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The capture of magnetic colloids at flow regimes specific to the capillary blood vessels

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Magnetic drug targeting (MDT) of tumors situated in the cavity of the human body is difficult because the magnetic field and its gradients decrease rapidly with the distance from the magnets. Here a dipolar magnetic device is used to investigate the magnetic capture of colloidal magnetic particles (MPs) in capillary tubes at flow velocities similar to that encountered in the capillary beds of tumours. The capture of MPs is influenced by the gradient of the magnetic field, the flow velocity, the particle concentration and their surface properties. This work shows the potential of MDT for targeting tumours positioned at medium distances from the surface of the body (e.g. head, neck, breast, hands and legs).

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1. Introduction

The active targeting of particulate drug carriers, bearing anticancer agents, can achieve more efficient drug delivery, so that the drug predominantly affects only the cancer cells, hence reducing the systemic side effects [1]. The magnetic drug targeting of anticancer drugs/agents (MDT) is an alternative to current systemic treatments. However, the challenge is to target the drugs precisely for the local treatment of solid cancer tumours [2]. The method uses the ability of the magnetic particles (MPs) to bear/entrap anticancer drugs that can be fixed and slowly released at the diseased site, by using an external gradient magnetic field. Despite real progress obtained with this new method (permanent remission of squamous cell carcinoma [3] and encouraging results in clinical trials [4]) a series of technical and physiological problems hinder the application of the method in clinical practice.

Therefore, a better understanding of the physical conditions for the magnetic capture of carrier particles is required. Moreover, the use of MPs capacity to block blood vessels and stop the nutrients supply to tumours can be an alternative or adjuvant method to treat cancer. The physical aspects of the MPs concentration into microvasculature have been experimentally investigated for MPs at high concentrations (up to 54%), magnetic fields with high strengths (0.5 – 1.0 T) and medium field gradients (0.2 T /cm) [5]. These results showed the possibility that embolization of blood vessels could be achieved within minutes, for an active magnetic space of maximum 4 cm. However, the conditions for high magnetic fields focused at any region of the human body are difficult to realise.

This paper presents and tests an experimental device for the MPs capture within fluidic systems simulating the flow regime in small blood vessels, by using a magnetic circuit having a large active space (the width of air gap - 8.7 cm), with a medium field of 0.3 T and medium field gradient of 0.15 T/cm). The aim of the study is to prove the possibility of MPs retention and entrapment inside plastic tubes ("blood vessels"), within regions that have similar sizes with the cancer tumours.

2. Materials and method

2.1 Materials

Iron(III) chloride hexahydrate p.a. and iron(II) chloride tetrahydrate p.a and polyvinyl acohol (PVA) (molecular mass, 72000, hydrolysis degree >98%) were purchased from Merck, Germany. The citric acid pure. p.a. and the sodium hydroxide pure p.a. were procured from Fluka, Germany.

2.2 Preparation and characterization of magnetite colloidal dispersions

The nanoparticles of magnetite were prepared by co-precipitation in aqueous media of the iron (II) and iron (III) salts with a concentrated NaOH solution, at a temperature of 70 °C with vigorous mixing for 30 minutes. The precipitate was cooled at room temperature and washed five times with distillated water. The obtained magnetic colloid was treated either with citric acid solution until the suspension reached pH 6-6.5 (MPs-CA), or was mixed with 1% aqueous PVA solution, and milled in a ball mill for five days (MPs-PAV). The size of the magnetite particles (MPs) was measured by dynamic light scattering (Nanotrac, Microtrac, Inc. US). To investigate the effect of particle aggregation on the polydispersity of MPs clusters two sets of measurements were performed, firstly with MPs sonicated for 10 minutes (30 mW sonicator, made in or laboratory) and secondly with particles left to settle for 15 minutes after sonication. The magnetization of MPs was measured using a magnetometer with vibrating probe (made in our laboratory) as follows: 0.2 g of air dried MPs where dispersed in 1.0 g of paraffin, the mixture was spherical shaped and the magnetization of the probe was tested for magnetic field values ranging between -7.0 to +7.0 kOe.

2.3. The principle of method and measurements

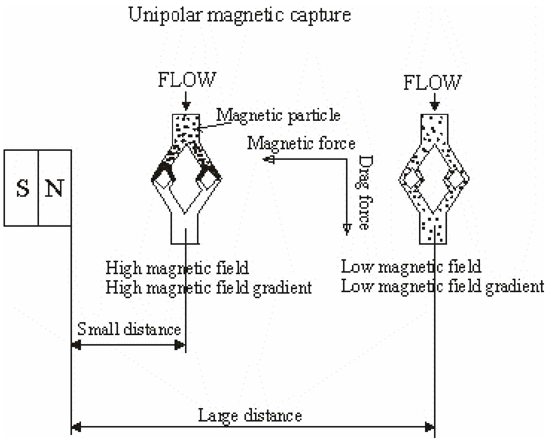


Fig. 1. The principle of MPs capture.

