



Nanotechnology in Urology- Is Small the New Big?

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Abstract

Nanotechnology, implying the engineering of miniscule molecules, of the sizes of 1 nm – 1000 nm, to effect macromolecular changes in various fields of human life, so as to bring about betterment in the quality of human lives, has garnered tremendous interest worldwide. Medical science has been the fore-runner in this regard and the field of Urology has embraced this technology with open arms. The current article highlights this very scenario, explicitly depicting the uses of nano-molecules as well as looks into what the future of this exciting technological advance can hold for us and whether they are really the way forward, so as to say: *Is Small really the new Big?*

Keywords: Nanotechnology; Nanomolecules; Medical science; Urology

What are Nanoparticles?

Nanoparticles, the DNA of the science of Nanomedicine are what the above stanza typically exemplifies. As miniscule as 1 nm – 1000 nm in dimension, with powers that still lay to be unearthed, these particles have laid the foundation for the very birth of the scientific discipline of nanotechnology [1]. So much interest have they generated, that the western world has been coaxed into adjudicating several millions of dollars from their corpuses, to harness these molecules and assess their widespread array of usefulness to the modern society [1,2]. K. Eric Drexler was the pioneer of the term “nanotechnology”, in the 19th century [2,3]. When Drexler first coined this term, it was meant to be for the world of physics, so as to popularize production of various machines, at a molecular scale. From such a humble beginning, this nanotechnological science has not only developed its own language, but also has its own stalwarts and specialists, dedicating their entire careers to the application of this technological advance for the betterment of human beings, in almost all fields of society.

Nanotechnology in Medical Science

Medical science too has readily embraced this technological advance and the field of Urology has been the fore-runner in this regard. The concepts of nanovectors and nanosensors for drug delivery and nanowires for early detection of pre-malignant lesions as well as nanopores for DNA sequencing are some of the applications that have grown from their infancy into maturing adolescents, as regards the domains of urology and uro-oncology [3].

Nanotechnology has found widespread applications in urology, ranging from diagnosis and treatment to even control and manipulations at the genomic level, so as to enable rooting out diseases from their very sites of origin.

Cancer, as rightly enunciated by Siddhartha Mukherjee, in his Pulitzer winning novel, “*The Emperor of all Maladies*” has been a thorn in the flesh of the entire medical fraternity and the urology community is no exception. Early and timely diagnosis as well as adequate assessment of the stage of the disease, and lymph node involvement is the main prognostic predictors for this “*disease*”. Imaging modalities such as Computerised Tomography (CT), Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET) and Single Photon Emission Tomography (SPECT) are important tools in the diagnosis, management as well as follow ups of human cancers. Herein, tumour targeted agents, based on nanotechnological formulations have been found to increase the accuracy of these imaging modalities.

In this context, Lymphotropic Nanoparticle-Enhanced MRI (LNMRI), which uses magnetic iron-oxide nanoparticles that are opsonised by the intra-nodal macrophages, are being used for detection of lymph node metastasis in Renal Cell Cancer (RCC), prostate cancer as well as retroperitoneal lymph node involvement in testicular cancer [4,5]. Statistical analysis has in fact proven a significant superiority (p<0.05) as regards the sensitivity and specificity of detection of lymph nodal metastasis with LNMRI, when compared with conventional MRI. Treatment decisions

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have been changed from radical (curative) to palliative intent as well as *vice-versa*, based on these reports.

