

INTERSTITIAL THERMOTHERAPY OF PROSTATE CANCER USING MAGNETIC NANOPARTICLES: RESULTS OF A PHASE I TRIAL

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Purpose

Thermotherapy using biocompatible superparamagnetic nanoparticles has been shown to inhibit prostate cancer growth in the Dunning rat model. Here we report on feasibility and toxicity of this novel technique in patients with locally recurrent prostate cancer.

Methods

Nine patients with biopsy-proven locally recurrent prostate cancer following primary therapy with curative intent and no detectable metastases have been entered on a prospective phase I trial. Primary endpoints were feasibility and toxicity, secondary endpoints were objective response and quality of life. CT of the prostate was performed before and after treatment. Transperineal intraprostatic injection of nanoparticle dispersion (MagForce[®]MFL AS, MagForce Nanotechnologies AG, Berlin, Germany) was carried out under transrectal ultrasound and fluoroscopy guidance. A software with a special nanotherapy module (MagForce NanoPlan[®]) was used for treatment planning as well as for non-invasive temperature estimations. In addition, invasive thermometry of the prostate was carried out in the first and last of 6 weekly thermotherapy sessions of 60 min duration (4 thermoprobes/prostate/session). Treatments were delivered in an AC magnetic field applicator for use in humans (MFH300F, MagForce Nanotechnologies AG, Berlin; field parameters: 100 kHz, 2.5-18 kA/m). NCI CTC 2.0 toxicity criteria and EORTC QLQ C30 and QLQ PR25 questionnaires were used to evaluate toxicity and quality of life, respectively.

Results

Nanoparticles are retained in the prostates for several months. AC magnetic field strengths of 4-5 kA/m were tolerated without anesthesia. The mean maximum temperature measured invasively in the prostates was 46.3°C (42.8-55.0), the mean T₂₀, T₅₀ and T₉₀ during the first and the last treatment taken together were 42.8°C (39.8-50.1), 41.3°C (39.2-47.1) and 39.7°C (38.0-42.1), respectively. Non-invasively calculated mean maximum intraprostatic temperature was 43.4°C (40.9-50.0), mean T₂₀, T₅₀ and T₉₀ were 41.9°C (40.2-47.4), 41.4°C (39.5-45.4) and 40.5°C (37.9-43.4). Mean urethral and rectal temperatures (measured intraluminally during each session) were 40.5°C (38.4-43.6) and 39.8°C (38.2-43.4), respectively. The median thermal dose resulting from the sum of all treatments, expressed as CEM T₉₀ 43°C, was 4.3 (calculated from invasive measurements) and 6.0 (calculated from non-invasive measurements), respectively. No systemic toxicity was observed. Acute urinary retention occurred in 4 patients (all with previous history of urethral stricture/impaired urinary flow rate), bladder spasms and urinary frequency grade 2-3 in 2, dysuria grade 1-2 in 5 and minor tissue reactions in 2 patients. A moderate PSA decline was observed in 7 and a rise in 2 patients at the end of treatment. Quality of life was only temporarily impaired.

Conclusions

Interstitial heating using magnetic nanoparticles was feasible in patients with previously irradiated and locally recurrent prostate carcinoma. Hyperthermic to thermoablative temperatures were achieved in the prostates at 25% of the available magnetic field strength, indicating a significant potential for higher temperatures. Intraprostatic nanoparticle distribution was still suboptimal and more homogeneous coverage must be attained. A non-invasive thermometry method specific for magnetic nanoparticle thermotherapy is being validated as a tool for thermal dosimetry in further studies. In the future, this treatment modality may be suitable for combination with irradiation in patients with localized prostate cancer.