The deviation of the injected MPs within the blood flux and their capture onto the wall of a blood vessel is usually obtained by positioning magnets or electromagnets in close proximity to the diseased area (Fig. 1). The magnetic capture is based on the competition between the magnetic force exerted by the magnetic field gradient on the MPs and the drag force from the fluid. The magnetic capture of MPs can be obtained by using either a single pole of the magnetic system (unipolar magnetic capture) or the both poles of the system (bipolar magnetic capture). In the first case, when the distance between the pole of the magnetic source and capillary bed is small (<1.5 cm), the gradients of the magnetic field are high (>0.2 T/cm) and the MPs from arterioles and capillaries (small blood velocities) can be captured onto the vessel walls and enable stable deposits to be formed. Alternately, at large distances (small magnetic field and field gradient) the chance of magnetic capture is small and MPs are flushed out from the blood vessels walls. However, for bipolar systems, if the magnetic field is high enough (>0.1T) to saturate the particles magnetization then the concentration of MPs can enable their magnetic clustering (c>0.02 g/ml). In these circumstances, it should be noted that the magnetic force acting on the MPs clusters is larger than that for individual particles and capture can be achieved even for small magnetic gradients (<0.05 T/cm), as encountered at large distances from the magnetic poles. Hence, bipolar systems can be used as an alternative to obtain magnetic fields >0.1 T (enough to saturate the magnetite) within magnetic active spaces that can be extended up to 10 cm. These systems can be useful for targeting zones deep within the body (e.g. head, neck, breast, hands and legs).

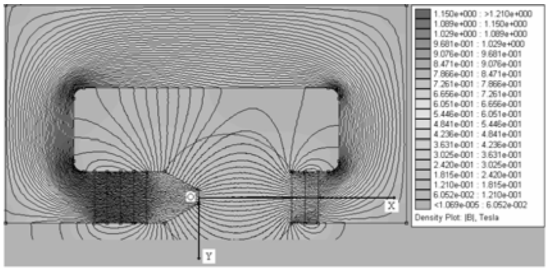


Fig. 2. Bipolar magnetic system and magnetic flux lines simulated using FEMM 3.4 program.

The present capturing system is a bipolar "C form" magnetic circuit and its design has been realised using the 2D "Finite Element Method Magnetics" program (FEMM 3.4) from Foster-Miller (http://femm.foster-miller.com) (Fig. 2). The system has an active space of 8.7 cm and the sizes of the polar pieces are 13.5mm and 50 mm, respectively. The yoke of the magnetic circuit was made from massive stainless steel (magnetization of saturation ~15,000 Gs) and the circuit was energized by 6 rectangular magnets (Sintered NdFeB, 35 MGOe, 50 × 50 × 12.5 mm, MMG MagDev Ltd, Swindon, UK). The experimental values of the magnetic field in the air gap were measured using a portable Hall effect Gaussmeter (MG-5DP, Walker Scientific Inc.,Worcester, USA), the magnetic field lines were plotted using the *ListPlotVectorField* function from *Mathematica 5.0* program (Wolfram Research, Inc. USA), and were compared with the numerical predictions. Also, contour plots of the magnetic filed gradient and the magnetization of MPs were drawn and their influence on the MPs capture is discussed.

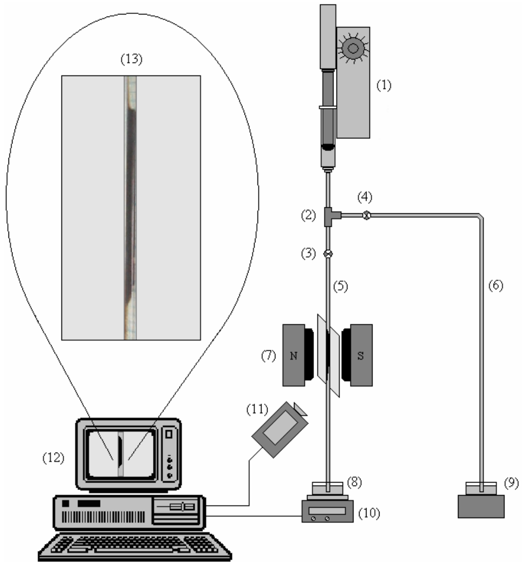


Fig. 3. Experimental device to prove the principle of magnetic particle targeting inside a "blood vessel".

The experimental setup simulates the deviation/capturing of MPs from the “blood flux” and the building of particle deposits onto the “blood vessel” walls (Fig. 3). About 5 ml of magnetic colloid (magnetite – size - 5 to 30 nm, magnetization of saturation - 340000 A/m) suspended in solution of citric acid (0.03 g/100 ml deionised water) or PVA solution (1g/ 100 ml deionised water) is pumped by the injection pump (1), through the vertical plastic tube (5), into the bipolar magnetic capture system (7). The MPs are attracted by the magnetic forces from the flow field and captured onto the tube’s wall into the region that is supposed to be affected by the tumour. The evolution of the particle buildup is monitored by the camcorder (11). The clean fluid passes to the collector (8), is weighed by a balance (10) and the data are stored on the PC (12). Alternatively, the colloid passes in a systemic way to the collector (9) through the ramification (2) and the plastic tube (6) that is not placed in the magnetic field. The valves (3) and (4) are used to vary the fluid flow rate.

The mass of the fluid that passes through the magnetic system is measured at one second time intervals. The evolution of the collected mass permits the evaluation of the flow conditions through a hypothetical region targeted by MPs. Also, it gives the time necessary for the blood vessel to be blocked. The evolution of the particle buildup is acquired at 30 frames/second. The length of MPs deposit is evaluated at time intervals of 30 seconds. This gives an indication of the affected area which can be targeted by the magnetic system. The above parameters are estimated as a function of the initial fluid velocity, the MPs concentration, and the position of “blood vessels” within the magnetically active zone.

