

# A SYSTEM FOR THE TREATMENT OF LIVER CANCER BY TARGETED HYPERTHERMIA USING MAGNETIC MICROSPHERES

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**ABSTRACT:** Sirtex Medical Limited is developing new technology to treat liver cancer by induced hyperthermia using magnetic microspheres. Eighty to ninety percent of patients presenting with primary or secondary liver cancer have inoperable disease and a poor prognosis [1-4]. The median survival for patients with non-resectable hepatocellular carcinoma is three to six months [5,6], and six to 12 months for patients with non-resectable hepatic colorectal metastases [7]. These patients must rely largely on various forms of chemotherapy, radiotherapy and other local or novel treatments. Although these treatments have at times shown promising response rates and symptom palliation and have occasionally down staged hepatic tumours to allow surgical resection, they have not improved five year survival rates which remain in the order of less than 1% [8]. The persisting poor survival among the vast majority of patients with hepatic malignancies has stimulated interest in the development of other treatment options, such as targeted hyperthermia.

In current clinical practice, hyperthermia therapy is mostly used as an adjunct to radiotherapy in the treatment of superficial and other easily accessible tumour sites. Restrictions to the wider application of hyperthermia to the treatment of tumours located at deep body sites are technological in nature. There are presently no reliable non-invasive techniques that can be used to deliver an adequate heat dose to a localized tumour in a deep body organ such as the liver without risking unacceptable heating of overlying and surrounding normal tissue.

The Sirtex technology uses the heat generated in small magnetic microspheres when exposed to a high frequency magnetic field to heat these tumours. It is well known that macroscopic liver tumours derive virtually all their blood supply from the hepatic artery, while normal liver tissue is predominantly supplied by the portal venous system [9]. Hence, an infusion of the magnetic microspheres through the hepatic artery results in embolisation of the tumour vasculature with an enhanced concentration of microspheres around any tumours in the liver. This concentration differential ensures only the diseased tissue is heated once the high frequency magnetic field is applied.

We have used a rabbit model of liver cancer to investigate different aspects of this new system, including the successful demonstration of tumour heating to therapeutic temperatures with minimal heating of the surrounding parenchyma and the consequent collapse of tumour growth [10]. Analysis of the distribution of the magnetic material shows a clear concentration around the edge of the tumour and this is reflected in the measured heating patterns which show the tumour core temperature generally lagging behind that of the tumour rim. This is in direct contrast to the situation in conventional hyperthermia where it is often much easier to heat the necrotic core of a tumour with

energy deposition from an external beam (e.g. microwave or ultrasound) than it is the highly vascular tumour rim which can be left with a sub-therapeutic thermal dose. Further analysis to compare the heating rate achieved in large and small tumours with the same average concentration of magnetic material showed that it is relatively easier to heat larger tumours compared to smaller ones using the arterial microsphere technique [11].

In another recently published study [12] we have compared the therapeutic efficacy of tumour heating via arterially infused microspheres against heating from magnetic material directly injected into the tumour milieu. Despite the generally inferior heating from the arterial microspheres, the therapeutic effect was clearly superior to the direct injection result.

These results highlight several unique advantages that this new form of hyperthermia may offer compared to more conventional methodologies. This paper reviews this research and discussed its implications for future clinical application of the technology.

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