlled locally by the effect of static magnetic field gradient and field free region. Lu *et al* [16] used magnets to focus the heat on a specific region. With their setup, both magnetic particle imaging and MFH operations can be performed together. Ma *et al* [17] used NdFeB magnets as static magnetic field source. It is observed that the temperature rise of MNPs is limited when they are in the static magnetic field gradient. Gradient pattern mapping was not studied in detail in any of these studies.

A comparison between workspaces and target objects in the literature for MFH tests is shown in Tab. 1. Workspace is usually the internal volume of the helically shaped work coil. Test tubes containing ferrofluid or regional tumor masses in small animals can be considered as target objects. For in vitro testing, small test tubes or a long test tube containing MNP can be used as target object. A long test tube can have a length of 47.5 mm and an outer diameter of 9.6 mm. The field free region can be overlapped with parts of the long tube. If the tumor mass in the small animal is target object, it may have point-like, line-like or surface-like geometries as indicated by the letters *P*, *L* and *S*, see Fig. 1(b).

Optimizing the distance between the static magnetic field sources and target object in the workspace may be necessary in different test setups. In this case, magnet arrays emerge as ideal candidates compared with coils and individual magnets. Halbach arrays are a permanent magnet configuration in which the magnetic field is maximum on one side and minimum on the other, see Fig. 2. This type of arrays increase the magnetic field intensity by 1.4 times compared to a standard magnetic array with the ability to orient magnetic field lines efficiently [18]. Halbach magnet arrays provide more remote intervention compared to other static magnetic field sources with their strong magnetic field generation properties. This allows for a localized flux concentration in the area of interest for operation. Correct positioning of dual array structure can create field free region in the workspace. In the light of the explanations above, the investigation of the usability of the magnetic field patterns formed by dual Halbach

**Table 1.** Comparison of workspaces and target objects in MFH experiment setup

Features of workspace	Features of target object	Reference
radius $\approx 2$ cm, height $\approx 6$ cm, crosssection of the workspace $\approx 24$ cm <sup>2</sup>	spherical plastic containers, $r \approx 0.2$ cm target area $\approx 0.126$ cm <sup>2</sup>	[15]
coil diameter = 3 cm	the two phantoms are located close to the heating zone of the coil (20 mm)	[17]
radius of the coil $\approx 5$ cm crosssection of the workspace $\approx 78.5$ cm	a test tube in the center of the coil, tube radius $\approx 0.5$ cm, target area $\approx 0.785$ cm <sup>2</sup>	[19]
coil diameter = 4 cm, length = 10 cm, crosssection of the workspace $\approx 40$ cm <sup>2</sup>	spherical core with a radius of 4.9 mm	(20)
circle diameter = 90 mm, a square of. 56 $\times$ 56 mm <sup>2</sup> can be fitted into	target object can be a small test tube array, a long test tube or a small test animal	proposed study

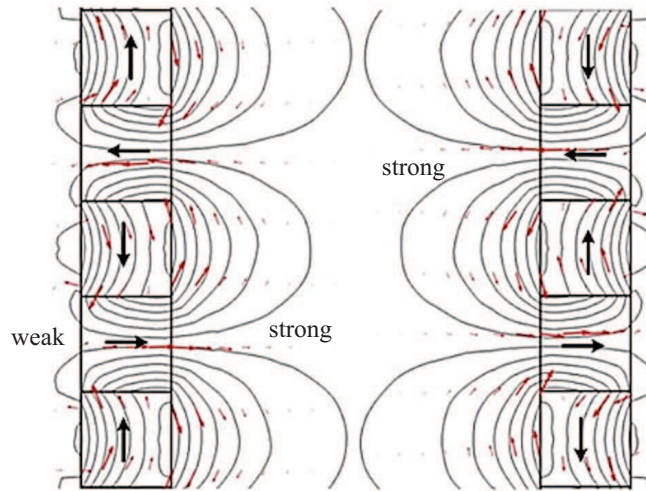


Fig. 2. Magnetic flux lines of dual Halbach array

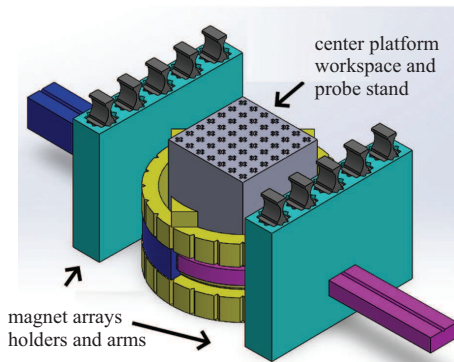


Fig. 3. Parts of the experiment platform

Table 2. Magnetization directions of array elements

Left array ( $x, y, z$ )	Right array ( $x, y, z$ )
(0, 1, 0)	(0, -1, 0)
(-1, 0, 0)	(-1, 0, 0)
(0, -1, 0)	(0, 1, 0)
(1, 0, 0)	(1, 0, 0)
(0, 1, 0)	(0, -1, 0)

array for MFH was examined for the first time in this study.