3. Results and discussion

3.1 The characterization of magnetic particles

The distribution of MPs-CA size following the sonication process and DLS analysis is presented in Fig. 4a. The dimensional analysis shows a log-normal distribution, the particles have sizes < 33 nm and their average diameter is x_c = 15.6 nm.

During the 15 minutes of settling the particles aggregate in clusters < 2 µm and their mean size is x_c = 0.61 µm (Fig. 4b). These clusters stay suspended in the absence of the magnetic field for ~30 minutes. For the MPs-PAV the particles size varies between 0.05 to 1.15 µm and their mean size is 0.36 µm (Fig. 4c). These values are much greater than that of the MPs-CA. Therefore, it is possible that PVA and magnetite to form a composite material with the particles and their clusters distributed within the mass of PVA. After 15 minutes settling these composites aggregate in clusters <4 µm and have an average size of 1.9 µm (Fig. 4d). These aggregates stay in suspension for ~ 20 minutes.

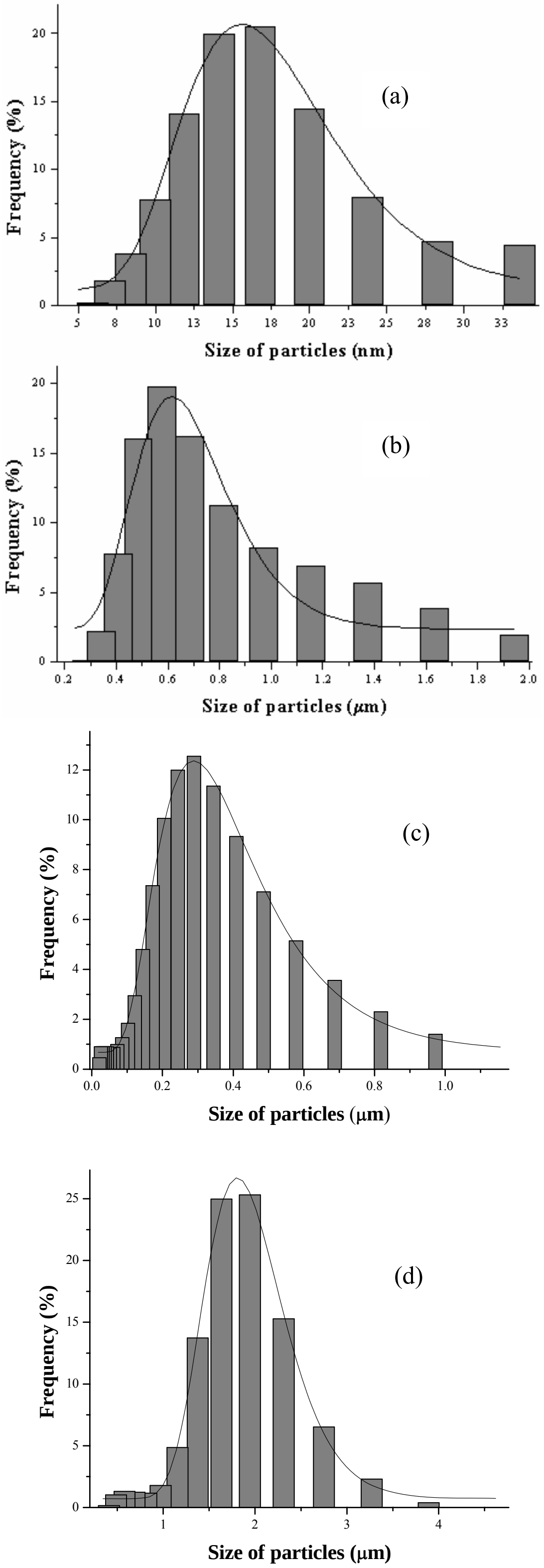


Fig. 4. a) The distribution of MPs size treated with citric acid after sonication. b) The distribution of MPs clusters treated with citric acid after 15 minutes of settling; (c) The distribution of MPs size treated with PAV after sonication; The distribution of MPs clusters treated with PAV after 15 minutes of settling.

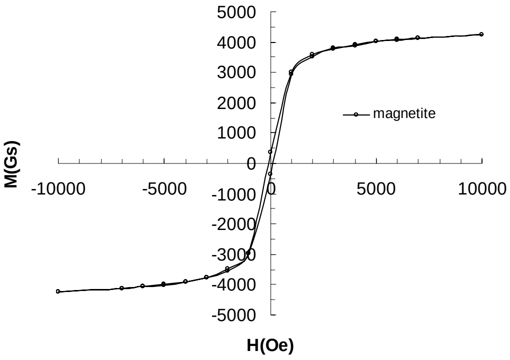
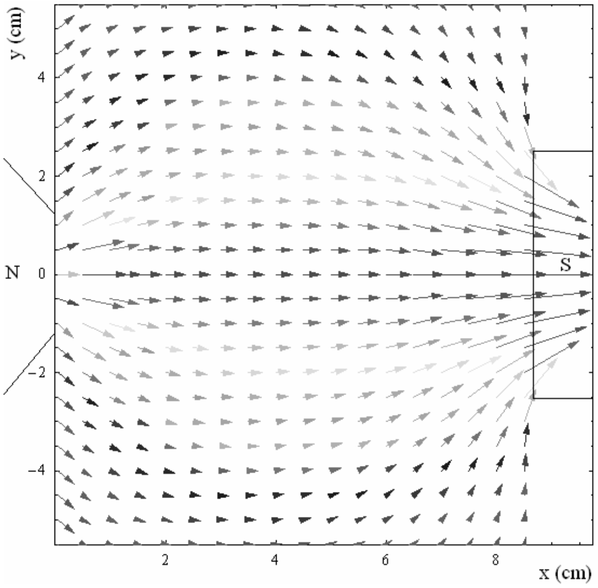


Fig. 5. MP magnetization as a function of the intensity of the external magnetic field - M_s =4.25 kGs (340000 A/m); M_r = 325 Gs (26000 A/m); H_c =110 Oe (8800 A/m).

