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P1_6 Golden Delivery

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Abstract

This article investigates the magnitude of the magnetic field gradient required to transport a gold nanoparticle of 1.9nm in diameter through the cardiovascular system. As an upper limit, the gradient required to overcome the blood flow velocity in the aorta was calculated by setting the force from the magnetic field gradient to be larger than or equal to the viscous drag from the blood. This yielded a magnetic field gradient of 1.3×10^{13} Tm^{-1} which is far higher than what is achievable at present. The effects of such a high magnetic field gradient on the biological processes in the body must also be considered as haemoglobin, for example, contains iron.

Introduction

Magnetic hyperthermia utilizes the unique characteristics of nanoscale particles to induce heat into the surrounding medium [1, 2]. Gold nanoparticles have particularly high extinction rates due to the surface plasmon resonance and the absorption cross-section of gold nanoparticles is approximately 10^5 times larger [2] than the strongest absorbing organic dyes currently used (the surface plasmon resonance occurs when electron cloud oscillates about the atoms [1]). This energy is transferred into heating the surrounding medium causing the tissue temperature to increase. Cells undergo apoptosis (automated cell death) when subjected to temperatures above 42^{o}C and so no inflammation occurs as with necrosis (sudden cell death) because the contents of the cell are removed by the immune system immediately [3]. This is one of the many advantages to using hyperthermia as a treatment for cancers. However, the particles must first reach their designated target. If this target is awkwardly placed and the aim is to be as non-invasive as possible, then transport through the body (via the cardiovascular system) with the use of a magnetic field gradient would be a possible solution. This paper aims to calculate the magnitude of the magnetic field gradient required to transport gold nanoparticles by overcoming the blood flow velocity in the aorta as an upper limit (this artery has the fastest flowing blood throughout the human body).

Theory

The magnetic field gradient required to force to particle in a z direction is given by [1, 4, 5],

$$\boldsymbol{F} = (m.\nabla)\boldsymbol{B} = m\frac{\partial B}{\partial z}, \qquad (1)$$

where m is the magnetic moment of the nanoparticle, and $\frac{\partial B}{\partial z}$ is the magnetic field gradient in one dimension. It has been assumed here that the patient is supine, the nanoparticle is suspended in the centre of the blood vessel and that the nanoparticle must travel in a straight line to reach its destination.

The force in *Equation 1* must overcome the drag due to viscous flow in order for the particles to move in the opposing direction to the blood flow. The force on the particle due to this is given by [6],

$$F = 6\pi\eta r\Delta v, \qquad (2)$$

where η is the viscosity of blood, r is the radius of the nanoparticle and Δv is the difference in the blood velocity and desired particle velocity. In this example we have assumed the practitioner would prefer a velocity of $\sim$1cms^{-1} for the nanoparticle so

that it can potentially be tracked. As the argument in *Equation 1* must be greater than or equal to that in *Equation 2*, then the magnetic field gradient must be,

$$\frac{\partial B}{\partial z} \geq \frac{6\pi\eta r\Delta v}{m}. \quad (3)$$

The viscosity of the blood η is taken to be 0.0027Nsm^{-2} [1], the radius *r* of the particle is 1.9nm (containing approximately 212 atoms of gold [7]) and the magnetic moment *m* equates to 0.4μ_B [7] where μ_B is the Bohr magneton (9.27x10^{-24}Am^{-2} [8]) (In reality, gold nanoparticles of larger sizes 9nm+ [1, 2, 6, 10, 11] are being investigated for hyperthermia treatment aids but as magnetic moments generally increase with increasing size, the magnetic field gradient calculated in this paper will be higher than that required. However, current research is still in the early stages and so hyperthermia via 1.9nm diameter nanoparticles cannot be neglected [1, 2, 6, 10, 11]).The velocity difference is calculated as the velocity of blood flow in the aorta (∼1ms^{-1} [12]) the desired particle velocity (taken as 1cms^{-1}). This gives a value for Δv of 1.01ms^{-1} (as they travel in opposing directions). When these values are substituted into *Equation 3*, the minimum magnetic field gradient required to overcome the blood flow in the aorta is 1.3x10^{13}Tm^{-1}.

Conclusion

The highest magnetic field gradient that can be applied from outside the human body is ∼50Tm^{-1} [1], and so the value calculated here of ∼10^{13}Tm^{-1} seems unlikely to be produced in the near future. This indicates the impractical use of a magnetic field gradient to transport gold nanoparticles. The magnetic field gradient also decays strongly with distance due to the attenuation of biological tissue [1] and would only penetrate a few mm into the human body. This limits the use of this technique to superficial regions only – highly impractical if the transport, as suggested here, was to be undertaken through the cardiovascular system.

Another application issue is exciting these particles for hyperthermia uses. 10nm gold clusters have the highest extinction efficiency at ∼500nm in blood [1] but biological tissue is also an excellent absorber of visible light.

A further issue is the effect of such a magnetic field gradient on the body. For example, haemoglobin contains iron and would therefore be forced against the blood flow. This would cause catastrophic health issues for the patient.

Another method of delivering the gold nanoparticles in a minimally invasive manner is to use biological targeting techniques. This involves knowing the specific antigens that the cancerous (or designated) cells express on their surfaces so that the exact opposite of their structures can be attached to the nanoparticles. This means that the nanoparticles will bind to these particular cells only. After this has been achieved, the process of heating the gold nanoparticles can be initiated. However, the specific antigens expressed are not always known and so this method will only work when sufficient research has been conducted.

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