Journal of Magnetism and Magnetic Materials 351 (2014) 1–7

Contents lists available at ScienceDirect

Journal of Magnetism and Magnetic Materials

journal homepage: www.elsevier.com/locate/jmmm

Investigation of heat distribution during magnetic heating treatment using a polyurethane–ferrofluid phantom-model

F. Henrich, H. Rahn, S. Odenbach *

Institute of Fluid Mechanics, Chair of Magnetofluiddynamics, Measuring and Automation Technology, Technische Universitaet Dresden, Dresden 01069, Germany

ARTICLE INFO

Article history:
Received 28 June 2013
Available online 25 September 2013

Keywords:
Hyperthermia
Magnetic heating
Phantom
Temperature distribution
Simulation
Heat transfer

ABSTRACT

Magnetic heating treatment can be used as an adjuvant treatment for cancer therapy. In this therapy, magnetic nanoparticles are enriched inside the tumour and exposed to an alternating magnetic field. Due to magnetic losses the temperature in the tumour rises. The resulting temperature profile inside the tumour is useful for the therapeutic success. In this context heat transfer between tissue with nanoparticles and tissue without nanoparticles is a highly important feature which is actually not understood in detail. In order to investigate this, a phantom has been created which can be used to measure the temperature profile around a region enriched with magnetic nanoparticles. This phantom is composed of a material, which has similar thermal conductivity as human tissue. A tempered water bath surrounds the phantom to establish a constant surrounding temperature simulating the heat sink provided by the human body in a real therapeutic application. It has been found that even at a low concentration of magnetic nanoparticles around 13 mg/ml, sufficient heating of the enriched region can be achieved. Moreover it has been observed that the temperature drops rapidly in the material surrounding the enriched region. Corresponding numerical investigations provide a basis for future recalculations of the temperature inside the tumour using temperature data obtained in the surrounding tissue.

1. Introduction

A new possibility for local cancer therapy is magnetic heat treatment. For this therapeutic approach, a biocompatible ferrofluid is enriched in the tumour tissue. Biocompatible ferrofluids are composed of magnetite (Fe_3O_4) or maghemite (γ-Fe_2O_3) particles suspended in water. In order to obtain a stable ferrofluid, the particles are coated with a surfactant, e.g. starch or dextran (e.g. [1]). To enable magnetically controlled heat generation in the tumour enriched with magnetic nanoparticles, an alternating magnetic field is applied to the target tissue. The alternating field drives a periodic change of the direction of the magnetic moment of the particles, and the corresponding magnetic losses lead to a temperature increase. The remagnetization can either follow the Néelian process, i.e. the magnetic moment changes its direction relative to the crystal structure of the particle, or by a rotation of the whole particle, i.e. the moment is fixed relative to the crystal structure, a process called Brownian relaxation [24]. In magnetic heat treatment, one distinguishes different approaches depending on the temperature reached during heating. If the temperature ranges from 41 °C to 46 °C, the process is called hyperthermia [16]. This treatment usually takes 45–60 min [26]. Hyperthermia is used as a complementary treatment to chemotherapy or radiation therapy [27]. At these temperatures, the cells are damaged, but not completely destroyed [2]. If temperatures above 50 °C are attained, the procedure is called thermoablation. The duration of this therapy is only a couple of minutes, since the human body cannot withstand a longer treatment at this temperature. In this process, the tissue is destroyed completely [12]. There are different ways to embed the ferrofluid in the tumour. One way is to inject the ferrofluid directly into the tumour [15,13]. The other way is to inject the fluid into a blood vessel and direct the particles into the tumour region afterwards with a magnetic field [1], a process called magnetic targeting. The advantage of the first technique is that a high concentration of magnetite can be injected into the tumour. However, the tumour tissue is injured. This can cause the tumour cells to spread. The second technique does not result in injury of the tumour tissue, but at present only a low concentration of magnetic nanoparticles can be embedded in the target region. A homogeneous distribution of the magnetic particles in the tumour is the optimal precondition for successful magnetic heat treatment. In reality, the particle distribution will be inhomogeneous [4], leading to an inhomogeneous distribution of heat sources and thus the temperature distribution will not be known. Experimental determination of the temperature distribution around a tumour filled with ferrofluid is already a complicated task. Determining the temperature distribution inside a tumour inhomogeneously filled with magnetic nanoparticles is even more complicated and possibly

* Corresponding author. Tel.: +49 351 46332 062.
E-mail address: stefan.odenbach@tu-dresden.de (S. Odenbach).

0304-8853/$ - see front matter © 2013 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.jmmm.2013.09.046

impossible. Numerous experimental and simulation studies have been conducted describing the temperature distribution around a tumour cell [3,26,9]. Andrä et al. [3] measure a temperature distribution and compares it to simulation predictions. Giordano et al. [9] describe a simulation of the temperature distribution and compares the results of Andrä et al. [3]. Wust et al. describe in [26] the temperature distribution inside a prostate carcinoma. All of these studies work with biological tissue, which is inhomogeneous, and whose thermal transport properties are highly influenced by blood flow. The results described by these papers do not give a deeper basic understanding of the physical effects of the temperature distribution as they worked with materials which have several not well known parameters. In order to obtain a better understanding of the heating effect, a phantom model made of a homogeneous and tissue-like material was built. In this paper we will describe the phantom system itself as well as experimental investigations of changes in the temperature distribution over time during a magnetic heat treatment with an alternating magnetic field. The experimental investigations are accompanied by numerical simulations. The nanoparticles distribution can e.g. be determined using X-ray microtomography [20–22].

