

Thermotherapy using magnetic nanoparticles

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The biological effectiveness of heat in treating cancer is known for decades and many of the corresponding molecular mechanisms are understood. Elevation of tissue temperature to above 41°C is termed hyperthermia, more than 46°C are called thermoablation. Hyperthermia alters the function of structural and enzymatic proteins within cells as a function of time and temperature, which in turn alters cell growth and differentiation, radiation sensitivity and resistance to certain drugs used in chemotherapy and also can induce apoptosis [1-3]. Thermoablation causes coagulation of cellular proteins, i.e. direct cell destruction.

The major problem of most conventional thermotherapy systems used is to achieve homogenous heat distribution and deep regional therapeutic temperatures in the treated tumor tissue. A failure may either lead to insufficient temperature rise in parts of the tumor, resulting in further tumor growth, or to negative effects on normal tissue by too high temperatures [4].

The MagForce Nanotherapy also termed “thermotherapy using magnetic nanoparticles” or “Magnetic fluid hyperthermia” is a new cancer therapy, which particularly faces these problems. Herein, a magnetic fluid is directly injected into a tumor and subsequently heated in an alternating magnetic field (100 kHz and variable field strengths of 0-18 kA). The magnetic fluid NanoTherm® MFL AS (MagForce Nanotechnologies AG, Berlin) consists of superparamagnetic iron-oxide nanoparticles in aqueous solution with an iron concentration of 112 mg/ml. The iron-oxide core (diameter 15 nm) is covered by an aminosilane type shell. The particles generate heat in an alternating magnetic field by Brownian and Néel relaxation processes.

This method has been developed by our group in more than 15 years of research at the Charité - University Medicine Berlin and is one of the first applications of nanotechnology in medicine [5].

First Clinical Experience

From August 2003 to July 2004 we performed the first phase-I trial on MagForce Nanotherapy with 14 glioblastoma multiforme patients [6]. All patients of this trial received stereotactic injection of the magnetic fluid into the tumor. Before starting thermotherapy, the position of the instilled nanoparticles was determined by computed tomography (CT). These data were matched to presurgical MR images by a specially designed software (MagForce NanoPlan®), thus allowing the calculation of the expected heat distribution within the treatment area in dependence on the magnetic field strength [7].

Another feasibility study enrolled 35 patients with local relapses of different tumor entities (e.g. cancer of the rectum-, ovarian-, prostate-, cervical- carcinoma and sarcoma). All of these patients received thermotherapy in combination with radio- or chemotherapy [8].

A feasibility-study with 10 patients with pre-treated prostate carcinoma, another main focus in the clinical use of the Nanotherapy, was closed in June 2006. The nanoparticles were injected transperineally into the prostate under transrectal ultrasound guidance and fluoroscopy [9, 10]. Another phase I study started in March 2006 on esophageal cancer, which, so far enrolled eight patients. Two phase II trials are in progress to evaluate the efficacy of the new approach on 72 patients with recurrences of glioblastoma multiforme and on 130 patients suffering from prostate carcinoma.

According to the experiences derived from these first clinical trials, the Nanotherapy is effective and can be applied without complications. The heat treatments were tolerated well without or with only minor side effects depending on the tumor location with therapeutically effective thermal doses. The follow-up showed encouraging results for severe oncological diseases.

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