Developing a Halbach array for targeted drug delivery to brain tumours

Areej Alghamdi[1], Munitta Muthana[1] and Martyn Paley[2]
[1]Oncology and Metabolism, University of Sheffield, Sheffield, United Kingdom, [2]Academic Radiology, University of Sheffield, Sheffield, United Kingdom

Rationale & Hypothesis:
Steering magnetic nanoparticles (MNPs) in a desired trajectory has been proposed for guiding magnetically labelled drugs to clinical targets. In order to steer MNPs to a desired location, a strong magnetic field and field gradient is necessary and the deeper the location, the stronger the magnetic force required. External permanent magnets can provide a strong magnetic field and gradient. We hypothesise that external magnetic field/field gradient arrays of a 1.1Tesla surface field can be designed to capture MNPs into brain tumours.

Methodology:
Computational model: A 2-D simulation model of a Neodymium-iron-boron (FeNdB-52) magnet was run using FEMM software.
In vitro model: The FEMM model was assembled and actually produced a magnetic strength of 1.1 Tesla and magnetic field gradient of 37.4T/m up to 3 cm as well as magnetic force of $43.4T^2/m$ and $11.2T^2/m$ up to 3cm and 12cm respectively. From optical and MR scan data, a 3D head/tumour model was printed which geometrically mimics the surface of the head of a patient. We also printed a brain tumour, with a positioning matrix allowing the tumour to be relocated anywhere within the printed head. A Halbach array was placed on the top of the head in order to trap Fe_3O_4 MNPs in the tumour, in contact with the surface of the head model (0.8 cm thickness). MNPs were run through a fluid flow system using a syringe pump of 10 ml/min (Master Dual Pump,WPI.) Basically, the experiment was performed in two parts; the first part was to flow MNPs with different concentrations ranging from 0.1mg/ml to 20mg/ml. The second part was to flow MNPs, with the same concentrations, but loaded with 50 million white blood cells (WBCs) to mimic circulation. The concentration of MNPs was quantified by inductively coupled plasma spectrometry (ICP). Images of the tumours with trapped MNPs were also obtained by MRI (3T) using a dual gradient echo sequence (TE= 4.60ms, 20ms).

Findings:
The strength of the modeled magnetic arrays was 1.6T whereas the actual assembled one was 1.1T. The concentration of trapped MNPs in the phantom flow model was different depending on the initial concentration of MNPs and the location of the tumours within the head phantom. As expected, the further away the tumour was from the magnet, the less MNPs were trapped. For example, at 5cm depth, the concentration of MNPs was 241 mg/l. Trapping was confirmed by both ICP and MRI. Also MRI scans showed that trapped MNPs into the tumours in presence of the magnet were higher/darker than the control samples where the magnet was not presence.

Conclusions:
Various Halbach array designs were modelled and an optimised design assembled. The *in vitro* experiments showed that the Halbach arrays could trap MNPs with/without WBCs inside the tumour at several distances. This suggest that Halbach arrays have the potential to trap therapeutic drugs labelled with iron particles at several distances and we believe this would be useful for targeting of anti-cancer therapies to brain tumours. We are currently testing the trapping potential of our Halbach arrays in more complex *in vitro* models with sophisticated tumour vasculature.