Additionally, nanocolloids have been used for descriptive mapping of Sentinel Lymph Node Anatomy (SLN) after an intraprostatic injection of technetium-99 m nanocolloid using a fusion SPECT-CT imaging. To our surprise, not only was the yield of lymph nodes higher, but the very location of this lymph nodal stations were way different and even more extensive than the traditional description in literature. So, it would be safe to say that these nanoparticles have now begun challenging the very basis of our oncological treatment strategies and may lead to a better and broader understanding of disease spread pathways, thus heralding a new dawn in the era of cancer therapy. This nanotechnology also enables cytotoxic drug delivery to specific cancer cells, thus enhancing efficacy as well as minimizing deleterious effects to all other organ systems. An example of this is the *liposomal drug delivery* that has now bypassed phagocytosis by the cells of the reticuloendothelial system and is at present a pillar of strength for patients with metastatic prostate cancer [6,7]. Leuprorelin conjugated within liposomal microspheres is in widespread use as monthly or three-monthly injections for preventing the progression of metastatic prostate cancer. This liposomal-drug delivery mechanism makes use of minute differences in cancer neo-vasculature to increase drug concentrations at desired tumour sites. Now that this drug-delivery mechanism has become a standard of care, efforts are on to further enhance drug delivery with the help of photosensitisers, local hyperthermia and ultrasound guided activation. In prostate cancers refractory to all other treatment modalities, the thermotherapy approach may give us some more "food for thought".

Current treatment of non-muscle invasive bladder cancer comprises of trans-urethral resection of the bladder tumor followed by intra vesical instillation of chemotherapeutic (mitomycin C) and/or immunotherapeutic (BCG) agents. However, the response of this intravesical therapy is both variable and partial among different patients, mainly due to the inability of the drug to percolate the bladder tissue. Thus the role of drug-loaded nanocarriers to increase the treatment efficacy needs complete evaluation. 'Paclitaxel-loaded gelatine nano-particles' and 'Transferrin mediated liposomal targeting of bladder surface receptors' are newer concepts being evaluated to enhance this intravesical drug-delivery [8].

This nano-carrier drug delivery system has now spilled over to the benign and chronic urological diseases as well. Diseases such as the Chronic Pelvic Pain Syndrome (CPPS) as well as psychogenic or organic Erectile Dysfunction (ED) which were a thorn in the flesh of the urologists due to the lack of definitive management options are being evaluated for cure. Intraurethral application of liposomal tagged Prostaglandin E1 (PGE1) has found many takers, especially in cases of psychogenic ED [8,9]. Nanotechnology has also encroached the holy-domain of "Renal transplantation" with improved survival patterns of graft kidneys seen in animal models. Intravenous administration of liposomal encapsulated methylprednisolone, once weekly, was found to have a higher efficacy for renal allograft survival [10]. How this correlates with the human transplant scenario, still remains to be explored.

Nanotechnology-What Lies in the Future?

Looking ahead, into the *not so far* future, where would this nanotechnology in urology lead us?

Gene therapy, an upcoming sub-domain of nanotechnology,

is one such aspect, where diseases can be dealt with, so as to say, at their "*grassroot levels*". Gene vectors may help us ferry certain wanted matter into cells as well as extirpate unwanted material out of the cell, which in turn may help modify the inheritance patterns of various hereditary diseases. A few studies have shown safety and high efficacy, albeit in the short term, with long term validation still mandated. Tissue regeneration and engineering of urinary tract structures would probably be the "*Eureka*" of our century, similar to what was proclaimed by Archimedes decades ago. *In vitro* development of three dimensional, porous scaffoldings, to regenerate seeded human bladder smooth muscle cells are currently being attempted, with promising results. If successful, this would open up a new dimension for treating almost all diseases, in particular for patients with End Stage Renal Disease (ESRD), where tissue engineered kidneys would be expected to have significantly improved outcomes rather than the live or cadaveric donated ones.

Limitation/Reality Check

No technology, however good, would be without its own set of limitations. Worldwide concerns on the health and economic impact of nanotechnology, as perceived by the general population, must be adequately addressed by the stalwarts in this field of science, so as to enable the best "*risk: benefit*" ratio. Thus, nanomedicine is still in its budding stage, with researchers *at their wits-end* to make optimum use of this exciting resource, in a cost-effective and cost-efficient manner.

To Extrapolate

We are all aware of the need for new revelations in medical science and nanotechnology is definitely the way forward. As things have now scaled down to "bare minimum" sizes, and the adage "Small is in" is definitely IN. Looking from the perspective of a "prospective new car buyer", "mileage" or rather "cost effectiveness" is a definite concern than just the comfort or features, hence, the 2500\$, Indian "Tata Nano" does an equivocal job to any other sedan, and thus, to extrapolate, maybe "*Size does matter*" and "*Small is the new Big*".

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