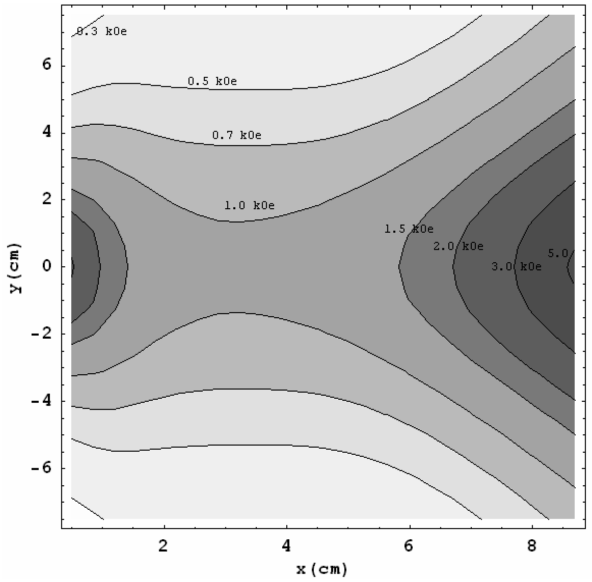
The magnetization of dry magnetite (Fig. 5) shows a saturation value of 4250 Gs (340000 A/m), 325 Gs (26000 A/m) for the remanency magnetization, and 110 Oe (8800 A/m) for the coercitive magnetic field. The magnetization of saturation for these nanometer scale magnetite particles is less than the bulk value (~6250 Gs (500000 A/m)) [6]. The remanency magnetization and the coercive magnetic field are probably consequences of the dipolar magnetic interaction between aggregated MPs, when they loose their superparamagnetic character.

3.2 The characterization of magnetic field

The values of the magnetic field were measured for the air gap of the magnetic system in a region of the Oxy plane surrounded by a rectangle (8.7×9 cm) which touches the magnetic poles (Fig. 6). The vector plot draw of the magnetic field vectors (Figure 6a) shows the directions of the field lines which qualitatively resemble those obtained from simulation (Fig.2). The contour plot shapes give the curves within the air gap which have the same value for the magnetic field intensity (Fig. 6b). A maximum value of 0.54 T (5.4 kOe) was measured on the face of the rectangular pole, the field is 0.45 T (4.5 kOe) on the conical pole, and decreases with the distance from the poles. The experimental values are ~ 80% less than that obtained from simulation, but this is a good approximation for a 2D simulation.

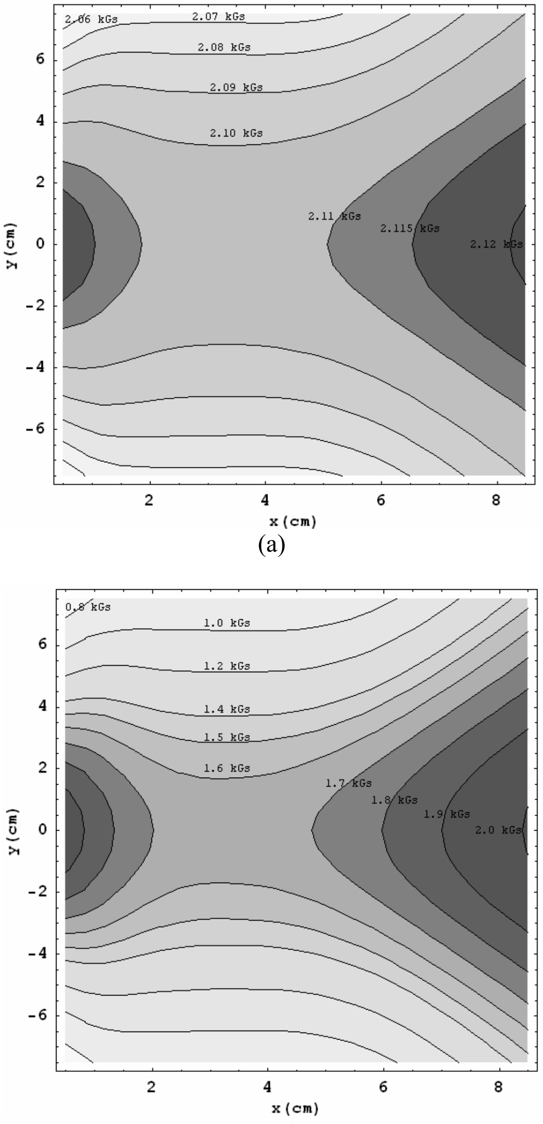


(a)



(b)

Fig. 6. (a) The magnetic field vectors (a) and the contour plot lines (b) in the air gap of the magnetic system as obtained from the processing of experimental data.

