CLINICAL HYPERTHERMIA OF PROSTATE CANCER USING MAGNETIC NANO PARTICLES – PRELIMINARY EXPERIENCE WITH A NEW INTERSTITIAL TECHNIQUE

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Purpose:
Thermotherapy using biocompatible superparamagnetic nanoparticles, also referred to as magnetic fluid hyperthermia (MFH), has been shown to inhibit prostate cancer growth in the Dunning rat model. Here we present the first clinical application of interstitial hyperthermia using magnetic nanoparticles in locally recurrent prostate cancer.

Methods:
Treatment planning was carried out using computerized tomography (CT) of the prostate. Based on the individual anatomy of the prostate and the estimated specific absorption rate (SAR) of magnetic fluids in prostatic tissue, the number and position of magnetic fluid depots required for sufficient heat deposition was calculated using the AMIRA software and a newly developed prostate module. Nanoparticle suspensions (MagForce® MFL AS, MagForce® Nanotechnologies GmbH, Berlin, Germany) were injected transperineally into the prostate under transrectal ultrasound and flouroscopy guidance. Treatments were delivered in the first magnetic field applicator for use in humans (MFH300F, MagForce® Nanotechnologies GmbH, Berlin), using an alternating magnetic field with a frequency of 100 kHz and variable field strength (0-18 kA/m). Invasive thermometry of the prostate was carried out in the first and last of 6 weekly hyperthermia sessions of 60 min duration. CT-scans of the prostate were repeated following the first and last hyperthermia treatment to document magnetic nanoparticle distribution and the position of the thermometry probes in the prostate.

Results:
Nanoparticles were retained in the prostate during the treatment interval of 6 weeks, as documented by CT. Treatment was well tolerated. During the first treatment, maximum intraprostatic temperatures measured by 4 thermometry probes at a magnetic field strength of 4.0-5.0 kA/m were 48.5, 43.0, 43.7 and 43.6 °C, whereas minimal temperatures were 41.2, 40.3, 40.0 and 41.1 °C, respectively. During the sixth and last treatment of the same patient, maximum intraprostatic temperatures were 42.5, 42.3, 41.5 and 40.7°C, whereas minimal temperatures were 40.5, 39.8, 39.7 and 39.4 °C, respectively. Mean temperatures measured in the urethra and the rectum did not exceed 42 °C. Using the AMIRA software, a non-invasive estimation of temperature values in the prostate, based on intratumoral distribution of magnetic nanoparticles, could be performed and correlated with invasively measured temperatures.

Conclusions:
Hyperthermia using magnetic nanoparticles is feasible and well tolerated in locally recurrent prostate carcinoma. Maximum intraprostatic temperatures achieved are in the thermoablative range. Interstitial deposition of nanoparticles in the prostate is stable for at least 6 weeks, allowing for sequential hyperthermia treatments without the need for repeated application of magnetic fluid. These first clinical experiences prompted us to initiate a phase I study to evaluate this technique in patients with local recurrence of prostate cancer following radiotherapy with curative intent. Further improvements will focus on optimization of intraprostatic application and distribution of nanoparticles as well as non-invasive temperature measurements.