## 2 Materials and methods

Five N54 grade NdFeB magnets were used to construct the Halbach arrays. Each magnet has a volume of  $10 \times 10 \times 40 \text{ mm}^3$ . Here,  $B_r$  and  $\mu_{recq}$  of magnets are 1.47 T and 1.05 T, respectively. Halbach arrays were created by rotating each magnet at an angle of  $90^\circ$  from the previous one, see Tab. 2. The dual Halbach array poles are arranged so that the strong magnetic fields of the arrays face each other, Fig. 2. Further,  $(d_1, d_2)$  are

the distances between the center of gravity of the arrays and the origin of the workspace. Six cases were chosen to investigate the effect of dual Halbach array positions on field free region, see Tab. 3.

Table 3. Array locations on both sides

Case	$(d_1, d_2)$
1	(-64, +64)
2	(-69, +69)
3	(-74, +74)
4	(-79, +79)
5	(-84, +84)
6	(-89, +89)

Table 4. Locations of array elements

Left array ( $x, y, z$ )	Right array ( $x, y, z$ )
$(d_1, 42, 0)$	$(d_2, 42, 0)$
$(d_1, 21, 0)$	$(d_2, 21, 0)$
$(d_1, 0, 0)$	$(d_2, 0, 0)$
$(d_1, -21, 0)$	$(d_2, -21, 0)$
$(d_1, -42, 0)$	$(d_2, -42, 0)$

### 2.1 Simulation medium

A multi-physics simulation software (COMSOL® Multiphysics 5.6, COMSOL AB, Stockholm, Sweden) was used for modeling. The simulation medium consists of dual Halbach array and target object. Locations of array elements are presented in Tab. 4. The target object is a cylinder with a radius of 28 mm and a height of 56 mm. A test tube or a small test animal can be placed in this area for in vitro or in vivo applications, respectively.

2.2 Experiment setup

Experiment setup consists of magnets, 3D-printed single magnet holders, magnet holders for five-element array, left and right arms, center platform and probe stand, see Fig. 3. Magnets are placed inside the single magnet holders. Then single magnet holders are inserted into array magnet holders. Five-element array magnet holders are attached to the arms. The array distances can be changed gradually by the help of arms. Holders, arms and center platform are connected together. Center platform keeps all system aligned and its center room is used for measuring. This room is a 90 mm diameter circle and a square of  $56 \times 56 \text{ mm}^2$  can be fitted into it. Probe stand is placed inside of this room.

The probe stand allows the measurement of magnetic flux density in the  $x$  and  $y$  directions ( $B_x$  and  $B_y$ ) from 49 points. Technical drawings of each part and information of 3D printing process can be found as a file in supplementary materials.

3 Results and discussion

3.1 Simulation results

Color maps of magnetic flux density and arrow representations of flux lines for six different cases are shown in Fig. 4(a)–(f), respectively. When the array positions are

close to the target object, the field free region is in a centrally focused dot-like form. It was observed that the field free region form became ellipse-like as the arrays moved away from the target object.

The MFH experiment conditions in the literature vary widely. For example, AMF intensity can range from 0.8 to 115 kA/m, [21]. To determine the field free region, an arbitrary cutoff must be chosen. Here limit value of static magnetic field is arbitrarily set to 20 G ( $\approx 1.6 \text{ kA/m}$ ). Contour lines are drawn at 20 G intervals and areas less than and equal 20 G can be considered as field free region for all cases. As seen in Fig. 5, field free regions ( $B \leq 20 \text{ G}$ ) are geometrically close to the elliptical surface area. Semi-major axis  $a$  and semi-minor axis  $b$  of field free regions were measured.  $(a, b)$  are  $(0.85, 0.7)$ ,  $(1.15, 0.95)$  and  $(2.1, 1.3)$  cm for cases 1–3, respectively. The equation  $A = \pi ab$  gives the area of the ellipse. The surface areas are 1.87, 3.43 and  $8.57 \text{ cm}^2$  for cases 1–3 respectively. It is found that, if the magnet arrays come closer to the target object symmetrically, the field free region can focus on a tiny area. If the field free regions for cases 4–6 are considered as rectangular form, their height is taken as 5.3 cm. The width of the rectangles can be taken as the average of the center width and the upper side width. The center widths are 3.3, 4.1, 5.1 cm, edges are 2.2, 3.6, 4.7 cm and rectangle-like surface areas are 14.58, 20.41 and  $25.97 \text{ cm}^2$  for cases 4–6, respectively. It is found that,

