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A CLINICAL EVALUATION OF THE OPTICAL CHARACTERISTICS OF THE PROSTATE IN MEN WITH PROSTATE CANCER

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INTRODUCTION & OBJECTIVES: The use of lasers is becoming increasingly common in urology, particularly in the prostate. Low power laser is used in photodynamic therapy in order to activate a photosensitising drug. The extent of the photodynamic effect is dependent upon the optical characteristics of the prostate. These characteristics, which encompass both scattering and absorption, can be expressed as the depth of penetration of the laser energy. We report a study using 763nm light to assess variability in laser penetration depth throughout the prostate.

MATERIAL & METHODS: The study was carried out in patients having high dose rate brachytherapy (HDRB). These patients have up to 22 hollow clear plastic needles in the prostate for 36 hours. The needles are inserted under general anaesthetic, using transrectal ultrasound and a perineal template. A CT scan is taken once the patient is awake, and the radiotherapy dose is planned by the radiotherapy medical and physics team. The radiotherapy dose is given by sliding an iridium wire along each needle, which rests at different positions along the needle for different times. The doses are given 6, 24 and 30 hours after needle placement. Prior to the first radiotherapy dose, we used the needles to position optical delivery and detection fibres in multiple positions throughout the prostate. A 763 nm laser was used to deliver light via a 2cm diffusing fibre. An isotropic optical detector was slid along nearby needles, and optical readings taken every 6mm. The exact separation distance of the delivery and detector fibre at each of the optical measurement positions was then measured on different slices of the CT scan. The Boltzmann approximation to the transport equation was used to calculate the penetration depth (PD), which is defined as the depth at which 63% of light intensity is lost.

RESULTS: Over 1000 data points in 8 patients were assessed. The mean PD was 3.7 mm with a range of 1.35 - 33 mm. The PD varied within patients by up to a factor of up to 12 times, with the mean variation within an individual patient of 4 times. Between patient variability of the PD was not as significant as intra patient variability. From examination of the CT scans of the patients it was not possible to identify any factors which would predict PD.

CONCLUSIONS: This study shows that there is marked variability of laser penetration both within and between patients with prostate cancer. It will be important to see if this translates to a difference in therapeutic effect in treatments which use lasers, in this patient group.

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VASCULAR-TARGETED PHOTODYNAMIC THERAPY IN ORGAN-CONFINED PROSTATE CANCER - REPORT OF A NOVEL PHOTOSENSITISER

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INTRODUCTION & OBJECTIVES: Photodynamic Therapy (PDT) uses a photosensitising drug, activated by single wavelength light from a laser to cause localised necrosis. Tookad is a vascular acting photosensitiser which is activated by 763 nm light. It has a short drug light interval, so that both drug and light are given in a single session. Due to rapid clearance, it has no skin phototoxicity after 3 hours. Vascular-Targeted Photodynamic therapy (VTP) with Tookad (WST09) has been evaluated in patients with post-radiotherapy prostate cancer recurrence. Here we report the use of Tookad VTP in the previously untreated prostate. The effect of different light doses with a constant drug dose was evaluated using gadolinium-enhanced MRI at 1 week.

MATERIAL & METHODS: Under general anaesthetic, using transrectal ultrasound guidance and a perineal template, two hollow, clear plastic needles were inserted into each of the right and left lobes of the prostate. On each side, the needles held one optical delivery fibre, and one optical detection fibre. Optical detectors were also placed within catheters in the urethra and rectum to monitor light levels throughout the light delivery phase.
Once needle positions were finalised, an infusion of 2 mg/kg Tookad was given over 20 minutes. After the infusion began, the light dose was given. The light dose was escalated throughout the study, with a minimum of 50 J/cm, and a maximum of 300 J/cm at a power of either 150 or 200 mW. The active length of the diffuser was chosen to leave a 5 mm margin at the base and apex of the prostate. A dynamic gadolinium-enhanced MRI was performed prior to and 1 week after the VTP procedure. PSA was measured prior to and at 1, 3 and 6 months after VTP.

RESULTS: Eleven men have undergone the Tookad VTP procedure and 1 week MRI to date. Prostate tissue necrosis, seen as absence of uptake of gadolinium, was observed in men receiving a light dose of 150 J/cm or more. The volume of necrosis varied with the light dose per cm, and the total light dose, but all patients had a PSA reduction at 1 or 3 months. All patients had a successful catheter removal the day after Tookad VTP, with four experiencing transient irritative urinary symptoms. Nine patients had a transient elevation of gamma GT and transaminases which resolved spontaneously within two weeks.

CONCLUSIONS: The Tookad VTP procedure is a promising minimally invasive treatment for prostate cancer. It can cause necrosis, as shown by lack of uptake of gadolinium on dynamic MRI at 1 week. This is accompanied by a PSA reduction. The procedure itself is safe and well tolerated. The study will continue using multiple optical fibres in each lobe.

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MATCH PAIR ANALYSIS HDR BRACHYTHERAPY VS. THERMORADIOTHERAPY USING INTERSTITIAL THERMOSEEDS

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INTRODUCTION & OBJECTIVES: There is still no standardised treatment of locally advanced prostate cancer. It seems to be that combined strategies are necessary for improving the outcome.

MATERIAL & METHODS: We studied two different dose escalation techniques of radiation therapy retrospectively using match pair analysis. Patients were matched according age, stage, grading, initial PSA and follow up time. Thermoradiotherapy using self regulating thermoseeds and high dose rate brachytherapy with iridium 192 were compared. The biological effective dose was for both regimen above 82 Gy. Biochemical failure was defined according to ASTRO criteria.

RESULTS: We were able to match 36 patients; who were treated in the same time period. Median follow-up time was 36 months in both groups. There was no statistically difference in the PSA decrease and progression free between therapy groups.

CONCLUSIONS: The combination thermoradiothearpy is able to reach high biological effective doses. Thermoradiotherapy and HDR-brachytherapy maybe had an equal oncological outcome. Long term toxicity data are not available yet. Quality of life data need to be investigated for high dose regiments.

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THERMOTHERAPY USING MAGNETIC NANOPARTICLES IN PATIENTS WITH LOCALLY RECURRENT PROSTATE CANCER: INITIAL RESULTS OF A PHASE I STUDY

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INTRODUCTION & OBJECTIVES: 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.

MATERIAL & METHODS: 9 patients with biopsy-proven locally recurrent prostate cancer following primary therapy with curative intent and no detectable metastases have been entered so far. 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[a]MFL AS, MagForce Nanotechnologies AG, Berlin, Germany) was carried out under transrectal ultrasound and flouroscopy guidance. A software with a special nanotherapy module (MagForce NanoPlan[a]) 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. Treatments were delivered in the first 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.

RESULTS: Nanoparticles are retained in the prostates for several months. The mean maximum and average temperatures measured in the prostates (4 thermoprobes/prostate/session) were 46.2°C (42.7-55.0) and 43.2°C (41.0-48.6), respectively. Mean urethral and rectal temperatures were 40.5°C (38.5-43.5) and 39.8°C (38.2-43.4). Non-invasively calculated mean maximum intraprostatic temperature was 44.1°C (41.0-52.0), the mean T90 was 41.0°C (39.7-45.0) and the mean T50 41.8°C (40.1-47.2). AC magnetic field strengths of 4-5 kA/m were tolerated without anaesthesia. 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 4 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 are achieved in the prostates already at 25% of the available power. Further optimisation will focus on intraprostatic nanoparticle distribution and patient tolerance at higher magnetic field strengths. In the future, this treatment modality may be suitable for combination with irradiation in patients with localised prostate cancer.