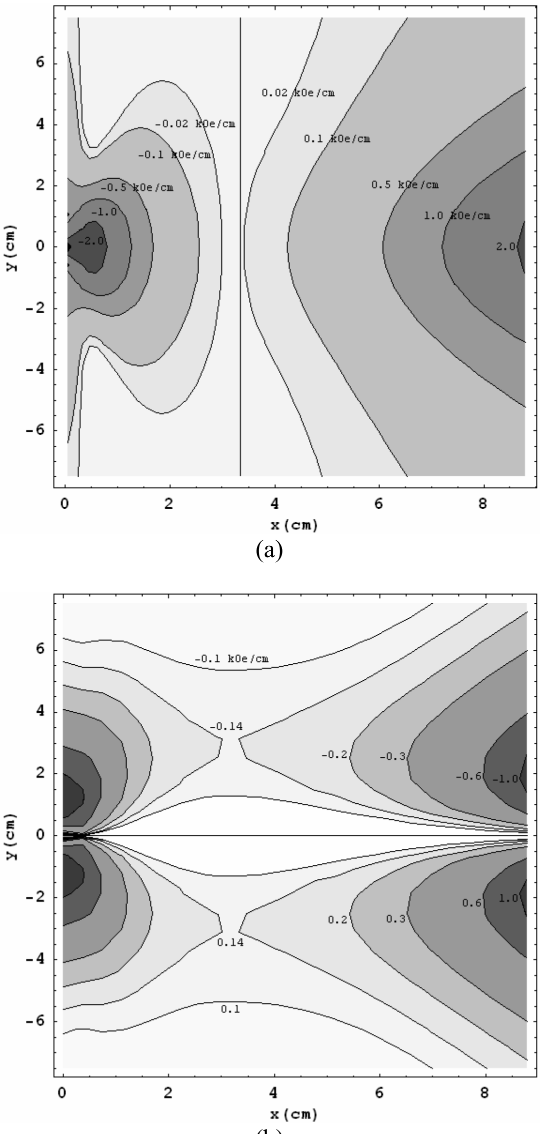


(a)

(b)

Fig. 7. The distribution of magnetization in the active space of the magnetic system for composite particles (50% magnetite and 50% PVA), as calculated from Langevin theory: (a) 30 nm MPs; (b) 10 nm MPs.

To estimate if the magnetic field values are high enough to magnetize the MPs at their saturation value, the curves of constant magnetization were plotted for the region of interest. When the particles strongly aggregate and the magnetic moments are in touch (e.g magnetite treated with citric acid) they attain a magnetization of saturation close to the dry material (M_s =4.25 kGs (340000 A/m)) (results not shown). However, if the particles are dispersed in a non-magnetic matrix (e.g. PVA), it is possible as the matrix to act as a spacer between the nanometer size MPs and prevent them to form strong aggregated clusters. In these circumstances the Brownian motion can play an important role in the economy of the magnetization for the assembly of MPs. By using the Langevin's theory for free magnetic dipoles (50% magnetite dispersed in PVA) [7], the assembly keeps its magnetization of saturation (~4.25/2 kGs= 2.125 kGs) all around the active region of the magnetic system, when the MPs size >30 nm (Fig. 7a). However, when the MPs size is <10 nm, the saturation is attained just around the magnetic poles (Fig. 7b). Therefore, it is possible that the performance of the magnetic system to be better for the MPs aggregates suspended in citric acid, which have higher magnetization of saturation than those suspended in PVA.



(a)

(b)

Fig. 8. The gradient of the magnetic field in the air gap of the magnetic system: (a) $(\nabla H)_x$; (b) $(\nabla H)_y$.

The gradient of the magnetic field is represented with its components ($(\nabla H)_x$ and $(\nabla H)_y$) in Fig. 8. The gradient is maximum at the surface of the polar pieces ($(\nabla H)_x$= -0.31 T/cm (-3.1 kOe/cm), $(\nabla H)_y = \pm 0.11$

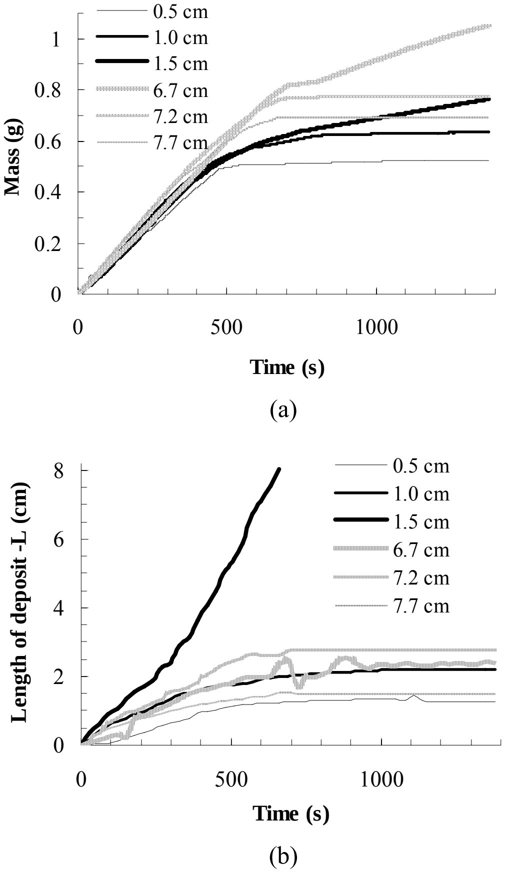
T/cm ($\pm$ 1.1 kOe/cm) - on the conical polar piece and $(\nabla H)_x$ = 0.2 T/cm (2.0 kOe/cm), $(\nabla H)_y$ = $\pm$ 0.1 T/cm ($\pm$ 1.0 kOe/cm) on the rectangular polar piece). The Ox component of the gradient is negative towards the conical magnetic pole, changes its sign when x = 3.35 cm and is positive towards the rectangular magnetic pole. This means that the magnetic force acting on MPs changes its direction when x increases from 0 cm to 8.7 cm and the deposits of particles will be formed on the left side of the vertical capillary tubes when $x<3.35$ cm, and reversely, on the right side of the tubes when $x>3.35$ cm. Also, given the values of the Ox component of the magnetic field gradient, the Ox component of magnetic force acting on the MPs should be higher towards the conical pole, lower at the middle of the air gap and moderate towards the rectangular pole. Accordingly, the capture of MPs must follow the same behavior. Because the vertical component of the magnetic field gradient is negative when $y>0$ and positive for $y<0$, the vertical magnetic force acting on the MPs will be pointed towards the axe Oy axis. This means that the deposit of MPs formed in the vertical tube will be compressed on the Oy direction.

