CHAPTER 4

Thermotherapy and Nanomedicine: Between Vision and Reality

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Summary

Although nanoparticles have been already applied on patients in clinical trials, generally nanotechnology in medicine is regarded rather a vision than a realistic option. Progress in this field arises particularly from the combination of molecular biology and nano(bio)technology. From the viewpoint of entrepreneurs nanotechnology is only a tool to develop new products, however nanotechnology itself is not a product. We developed a new cancer treatment platform technology termed MagForce Nanotherapy, in which nanotechnology has the potential to cause a revolution in tumor therapy.

Introduction

The idea of traveling through the vessels of a body in a “nanobot” to heal diseases from “the inside”, as shown in the Oscar-awarded movie “Fantastic Voyage” (Stephen Boyd, 1966), is indeed quite attractive, but unfortunately it also inherits general difficulties, especially in combating cancer. Theoretically, an ingeniously built nano-vehicle, controlled from outside the body, could move through vessels. Nevertheless, the fantasy story would end very fast, because the immune system of the human body would quickly destroy the submarine, as it does enduringly with bacteria, viruses and other foreign particles. But even if this problem could be solved, the submarine would still not know how to destroy cancer cells selectively while sparing normal cells. Hereto defined molecules on the surface of tumor and normal cells (“targets”) have to be identified for distinguishing between these cells. A solid tumor consists of a number of different sub-populations, whose genomes are different from each other expressing those targets or not. Therefore not all cells of the tumor are recognized by their specific target molecules, which build the source of recurrent, often multi-resistant tumor growth. Even the mixture of different target recognizing molecules is not a guarantee that all tumor cells are affected. This general problem cannot be solved by any “nanobot” approach.

How we get along with this new knowledge without “nanobots”, future will tell. Answers to these problems may rather derive from research in the fields of molecular biology, where certain success has already been obtained concerning different tumor entities.

Boundaries between nanotechnology and molecular biology blur. It is of general acceptance, that in the future even single molecules and atoms are to be controlled, and then nanotechnology will probably gain the same importance that molecular biology has today.

As one of the first applications of nanotechnology in medicine the group of the authors developed a worldwide new Nano-cancer-therapy in more than 15 years of fundamental

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research at the Charité - University Medicine Berlin. Via foundation of the MagForce®
Nanotechnologies GmbH in Berlin, research lead to products, which have already been tested
in clinical trials and which are already requested by numerous cancer clinics, even before their
approval.

The principle of the method termed MagForce Nanotherapy is simple: Iron-oxide
nanoparticles are directly injected into the tumor and release heat after inductively induced
activation by an alternating magnetic field. Despite this simple-sounding approach, it was
nanotechnology to be the key for realizing this new cancer-therapy:

- Only nanoparticles extract high energy per applied mass from a magnetic field
- Due to their enormous surface only nanoparticles are able to carry a huge number of bind-
ing sites for cancer cells /target molecules
- Only nanoparticles are able to intrude deeply into tumor tissue
- Only nanoparticles with special coatings
  - are recognized delayed by the immune system and thus reach their targets
  - can be ingested in great quantities by tumor cells
  - form a homogeneous fluid of low viscosity in water
  - remain in the tumor tissue even after interstitial application for a long time and are not
    being washed out

So far, the MagForce Nanotherapy is, in a first step, a new form of local thermotherapy of
deep-seated tumors. Clinical trials in this field done so far demonstrated a good feasibility and
tolerability of the new technique. Later the nanoparticles are supposed to function as transport
vehicles for medical agents, isotopes or genes. MagForce is doing research in this field for years
now, predominantly in cooperation with the Leibniz-Institute for New Materials (INM),
Saarbrücken, Germany and different departments of the Charité - University Medicine, Ber-
lin, Germany.

The MagForce Nanotherapy offers the possibility of repeated heat treatments of basically
every region of the body very precisely without repeated application of the particles. Intratumoral
temperatures can be varied according to clinical requirements between hyperthermia (up to
45°C for supporting radiochemotherapy) and thermoablation with temperatures of up to 70°C.

The method is based on the defined power transfer to biocompatible iron-oxide nanoparticles
in an alternating magnetic field. The patented nanotechnological design of the MagForce
nanoparticle shell leads to preferred intracellular absorption into proliferating cells like tumor
cells (Fig. 1). The particles function as “Trojan horses”, thus destroying tumor cells, whereas
healthy tissue is spared. Particles generate heat by relaxation processes of the particle core and
emit it into the surrounding tissue.¹

Thermotherapy is performed in a specially designed magnetic field applicator (Fig. 2). Due
to its construction and safety standards, the system can be applied on different tumor entities
in every region of the human body.

To date, the MagForce Nanotherapy is being investigated only at the Charité - University
Medicine Berlin, Germany. Treatment modalities are shown in Figure 2.

In early 2007 the new method is supposed to be available for all clinics in Europe.

From March 2003 to July 2004, the worldwide first feasibility study on thermotherapy
using magnetic nanoparticles was performed on 14 patients with glioblastoma multiforme. In
Germany, more than 2000 patients (Incidence: 3/100,000) die on this aggressive tumor every
year. Median overall survival after first-line therapy does not exceed 12-15 months and no
significant increase has been achieved over the last decade, despite modern diagnostics and
treatments with surgery, radiotherapy and chemotherapy.²⁴

The therapy was tolerated well by all patients, and in all cases intratumoral temperatures of
42-45°C could be achieved, even in deep-seated tumors. Signs of local efficacy could be ob-
served in all patients. Detailed results will be published soon.