THE CROSSROADS OF PROSTATE CANCER AND THERMAL MEDICINE

MARK HURWITZ

Dana-Farber/Brigham &
Women's Cancer Center,
Harvard Medical School,
Boston, MA, USA

Int. J. Hyperthermia, December 2010; 26(8): 735-736

Prostate cancer has been a focus of thermal therapy research for many years. The principles of thermal biology, as for other disease sites, provide a compelling rationale for combining heat with radiation in the treatment of prostate cancer. For example, hypoxia is commonly associated with prostate cancer leading to radiation resistance which may be addressed with hyperthermia. Beyond classic thermal biology there is increasing appreciation for the relevance of heat shock proteins (HSPs) to prostate cancer. For targets as diverse as androgen receptors and the PI3-kinase/ATP pathway, HSPs have a role in the development and regulation of prostate cancer.

From a clinical standpoint, prostatic anatomy allows for numerous heating approaches including non-invasive, trans-rectal, trans-urethral, and trans-perineal techniques. The relevance of hyperthermia with its favorable morbidity profile has grown in recent years as both the importance of radiation dose escalation and impact of treatment on quality of life have become increasingly apparent. Prostate cancer is often associated with an indolent course. Many men contemplating treatment will die of causes other than prostate cancer. The potential benefit of treatment has to be carefully weighed against the prospect of short-term side effects which impact quality of life. There is growing evidence that hyperthermia provides benefit to patients treated with radiation therapy with modest impact on quality of life. Notably, thermal enhancement of radiation therapy as demonstrated in a review of clinical literature by Maluta et al. in this special edition appears similar to the added benefit of androgen deprivation therapy to radiation in patients with adverse risk factors. Provided efficacy of hyperthermia can be definitely established, heat as opposed to testosterone suppression with its incumbent sexual and metabolic side effects, or radiation dose escalation with associated genitourinary and gastrointestinal effects would be a preferred choice for patients to optimize local control.

The same properties of the prostate and limitations of standard treatments that lend appeal to traditional hyperthermia also make thermal ablation attractive. The past several years have seen a rapid increase in use of high intensity focused ultrasound for ablation of prostate cancer. The application of MR to HIFU and other ablative therapies provides further impetus for integration of thermal ablation into the therapeutic armamentarium used against prostate cancer. Lessons learned by incorporation of hyperthermia with radiation or chemotherapy are as relevant as ever before. While significant strides have been made in the use of thermal ablation as monotherapy, similar to other modalities, thoughtful application of ablation as part of combined modality therapy holds tremendous promise. Future clinical trials should be designed to asses this yet to be explored therapeutic strategy.

This special edition includes seven outstanding reviews that encompass wide ranging topics of interest in regard to prostate cancer and thermal medicine. In the first paper, Ciocca et al. provide a comprehensive review of the significance of HSPs in prostate cancer including their role in carcinogenesis, prognostic implications, and potential as therapeutic targets. Rylander et al. then explore the relationship of hyperthermia protocols with HSP expression kinetics and cell death. The authors present how in vitro experiments can be used to develop elegant models of HSP expression and cellular injury that hold great promise for advancing thermal therapy via future clinical translation.

Moving from bench to clinic, Maluta et al. provide an extensive assessment of the current status of radiotherapeutic management of prostate cancer. A thorough review of clinical trials exploring the role of hyperthermia for prostate cancer including the long-term results of a newly published positive phase II trial from the Dana-Faber Cancer Institute at Harvard Medical School are then provided. The rapidly expanding applications of nanotechnology in thermal medicine are explored in two subsequent papers. Krishnan et al. provide an excellent overview of nanotherapeutic strategies currently being used for thermal therapy including their work with near infrared stimulation of gold nanoshells. Exciting clinical avenues for application of nano-thermal therapy are presented including active tumour or vascular targeting, precise payload delivery, and radiation sensitization. Johannsen et al. review their clinical work with interstitial application of magnetic nanoparticles via a trans-perineal route as is commonly utilized for prostate brachytherapy. The results of two completed phase I studies, one on use of magnetic nanoparticle thermotherapy alone and a second in combination with prostate brachytherapy are presented. These trails are notable examples of leading-edge clinical application of nanotechnology in oncology.

The final two papers address the rapidly expanding field of thermal ablation as applied to prostate cancer. Crouzet et al. provide an outstanding synopsis of the current status of ultrasound guided high intensity focused ultrasound (HIFU) for treatment of prostate cancer. In the final paper, Chopra et al. provide a comprehensive review of one of several eloquent strategies combining MR with thermal ablation. In this case, the combination of trans-urethral treatment with MR imaging, thermal dosimetry, and treatment verification provides a compelling example of the prostate of MR in advancing thermal therapy

The breadth of topics and elegant research presented in this special edition clearly demonstrate the value of thermal medicine in the fight against prostate cancer. Efforts put forth to date have yielded meaningful results yet much remains to be accomplished. The collective efforts of biologists, physicists, engineers, and clinicians committed to advancing thermal medicine will no doubt lead us and our patients along not one but rather many paths towards improved prostate cancer therapies.