3.3. The capture of MPs suspended in PVA

The time interval necessary to block the capillary vessels with magnetic particles (blocking time) is an important parameter when is necessary to establish the time scale for an *in vivo* treatment procedure. This temporal interval gives the approximate time of injecting MPs into the blood stream. Also, the extension of the particle deposits onto the tube's walls is important to estimate the volume of tissue which can be treated by the magnetic targeting procedure. The blocking time and the length of particle deposits vary with the process parameters (tube position in the magnetic field – x, the strength of the magnetic field and its gradient, the initial fluid velocity/flow rate, the MPs concentration and their magnetisation).

Fig. 9a presents the mass of the fluid depleted by MPs-PVA after it passes through the magnetic system (7) and is collected in the collector (8) as a function of time. The distance *x* between the plastic tube (5) and the conical magnetic pole is a variable parameter. The saturation of the mass values indicates the blockage being achieved within the tube as previously was found for high concentrations of MPs [5]. This means that once the MPs-PVA build-up a strong "embolus" then all of the suspension is diverted through the by-pass tube (6). However, the tube (5) is not always blocked. The blockage appears earlier in the proximity of the rectangular magnetic poles (t = 677 s at x= 7.7 cm and t = 723s at x =7.2 cm), later in the proximity of conical magnetic poles (t = 1103 s at x = 0.5 cm and t = 1224 s at x = 1.0 cm) and does not appear in the middle of the air gap (x = 1.5 and 6.7 cm). The length of the deposits varies between L = 1.26 cm and L = 2.78 cm, being higher in the proximity of the rectangular poles, where the gradient of the magnetic field/magnetic force is intermediate (Fig. 9b). However, the capture takes place even at larger distances from the poles (x = 1.5), where the gradient is smaller. A maximum deposit length of 7.7 cm was observed, but the deposit was not stable. Moreover, when the tube is placed at x = 6.7 cm the appearance of avalanches is evidenced and the length of MPs-PAV deposit fluctuates (Fig. 9b).

The variation of MPs-PAV concentration and the fluid velocity affects the time of blockage and the length of deposit (Fig. 10). At low velocities (v = 0.43 cm/s) that is are similar to that found in diseased capillaries the blockage takes place even at very low concentrations. But, the time necessary to block-up the tube increases and the length of deposit decreases (t = 1074 s, L = 2.79 cm for c = 0.02 g/ml and t = 1954 s, L = 2.23 cm for c = 0.01 g/ml). When the fluid flows at a rate representative of normal arterioles (v = 0.86 cm/s) the deposits of particles are longer (L = 7.7 cm) but unstable and the tubes are not blocked.

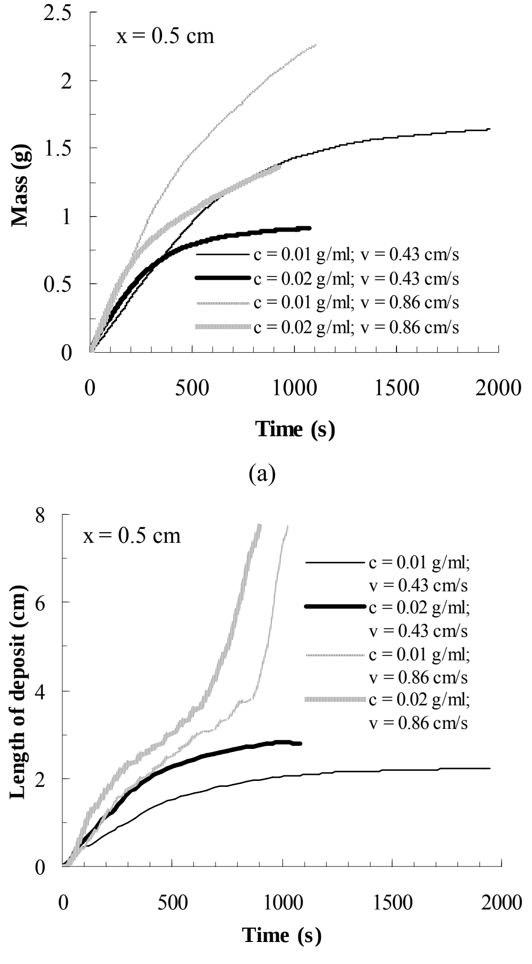


(a)

(b)

Fig. 9. (a) The mass of fluid collected in the collector (8) after the suspension of MPs-PAV passes through the magnetic system (7) as a function of time. (b) The variation of the length of deposit as a function of time. Parameters used in the experiments were: the initial velocity (calculated at the beginning of the capture process) of the fluid – v = 0.29 cm/s; the concentration of MPs – c = 0.02 g/ml; the tube was positioned at various distances in the air gap of the magnetic system.

