

## Nanotechnology as a Platform for Thermal Therapy of Prostate Cancer

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### Abstract

Over the past several years, there has been increasing research and clinical interest in using nanotechnology for cancer therapy. Nanoparticle provides tremendous potential for future medical therapy. Besides targeting cancer cells, delivering and releasing drugs in a regulated manner, the specificity of nanoparticles is what makes thermal therapy as attractive as a cancer therapy. In this mini review, we discuss some of the recent advances of nanotechnology for thermal therapy of prostate cancer.

**Keywords:** Cancer therapy; Nanoparticle; Thermal therapy; Prostate cancer

Since 2005, cancer has become the leading cause of death in individuals under age 85 in the USA [1] and Prostate cancer (PCa) is the most common non-skin cancer diagnosed in the USA [2]. It is estimated that approximately 238,590 new cases and 29,720 prostate cancer-related deaths will occur in the United States in 2013. Prostate cancer is now the second leading cause of cancer death in men, exceeded only by lung cancer. It accounts for 28% of all male cancers and 10% of male cancer-related deaths. The PSA (prostate specific antigen) test has been used for initial diagnosis of disease, and monitored for recurrence after initial therapy and for prognosis of outcomes. Diagnosis of prostate has been substantially improved with the combined use of digital rectal examination, measurement of serum PSA levels and transrectal ultrasound [3]. Nearly 90% of men with prostate cancer were diagnosed with clinically localization [4]. Therefore, an early intervention to the disease could be more appropriate for such patients.

Currently chemotherapy is a preferred modality in the treatment of prostate cancer, [5] for example; docetaxel and mitoxantrone are considered first-line chemotherapeutic options in patients with hormone-refractory prostate cancer (HRPC) [6]. But modest drug response and significant toxicity by conventional methods of administration limit their efficacy. For these issues, targeted cancer therapies offer significant therapeutic benefits over existing chemotherapy regimens since the drug is preferentially delivered to the cancer tissue. The side effects associated with chemotherapy can be minimized by targeted drug delivery. Nanoparticles have large flexibility in engineering design with sustained-release characteristics are the most promising candidates as drug delivery carriers. Over past a few years, researchers have developed different types of nanoparticles for treatment of cancer [7]. For targeting of prostate cancer, one such antigen is the prostate specific membrane antigen (PSMA) [8,9]. PSMA is a protein abundantly expressed on the surface of prostate cancer cells, metastatic disease and the hormone-refractory form. Anti-PSMA mAbs that bind the extracellular PSMA domain were used in targeting cells for prostate cancer therapy and imaging by several research groups [10-12]. Not limiting to antibody, aptamers, also known as chemical antibodies have recently been demonstrated as ideal candidates for molecular targeting applications. Many groups developed aptamers conjugated with nanoparticles for prostate cancer therapy and molecular imaging. For example, Chu et al. [13] used A9 RNA aptamer: gelonin as conjugates to target and destroy prostate-specific membrane antigen (PSMA)-positive PCa cells. Dhar et al. [14]

reported the use of A10 PSMA Apt conjugation with PLGA for targeted delivery of cisplatin to prostate cancer cells. Javier et al. [15] developed aptamer-based gold nanoparticles as contrast agents for imaging of PSMA (+) prostate cancer cells.

After we mentioned the strategy of targeting for prostate cancer above, we will discuss the treatment of prostate cancer. As low-risk clinically localized disease, the treatments of prostate cancer include watchful waiting, radical prostatectomy, external beam radiation therapy (RT) and interstitial RT (brachytherapy), freezing the prostate (cryotherapy), and androgen deprivation therapy (ADT). And for prostate cancer recurrence, the patients would be offered radiation therapy, androgen deprivation therapy (ADT), thermal therapy and others. Among of these, thermal therapy was very interesting and promising for prostate cancer locally therapy.

Thermal therapy (also called hyperthermia or thermotherapy) is a type of cancer treatment in which body tissue is exposed to high temperatures (up to 113°F). Research has shown that high temperatures can be used to damage and kill cancer cells without damage to normal tissue [16]. Thermal therapy may shrink tumors by killing cancer cells and damaging proteins and structures within the cells [17]. Several methods of hyperthermia are currently under study, including local, regional, and whole-body hyperthermia. Recently, nanoparticles for local hyperthermal show tremendous promise in the safe and effective transducers for cancer therapy. Ji et al. [18] summarized carbon nanotubes as carriers for drug delivery and thermal therapies. Kennedy et al. [19] reviewed gold-nanoparticle-mediated thermal therapies. Kumar and Mohammad [20] reported magnetic nanomaterials for controlled drug delivery and hyperthermia-based therapy. Here, we highlighted three types of nanoparticles (carbon nanotubes, gold

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nanoparticles, and magnetic nanoparticles) for prostate cancer thermal therapy.

Carbon nanotubes (CNT) as a class of nanomaterials holds great potential for various biomedical applications including extrinsically activated hyperthermia for prostate cancer therapy. Fisher et al. [21] demonstrated the capability of multiwalled carbon nanotubes (MWNTs) coupled with laser irradiation to enhance treatment of Human prostate cancer. Ghosh et al. [22] reported DNA-encases multiwalled carbon nanotubes (MWNTs) were used to safely eradicate prostate cancer *in vivo* following NIR irradiation of MWNTs. Despite these promising results, the toxicity of carbon nanotubes has been an important question in nanotechnology. CNTs from manufactured and combustion sources in the environment could have adverse effects on human health [23]. From this issue, gold nanoparticles are especially appealing due to bioinertness and biocompatibility for biomedical use. For thermal therapy of prostate cancer, Stern et al. [24] used laser activated gold nanoshells for selective prostate cancer thermal ablation. Gobin et al. [25] demonstrated elective photo-thermal destruction of prostate cancer upon application of prostate-specific EphrinA1-conjugated gold nanoshells with the NIR laser irradiation. Normally, the size of gold nanoshells is more than 100 nm which is not suitable for *in vivo* application. Therefore, a gold nanorod is more attractive to researchers due to small size, easily surface function and with tunable plasmon resonance (SPR) in NIR region. As agents for prostate cancer therapy, Gormley et al. [26] evaluated gold nanorods conjugated with the cyclic RGD fK peptide for prostate cancer treatment. In addition, thermotherapy using magnetic nanoparticles represents another interesting area of magnetically mediated hyperthermia for prostate cancer treatment. Johannsen et al. [27] analyzed the effects of thermotherapy using magnetic nanoparticles combined with external radiation on prostate cancer and demonstrated this technique was feasible for prostate cancer treatment. Further, morbidity and quality of life were investigated during thermotherapy using magnetic nanoparticles in locally recurrent prostate cancer, the results showed interstitial heating using magnetic nanoparticles was feasible and well tolerated in patients [28]. These promising results show nanoparticles-mediated thermal therapy can be as a minimally invasive method for hyperthermia treatment of prostate cancer.

In this mini review, we collected some examples where nanoparticles were employed to induce localized heating for thermal therapy of prostate cancer. We hope that readers will find them beneficial to their works including molecular targeting.

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