

PRECLINICAL AND CLINICAL EXPERIENCES WITH MAGNETIC DRUG TARGETING – DIAGNOSIS AND THERAPY – POSSIBILITIES AND LIMITATIONS

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INTRODUCTION: A major challenge in cancer therapy is the delivery of antineoplastic agents to remote, difficult to reach anatomic sites. Specific targeting enhances the delivery efficiency and at the same time reduces the toxicity. In magnetic targeting, a drug or therapeutic radioisotope is bound to a magnetic compound, injected into a patient's blood and then stopped with a powerful magnetic field in the target area. It is thus possible to replace high concentrations of freely circulating drug with much lower drug concentrations (Fig. 1). This decreases side effects and whole body toxicity substantially, and at the same time increases localized drug levels several fold [1-3].

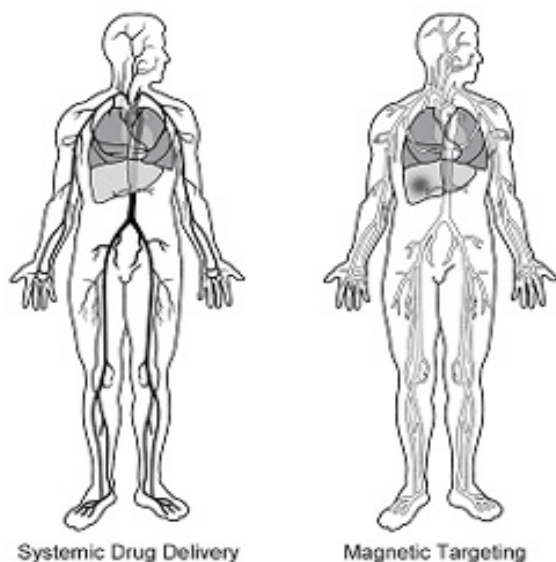


Fig. 1. Concept of magnetic drug targeting.

METHODS: Preclinical targeting tests and experimental treatment trials have been performed in cell culture, in mice growing EL-4 lymphomas and in rats with 9L-glioblastomas. Biodistribution and toxicity evaluations were performed in a swine model. A clinical trial is ongoing with doxorubicin loaded magnetic microspheres for the treatment of unresectable liver tumours.

RESULTS: Our animal studies confirmed that magnetic microspheres can be magnetically concentrated in different areas of the liver. Fig. 2A shows that the liver is homogeneously filled with magnetic microspheres sized 1-5 μm with no magnet present. Positioning a permanent rare earth magnet above the liver during and for 15 minutes

after injection leads to accumulation of more than 90% of the microspheres in the target area (Fig. 2B). Double injections, for example for the treatment of two distinct metastases, are also possible, as shown in Fig. 2C.

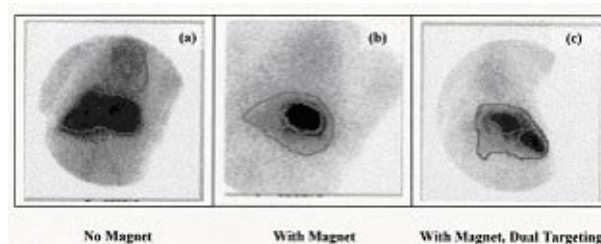


Fig. 2: Targeting of radio-labelled magnetic microspheres to specific liver sections.

DISCUSSION & CONCLUSIONS: Our experiments confirmed the promises of magnetic targeting such as low toxicity, few side effects and high target organ uptake. The microspheres seemed to stay in the target area even after removing the magnetic field. Histological studies showed that the magnetic carriers extravasate. They are "pulled" through the capillary walls of the target organ and remain in the target tissue for long times. This effect can be exploited by making magnetic microspheres, which slowly release a (chemotherapeutic) drug, or encapsulate a therapeutic radioisotope for local tumor therapy.

Areas of further research are magnetic microsphere synthesis (more responsive, homogeneous size, biocompatibility, target cell affinity), magnet optimisation (shape and strength) for more precise targeting control, imaging method development during magnetic targeting, and extension of magnetic targeting to other organs than the liver.

REFERENCES: ¹K. J. Widder, A. E. Senyei, and D. F. Ranney (1979) *Adv. Pharmacol. Chemother.* **16**:213-271. ²P.K. Gupta, C. T. Hung (1989) *Life Sciences* **44**:175-186. ³U. Häfeli, W. Schütt, J. Teller, M. Zborowski (1997) *Scientific and clinical applications of magnetic carriers*, Plenum.

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