Predicting The Future Of Urology – Looking Beyond The Horizon!

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Introduction : The only thing constant in life is "Change". One must constantly learn, unlearn and relearn in order to keep pace with advancements. The field of urology continues to make extraordinary advances in knowledge, skill, technology and healthcare delivery. Urologists have seen major changes during their lifetimes that have transformed the practice of urology in significant ways[1]. The introduction of ESWL and endourology, the advent of medical therapy for BPH and the introduction of serum PSA are a few examples that have revolutionized the way urology is practiced throughout the world. Laparoscopy is now becoming the standard of care and robotic surgery is making great inroads. Urology has truly become Minimally Invasive surgery!

Predicting the future is a difficult proposition. What can happen in future is one's imagination but what one can predict in near future is from a probability viewpoint. This article approaches the future of urology on the basis of the direction of the ongoing research.

Proteomics: Proteomics (the branch of genetics that studies the full set of proteins encoded by a genome) may be the most powerful way to uncover biomarkers of detection, prognosis and prediction as proteins represent the majority of diagnostic markers and drug targets today. In recent years, **mass spectrometry and** associated technologies have been explored to identify proteins or a set of proteins specific to a given disease, **for** the purpose of disease detection and diagnosis. Proteomics coupled with bioinformatic tools and nanotrap will pave the way for personalization of therapies tailored to each tumor's unique pathway activation network, in future[2].

Application Of Genomics: Current developments in genomics are showing a dramatic impact on the whole field of research. The human genome having been fully sequenced, it provides the 'book of life' as a basis for the understanding of human disease. New technologies have emerged to translate the human genome sequence into gene function and improved diagnostics or treatment modalities. DNA microarrays make it possible to analyze the mRNA expression of thousands of genes simultaneously. The resulting comprehensive gene expression surveys lead to the identification of new genes and pathways with importance in cancer development and progression, or as targets for new therapies. DNA microarrays and TMAs (Tissue microarrays) provide a powerful approach to identify large numbers of new candidate genes, and rapidly validate their clinical impact in large series of human tumours. These technologies will hopefully lead to a better molecular understanding of urologic tumours, and accelerate the identification of new prognostic markers or therapeutic targets[3].

Organ Engineering: Patients suffering from diseased or injured genitourinary organs are often treated with reconstructive surgery or transplants, but there is a severe shortage of donor tissue and organs. The aging population grows, and the need for organs grows with it. Physicians and scientists have begun to look to the fields of regenerative medicine and tissue engineering to provide new options for these patients[4].

Organ engineering is an area that is developing rapidly. Stem-cell biology is concerned with the understanding of which differentiation pathways are activated in embryonic cells, and with the manipulation of those pathways to produce differentiated cells. Autologous cells can be harvested from patients and grown in a laboratory culture. Laboratory techniques can be used to change the character of those cells. For example, by using a variety of transfection approaches, researchers can transform fibroblast cells into smooth muscle cells[1].

An example of how this might be applied in the future might involve a newborn with exstrophy of the bladder. In this case, stem cells could be isolated from the umbilical cord blood and coerced into differentiating into myoblasts. Those cells could be programmed to develop into a striated muscle phenotype expressing a growth factor that would not only allow the development of the striated sphincter, but also its innervation. Smooth muscle cells could be induced to mature and develop a so-called contractile phenotype and allow the in-growth of nerve cells. By using these approaches it is possible to grow these cells over an acellular tissue scaffolding, and by adding myoblast cells that would become a striated sphincter mechanism, develop an artificial bladder in vitro.[1]

Efforts in regenerative medicine are currently underway experimentally for virtually every type of tissue and organ in the human body. In urology, Urethra, Bladder, kidney and Genital tissues are at various stages of development. These engineered tissues may have an expanded clinical applicability in the future and may represent a viable therapeutic option for those who would benefit from the life-extending benefits of tissue replacement or repair[4].

Drug Delivery Systems: Advances in Material science are shaping the future of urological practice. Novel drug delivery approaches like Biodegradable Shape-Memory polymers, "Smart Gels", Targeted Nanoparticles and Miniaturized Drug Delivery Devices promise a bright future ahead.