Using the MPs-PVA and the results for their deposit lengths, and taking into account that the magnetic field has an axial symmetry within the active space of the magnetic circuit, it is possible to appreciate that the maximum volume of diseased tissue hypothetically blocked at the capillary level is ~100 cm^3. This suggests that using the “C form” magnetic circuit and colloidal magnetite particles suspended in PVA is possible to block the capillary vessels from medium size tumours, which will be starved from blood supply and will become necrotic.



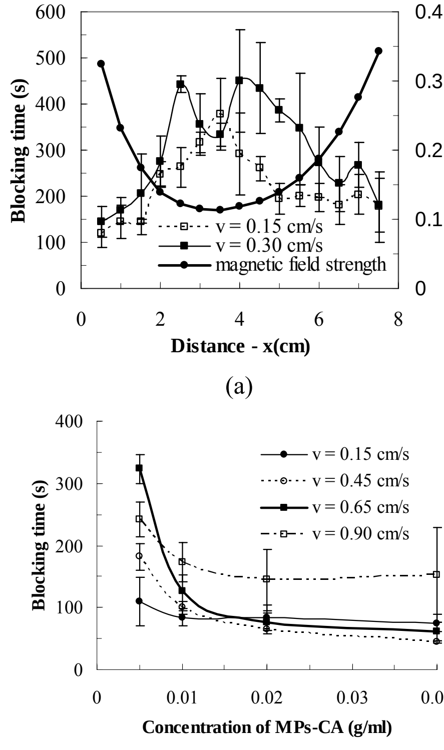
(a)

(b)

Fig. 10. (a) The mass of fluid collected in the collector (8) after the suspension of MPs-PAV passes through the magnetic system (7) as a function of time. (b) The variation of the length of deposit as a function of time. Parameters used in the experiments were: the initial velocity of the fluid – v = 0.43 and 0.86 cm/s; the concentration of MPs – c =0.01 and 0.02 g/ml; the tube was positioned at x = 0.5 cm from the conical magnetic pole.

3.4. The capture of MPs treated with citric acid

As seen from Fig. 11a the blocking time for MPs-CA colloid increases when the tube is far away from the magnetic poles. This behavior is in agreement with the conditions of magnetic capture that are more favorable for capillary vessels placed in the proximity of the magnetic poles (7 cm<x <1 cm), where the intensity and the gradient of the magnetic field have maximum values (B =0.35 T and $|\mu_0 \text{grad}B|$ = 0.2 T/cm). Blocking times *t*< 150 s were obtained when the concentration of magnetite MPs-CA (c =0.02 g/ml) and the fluid velocities were similar with those encountered in the diseased capillary vessels (v < 0.5 cm/s). As opposite to MPs-PAV colloids, when the capillary vessels are placed in the regions with the lowest magnetic field (B =0.1 T) and small field gradient ($|\mu_0 \text{grad}B|$ <0.05 T/cm) the blockage takes place. The blocking time increases up to *t* = 450 s. We believe that the magnetic capture in the regions with small magnetic field gradients is favored by the strong aggregation of magnetic particles. Hence, the magnetic force exercised by the external magnets increases with the volume of the MPs-CA aggregates. Even though the MPs-PAV aggregates have a greater size than the MP-CA ones, it is possible that their magnetic content to be much lower because of the 3D structure of PAV, and are not captured at small field gradients. Moreover, for MPs-CA particles the strong dipolar interactions between the magnetic moments modify the rheology of the suspension and solid-like architectures may appear [8]. Therefore, the concentration of MPs-CA suspended in the carrier fluid



(a)

(b)

Fig. 11. The blocking time of the capillary vessel for MPs-CA and a plausible range of the process parameters that influence the magnetic capture: (a) dependence on the position of the tube and the initial fluid velocity – c = 0.02 g/ml; (b) dependence on the concentration of MPs-CA and the initial fluid velocity – distance – x =1.0 cm.

must have an effect on the time interval necessary to block the capillary tube. Fig. 11b shows a decrease of the blocking time when the concentration of MPs-CA increases, but the effect is less important when the particle concentrations are >0.015 g/ml. Concerning the influence of the initial fluid velocity/flow rate on the length of the blocking time, there is not a clear rule. It appears that for small concentrations of the MPs-CA (c<0.015 g/ml) the time necessary to block the tube increases when the fluid flows faster. However, at larger concentrations (e.g. c = 0.04 g/ml) this rule is true just when the initial flow velocity attains levels encountered in healthy arterioles (v ~1.0 cm/s).

The above experimental data suggests that using MPs-CA parts of the human body should be exposed for < 10 minutes with medium intensity magnetic fields (<0.35 T) to block capillary vessels from tumour tissues. When MPs-PAV are used the blocking time rises up to 20 minutes. This is well within the US Food and Drug Administration regulations (http://www.fda.gov/cdrh/ ode/mri340.pdf), which stipulates a maximum magnetic field intensity (2.0 T for head and 5.0 T for extremities) when applying MRI procedures lasting < 30 minutes.

