New antitumor therapies are urgently needed for glioblastomas (GBM), the most frequent and malignant of brain tumors, after failure of first-line therapy. Hyperthermia and thermoablation kill, disable, or sensitize tumor cells to concurrent anticancer treatment depending on duration and temperature, and possibly inhibit the cells’ repair system in contrast to normal brain cells. The challenge is to get enough heat into the tumor. While different thermotherapy methods are used (e.g., radiofrequency, ultrasound, hot water tubes, laser fibers, or microwave antennas), these methods have several disadvantages when it comes to including application procedures, accuracy to the targeted treatment area, and safety issues.

The MagForce NanoTherm™ Therapy is a new thermotherapy based on 5 class I to III medical devices. The main components are coated iron oxide nanoparticles (NanoTherm™), simulation software (NanoPlan®), an alternating magnetic field device (NanoActivator®), and a Pebax closed-end catheter (50 cm long, external diameter: 1.0 mm) for the insertion of the thermometry probe.

After stereotactic injection of biocompatible aminosilane-coated superparamagnetic iron oxide nanoparticles (diameter: ~12 nm) into the tumor, the particles agglomerate immediately in the tumor tissue. They are stimulated by the external alternating magnetic field, which is of no harm to humans, generating heat within the tumor while sparing the surrounding healthy tissue.

Preclinical studies with the RG-2 glioblastoma rat model showed enhanced survival rates with increasing magnetic field strengths (and thus increasing temperatures in the tumor).

MagForce has successfully conducted clinical studies in diverse cancer indications.

Recurrent glioblastoma feasibility and safety/efficacy studies of NanoTherm Therapy in combination with percutaneous radiotherapy showed that this combination therapy was feasible and safe. Therapeutic hypertermic and thermoablative temperatures could be reached in the treatment area with promising therapeutic effect (mOS after recurrence = 13.4 months) and moderate side effect profile.

Further advantages of the therapy are the minimally invasive procedure of the nanoparticle instillation, treatment of tumors with unlimited treatment depth, the constant dosage control throughout thermotherapy, and being independent of tissue characteristics.

The current impairments of the NanoTherm therapy are that metallic bodies within 40 cm/15.7” of the treatment area are not allowed and that MRI cannot be used for further diagnosis in the region of nanoparticle placement due to artifacts. However, MR imaging in other body areas as well as other imaging modalities in the nanoparticle area (e.g, CT, PET, PET-CT) are not affected.

Based on the preclinical and clinical data collected, the European certification (CE mark) for the treatment of brain tumors was granted in 2010 for the 2 molar NanoTherm Therapy.

A new clinical study in recurrent glioblastoma was initiated in Europe with the first patient enrolled in March 2014. The objective is to evaluate the effect of 6 molar NanoTherm monotherapy in a run-in phase (up to 24 subjects) and, if effective, in the main study versus the combination with hypo-fractionated stereotactic radiotherapy (HFSRT) and HFSRT alone (245 subjects).

Eligible subjects must have radiographically and histologically confirmed first progression of supratentorial glioblastoma, a maximum tumor volume of 25 ml, standard radiochemotherapy or radiotherapy alone, at least six months off RT, no proximate metallic material, and no previous and concurrent antiangiogenics. After stereotactic deposition of nanoparticle depots in the tumor, six magnetic field sessions alternating every one hour are applied twice weekly in the HFSRT combination arm within two hours after HFSRT, which is applied as 2.66 Gy fractions (40 Gy in total) five days a week for three weeks. During the instillation procedure a Pebax closed-end catheter (50 cm long, external diameter: 1.0 mm) is placed in the direct vicinity of the nanoparticle depots for direct temperature measurement and control via an inserted thermometry probe during at least the first of the six non-invasive thermotherapy sessions in the NanoActivator.

MagForce is planning to expand the study to other European and non-European countries and to the United States. A pre-IDE meeting with the FDA took place in 2014 with positive and constructive feedback from the FDA. Preparation of IDE dossier is ongoing with IDE submission planned for 2015.

Further research projects at MagForce concern the linkage of drugs and biologicals to nanoparticles for targeted drug delivery.