Table 5. Point probe measurements

Supplementary material

Point probe measurements in simulation medium, technical drawings of each part and information of 3D printing process for experiment setup are available online at <https://docs.google.com/document/d/1lWfWtoov9hdyQCW3tHoZWKPmjE8TpXb1/>

B (G)	Case 1						Case 2						Case 3									
	$x$ -axis probe position (mm)						$x$ -axis probe position (mm)						$x$ -axis probe position (mm)									
	-24	-16	-8	0	8	16	24	-24	-16	-8	0	8	16	24	-24	-16	-8	0	8	16	24	
$y$	24	209	128	92	82	91	127	208	149	93	69	59	68	93	150	106	66	50	47	47	68	108
-axes	16	209	129	79	67	78	120	219	145	89	59	48	57	84	150	104	66	44	38	44	65	109
probe	8	192	113	55	40	55	102	192	136	81	39	25	39	73	133	96	57	29	20	29	51	95
pos.	0	196	91	49	3	45	94	177	136	64	36	6	34	68	124	94	49	22	2	21	52	85
(mm)	-8	190	109	53	41	55	101	200	136	77	40	30	42	73	129	95	54	28	19	33	52	98
	-16	218	126	76	69	78	119	204	150	88	54	50	60	82	146	107	65	39	36	42	61	105
	-24	213	128	94	82	90	132	210	149	90	68	61	64	97	148	102	64	50	42	52	68	108
B (G)	Case 4						Case 5						Case 6									
	$x$ -axis probe position (mm)						$x$ -axis probe position (mm)						$x$ -axis probe position (mm)									
	-24	-16	-8	0	8	16	24	-24	-16	-8	0	8	16	24	-24	-16	-8	0	8	16	24	
$y$	24	77	51	41	36	39	49	74	56	37	29	23	29	36	53	42	29	24	18	21	27	38
-axes	16	75	45	30	25	33	48	77	52	33	26	23	26	37	55	37	27	15	16	15	24	41
probe	8	68	40	20	14	25	39	67	47	29	18	11	16	30	48	34	25	10	12	13	22	33
pos.	0	69	38	16	2	20	35	60	51	24	16	4	16	26	46	39	21	9	5	11	23	34
(mm)	-8	67	42	23	13	23	37	66	46	32	19	10	19	28	49	33	23	11	8	14	23	36
	-16	74	45	31	30	32	45	71	56	35	22	22	24	33	50	42	25	16	16	17	23	41
	-24	76	47	38	35	35	49	78	57	37	30	28	28	35	53	38	30	24	17	22	31	39

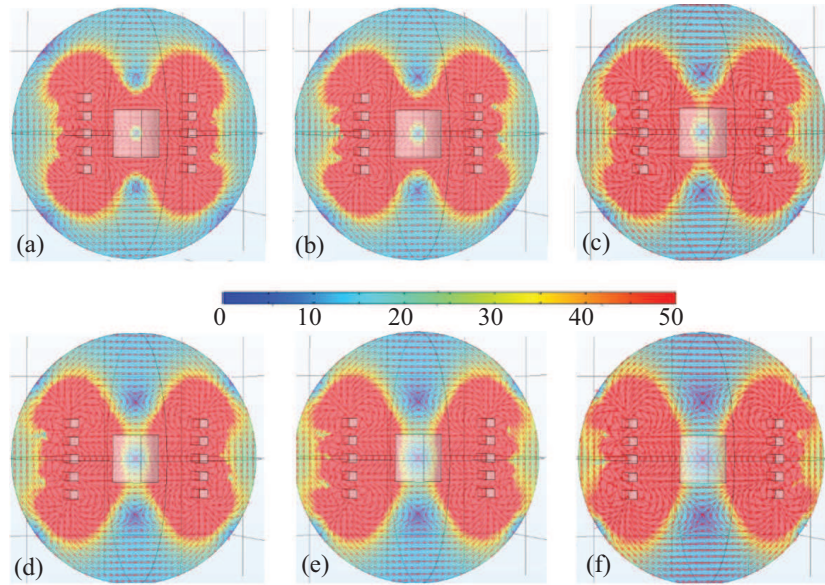


Fig. 4. Color maps and arrow representations for (a) – case 1, (b) – case 2, (c) – case 3, (d) – case 4, (e) – case 5 and (f) – case 6