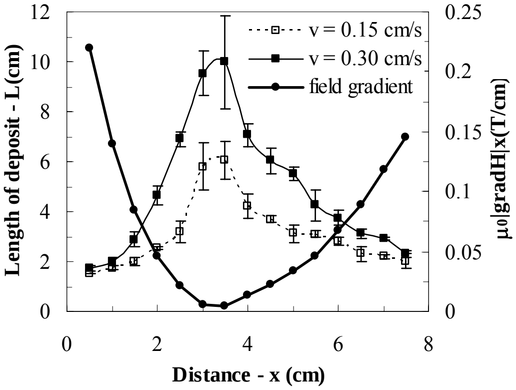


Fig. 12. The length of MPs-CA deposit vs. the position of the capillary tube. The concentration of MPs – CA was c =0.02 g/ml.

The length of the MPs-CA deposits varies with the position of the capillary tube relative to the magnetic poles, being smaller in the proximity of the poles (L = 1.5 – 2.0 cm) where the intensity and the gradient of the magnetic field are maximum, and larger at the centre of the active space (L ~ 6.0 - 6.5 cm) where the magnetic field and its gradient are minimum (Fig. 12). The increase of the initial fluid velocity from v = 0.15 cm/s to v = 0.30 cm/s means larger drag forces on the MPs-CA and their trajectories are therefore longer. Hence, the length of the particle deposits increases. A maximum length of 9.9 cm was obtained when the capillary tube was positioned at 3.5 cm (the point of minimum magnetic gradient < 0.05 T/cm) from the conical magnetic pole.

The influence of the MPs-CA concentration on the deposit length was determined when the tube was positioned at a distance x =1.0 cm from the conical magnetic pole, and the initial fluid velocity was varied between v =0.15 to 0.90 cm/s (Fig. 13). For small fluid velocities (v <0.45 cm/s) there is a slow monotone increase of the deposit length when the MPs concentration increases from c = 0.005 to 0.04 g/ml. When v = 0.65 cm/s the deposit has a constant length (L ~ 2.4 cm), and for higher initial fluid velocities (v = 0.90 cm/s) the *length – concentration* profile passes through a minimum value (L =2.85 cm / c = 0.01 g/ml) and goes to maximum values at the extremities of the concentration interval (L =3.1 cm / c= 0.005mg/ml; L = 3.4 cm / c =0.04 g/ml).

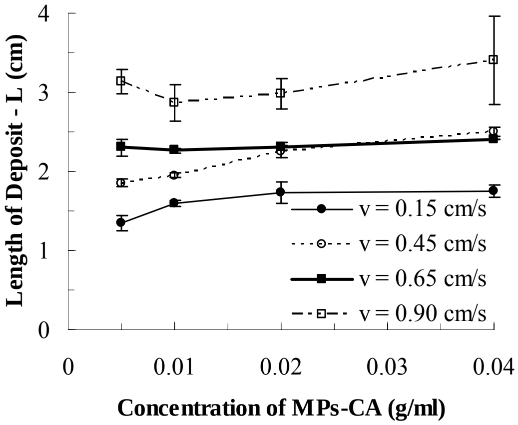


Fig. 13. The length of MPs deposit vs. the concentration of MPs. The position of the capillary tube was x =1.0 cm and the initial velocity of the carrier fluid varied between v =0.15 to 0.90 cm/s.

Using the MPs-CA and the results for their deposit lengths, it is possible to estimate that the maximum volume of diseased tissue hypothetically blocked at the capillary level is ~350 cm^3. Hence, where the technical conditions permit the intra-arterial administration of the MPs-CA by blood vessel catheterization, a refinement of the targeted volume should be possible. Moreover, the lower velocities encountered within the diseased capillaries (<0.5 cm/s) when compared with the healthy ones (>1.0 cm/s) [9], will help the selectivity of the MDD process. This is in contrast with the use of larger magnetic particles [10], where healthy blood vessels at the capillary and arteriolar level were blocked within the liver of pigs.

4. Conclusions

The magnetic capture of magnetite MPs (~15 nm) was achieved in a small "blood vessel" (capillary tube) placed in the air gap of a "C form" magnetic circuit, at magnetic fields strengths within the range stipulated by the US Food and Drug Administration. Stable deposits of particles were obtained fairly rapidly (~10 minutes for MPs-CA and ~20 minutes for MPs-PVA) at low MP concentration (0.01 g/ml< c <0.04 g/ml) and low fluid velocities (<0.90 cm/s) that are parsimonious with tumour microcirculation. By using the image analysis technique it was possible to show the distribution of MPs and to analyse the stability of their deposits within the "blood vessels" from hypothetical tumours. The capture was stable along the magnetically active space for MPs-CA (8.7 cm wide) and the length of MPs-CA deposits extended up to 9.9 cm. For MPs-PAV particles the capture was stable just in the proximity of the magnetic poles (distances < 1cm). The maximum diseased volume covered by the magnetic system was ~350 cm^3 which is the size of a medium tumour. The use of small MPs is particularly convenient to avoid the blockage of healthy blood vessels as encountered in animal tests for micrometer sized particles. These results indicate that the magnetic drug targeting technique using gradient magnetic fields (particularly a “C form” magnetic circuit) is suitable for the sub-surface treatment of cancers within the human body (head, neck, breast, hands and legs) by either concentrating drugs within the tumor or embolization to block the blood supply to the tumor.

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