The Jacket with Pulling Power-a novel approach to early stage evaluation of magnetic nanoparticles

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Introduction

As a cancer research group, one of our aims is to develop more efficient methods of compound delivery. One area we are investigating is that of the delivery of **theranostic nanoparticles**, which combine both therapeutic and diagnostic agents that directly target a tumour, thus reducing potential side effects from systemic therapies.

One delivery method is to magnetise the nanoparticles during formulation and, after injection, they are exposed to a magnetic field located close to the tumour (Fig 1).

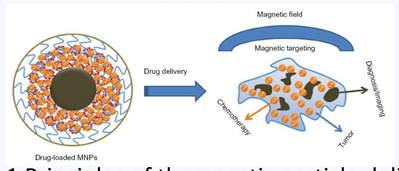

Fig. 1 Principles of theranostic particle delivery

In order to study the targeting efficiency as well as the theranostic properties of these magnetised nanoparticles, they need to be tested *in vivo.*

Researchers have used a variety of methods to expose the particles to a magnetic source, including

i. MRI-expensive, therefore impractical for early stage testing, requires lengthy anaesthesia and specialist equipment
ii. sticking a magnet to the animal's skin with tape or superglue-can damage the skin and is difficult to remove
iii. surgically implanting subcutaneously-requires full aseptic surgery and remains in place until termination.

However, it is very difficult to reproduce reported results as methodology details are scant and often rely on cartoons rather than photographs (Fig 2).

Fig. 2 Representations of *in vivo* testing of theranostic particles

Materials & Methods

We wanted to develop an early stage testing system which would allow us to fine-tune the formulation of our nanoparticles prior to full translationally-relevant testing, and which would demonstrate the efficiency of the targeting without the need for invasive, damaging or uncomfortable procedures.
To this end, we decided to develop a novel, inexpensive and non-harmful way to present the magnet to the tumour and took our inspiration from the already widely-available infusion jacket.
Working with the manufacturer, we designed a Spandex jacket (Figs 3 and 5) with a pocket to house the magnet (Fig 4) and proceeded to test our nanoparticles.

Fig. 3 Skin side of jacket

Fig. 4 Magnet

Fig. 5 Outside of jacket

Thus, we hoped to deliver the particles intravenously and then direct them towards an established subcutaneous tumour using the magnet.
After injecting the magnetic nanoparticles intravenously via the tail vein, the mouse was lightly anaesthetised with an injectable anaesthetic, the jacket was fitted and remained in place for one hour (Fig 6)
After this time, the jacket was removed and the animal was imaged for fluorescence in the IVIS Spectrum (Fig 7) under the same anaesthetic event.

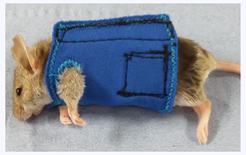

Fig. 6 Mouse wearing jacket

Fig. 7 IVIS Spectrum imaging system

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Results

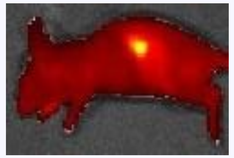

Fig. 8
With magnet

I hr post injection fluorescent images

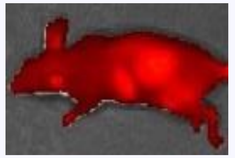

Fig. 9
Without magnet

It can be seen from the images that the Cy5 fluorophore conjugated magnetic nanoparticles have accumulated in the region of the tumour in the presence of the magnet (Fig 8), but not in its absence (Fig 9).

However, *ex vivo* analysis showed that the particles had not actually penetrated the tumour, which we believe is due to the encapsulated nature of the subcutaneous tumour.

Conclusions

Preliminary data is very promising in that it demonstrates the ability of the magnet to attract the magnetic nanoparticles when housed in the jacket. Moreover, this pilot study has also identified a number of areas for improvement, particularly in facilitating tumour uptake of the nanoparticles. To this end, we intend to further test the system against other tumour models, including an orthotopic intraperitoneal model.

However, we believe that, with some further refinements, this system could be used to quickly and easily test different nanoparticle formulations, giving us the opportunity to improve and reformulate them prior to taking them forward into more translationally relevant studies, while ensuring high welfare standards for the mice throughout the procedure.