2. Phantom

In this section the development of an adequate phantom is described including detailed explanations of the phantom components, the geometry and the production process.

2.1. Phantom material and ferrofluid

The material of the phantom should have the following properties:

- properties similar to human tissue with respect to thermal conductivity;
- homogeneous structure;
- long-term stability;
- thermal stability up to 100 °C;
- magnetic particles must be immobilized in the material.

Polyurethane (PUR) is used in forensics, wound ballistics and medicine as a basic material for body part phantoms [25]. Rahn et al. [23] have already used PUR as a tissue substitute. PUR is part of polyesters and is produced via polyaddition of isocyante and alcohol. PUR fulfils the stability requirements listed above. As already mentioned, the phantom material must have a thermal conductivity similar to human tissue. The thermal conductivity of human tissue is dependent on the blood flow. Bloodless tissue has a thermal conductivity of about $\lambda = 0.477$ W/(m K), for normally perfused tissue $\lambda = 0.511$ W/(m K) and for well-perfused tissue the thermal conductivity reaches values of about $\lambda = 0.641$ W/(m K) [10]. Since tumour tissue usually has a strong blood circulation [5], a material with thermal conductivity of around 0.641 W/(m K) was chosen. The selected material, manufactured by ELANTAS Beck GmbH, is called Bectron® PU 4526. It is a combination of the filler material Bectron® PU 4526 and the hardener Bectron® PH 4912, with a mixing ratio of 6:1 by weight [7]. Due to the fact that mixtures of PUR and water or water-based ferrofluids form foams, and the fact that the heat treatment will depend only on the magnetic properties, a commercial ferrofluid containing magnetite particles was used. The ferrofluid used, APG513, is produced by Ferrotec GmbH [8] and contains 7.2% of particles with a mean diameter of about 10 nm suspended in a synthetic ester. An example of a PUR–gel mixture with this ferrofluid is shown in Fig. 1a, while Fig. 1b shows the foam formation problem of a biocompatible water-based ferrofluid.

2.2. Phantom layout

As mentioned in the introduction, the primary goal of the experiments described here is the evaluation of heat transfer from tumour tissue enriched with magnetic nanoparticles to tumour tissue without particles. For the model to be transferable to actual animal tests, and for the experimental data to be aligned with numerical simulation, a couple of structural boundary conditions must be fulfilled. The phantom is composed of two concentric cylinders. The inner cylinder is made up of a PUR–ferrofluid mixture. It has a magnetic particle concentration of approximately 13 mg/ml. This concentration was chosen since it is one of the lower concentrations used in magnetic heating treatment experiments [11]. Thus the phantom experiments provide data which enable a critical check of temperature profile determination from measurements inside healthy tissue for possible later clinical applications. The concentration was checked using a vibrating sample magnetometer (VSM). The outer cylinder simulating the tissue without magnetic particles is made up of pure PUR. To measure the temperature distribution in the model, four thermocouples were distributed at different positions inside the phantom. Thermocouples of type T consisting of copper and copper constantan with a negligible nickel concentration and a polytetrafluoroethylene (PTFE) insulation were chosen, since an alternating magnetic field has little influence on this type of thermocouple. The conductors have a diameter of 0.08 mm and the thermocouple can measure temperatures up to 260 °C [19]. In Fig. 2 the dimensions of the phantom as well as the positions of the thermocouples are shown. Thermocouple T_1 is located in the centre of the inner cylinder; thermocouple T_2 measures the temperature at the interface of the two cylinders, while thermocouples T_3 and T_4 provide measurements

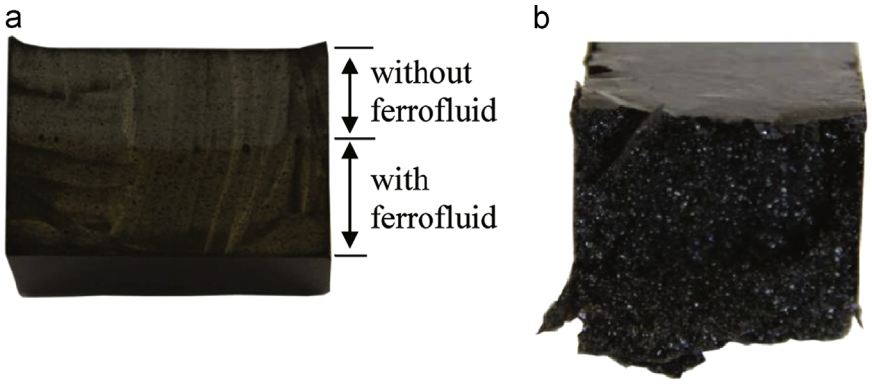

Fig. 1. Photos of PUR with suspended magnetic particles: (a) an unfoamed solid gel consisting of a section enriched with particles from ferrofluid APG513 at the bottom, and pure PUR at the top and (b) a PUR foam created using a biocompatible water-based ferrofluid.