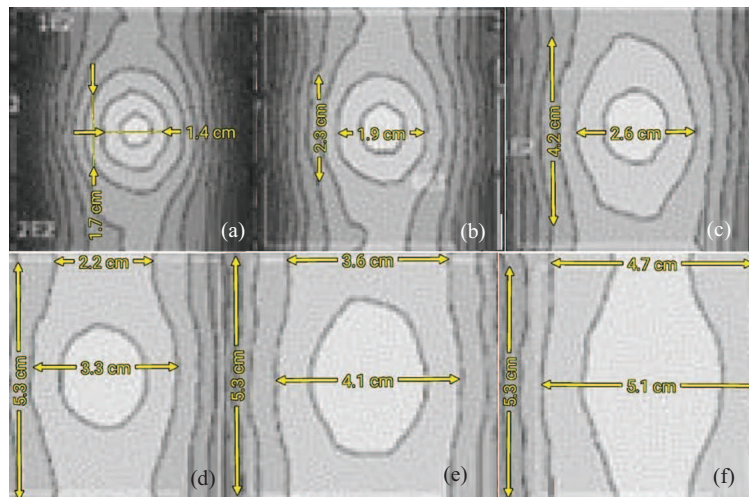


Fig. 5. Field free region contour plots and axis measurements for (a) – case 1, (b) – case 2, (c) – case 3, (d) – case 4, (e) – case 5 and (f) – Case 6

the field free region form broadens when the dual Halbach array moves away from the target object. Among the resulting field free regions in these six cases, appropriate ones can be selected, taking into account target object s such as small test tubes, a long test tube or a small test animal.

As much as 49 measuring points were identified on the  $x$  and  $y$  axes at 8 mm intervals from  $-24$  mm to  $24$  mm in the workspace. Point probe measurements of the static magnetic field for the simulation medium were generated for all cases. Related tables can be found as a file in the supplementary materials.

### 3.2 Experiment setup

Point probe measurements were taken at the same probe positions as in the simulation. Magnetic flux mea-

surements in the  $x$  and  $y$  directions ( $B_x$  and  $B_y$ ) were taken for all cases with WT10A commercial magnetic flux meter. The magnitude of magnetic flux density for every point was  $B = \sqrt{B_x^2 + B_y^2}$ . Measurements were repeated four times in a row and the average values were transferred to Tab. 5. The number of points forming the field free region (red-colored regions in Tab. 5,  $B \leq 20$  G) are 1, 1, 3, 5, 9 and 17 for case 1–6, respectively. It is seen that point probe measurements in experiment setup give information about position and flux density levels of the field free regions.

### 3.3 Discussions

Small deviations of point probe measurements between simulation medium and experiment setup may have various reasons. For instance, magnets are identical in simula-

tion medium but in real life they may not be exactly the same. Commercial flux meter measurements were done with hand and probe alignments can't be perfect as in the simulation. Some gaps should be added to the 3D printed objects for assembly. For example, the magnet edges should be set to 10 and 40 mm, while the room edges in the holder should be set to 10.3 and 40.3 mm (see supplementary materia). 3D printouts may differ from the ideal dimensions in the drawing. This can lead to inevitable alignment and measurement differences.

#### 4 Conclusions

In this study, gradient pattern mapping produced by parametric position changes of a dual Halbach array for using in focused MFH tests was investigated for the first time. It is found that, symmetric displacements of a dual Halbach array can manipulate field free region form (changes its shape to rectangle-like and ellipse-like forms) and location (can be focused to center of the target object). Field free region structures were analyzed with color maps and arrow representations, axis measurements and area calculations from contour representations, point probe measurements and mappings of gradient patterns. The utilized system in this study could be used in real scenario if the specific conditions of each experiment are taken into account. For in vitro tests, field free region can be applied to test tubes in a periodic array or a long tube with horizontal positioning. For MFH test with small animals, field free region and target tissue overlap can be achieved by appropriate placement of the static magnetic field source and/or target object.

The obtained results provide data for in vitro and in vivo MFH tests performed prior to clinical trials. With the help of gradient pattern mapping, suitable field free regions for different tumor geometries can be determined. The ability to ablate a tumor of any possible geometry by moving the field free region over the tumor is important for future studies. This highlights the importance of adapting the position and shape of the field free region in MFH applications. In the future, designs may be considered to focus field free region with highly sensitive robotic devices for each patient's unique individual conditions.

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