The advent of biodegradable shape-memory polymers has ushered in a new era of unlimited endoscopic possibilities[5,6]. Biodegradable shape-memory polymers possess the ability to "memorize" a permanent shape that can differ substantially from their initial temporary shape. Thus, bulky devices can be introduced endoscopically in a compressed temporary shape (e.g., a "coil") that can then be expanded on demand into a permanent shape (e.g., a rod"). Additionally, these polymers can be engineered into sutures that possess the ability to tie themselves on demand as a result of a temperature shift (e.g., from room to body temperature). In urology, these Materials hold the promise for developing degradable drug-eluting stents[7] . Initially, at room temperature; a shape-memory stent could be delivered endoscopically in a compressed state. When the temperature increases to that of the human body (i.e., greater than the switching transition temperature of the polymer), the stent will expand into a coil.[5] Biodegradable stents obviate the need for repeat interventions for removal[8] and can serve as reservoirs of active agents (e.g., antibiotics, alkalizing agents), which can bulk the device and be released from the surface[9].

During the past two decades, hydrogels have been developed as "smart" carriers in controlled drug delivery systems[10]. Their physical and chemical properties have been engineered at the molecular level to optimize their properties, such as perme-ability (e.g., sustained release applications), environmentally responsive nature (e.g., pulsatile release applications), surface functionality (e.g., polyethylene glycol coatings for stealth release), biodegradability (e.g., bioresorbable applications), and surface biorecognition sites (e.g., targeted release and bioadhesion applications). Their release kinetics make them useful as "smart" Materials for diabetes applications, or, in the case of incontinence, these gels can in future provide "remote control" and ongoing readjustment of implants[9].

Microscale and nanoscale devices are attractive platforms for urologic therapies. Microscale approaches, such as microfluidics, microdevices, and micropatterning, provide a particularly useful method of delivering molecules to various tissues of the body[11,12] .These technologies, known as microelectromechanical systems (MEMSs), have been used in performing microsurgery and delivering drugs. Micropumps may be used in future for intrarenal and intraprostatic delivery of drugs[9].

Medical Management: Urology is going to see increasing use of medications for the treatment of various urological diseases which at present are being treated with surgery, namely bladder outflow obstruction, neurogenic vesical dysfunction, etc[13]. Future treatment for BPH may begin with an assessment of the baseline risk of progression of prostatic size, by using tissue genotyping and phenotyping using microarray technology. Alternatively, new imaging studies such as NMR spectroscopy or PET may be used to noninvasively `biopsy' the tissue. Intervention with therapy would be based purely upon that information and again would be highly individualized[1].

In urologic oncology, the treatment will shift towards oral outpatient selective chemotherapy. [13] Other medical therapies are likely to be developed in the coming years. These include truly effective angiogenesis inhibitors and anticancer immunotherapeutics that can be combined with cytotoxic agents for treating a variety of tumours, not just RCC. Kinase inhibitors and growth factor receptor antagonists will become popular as new forms of chemotherapy with organ-specific localization. Novel therapeutic agents will change the environment of e.g. tumour cells, limiting the ability of prostate cancer cells to interact with bone to cause skeletal metastasis. Chemotherapy may be combined with gene therapies, to reactivate apoptosis and combat drug resistance with future medical treatments[1].

Nanotechnology: Nanotechnology is the study, design, creation, synthesis, manipulation, and application of functional Materials, devices, and systems through control of matter at the nanometre scale.

Currently, the three main areas of integration of synthetic nanotechnology with potential availability to urologists are either for the delivery of pharmaceuticals, for tissue engineering, or as an adjunct to conventional imaging.

A number of important nanotechnology concepts include nanovectors, nanotubes, and nanosensors for targeted drug delivery; nanowires and nanocantilever arrays for early detection of precancerous and malignant lesions; and nanopores for DNA sequencing. These advances will lead to significant applications relevant to the diagnosis, management, and treatment of all urological conditions, allowing the urologists to intervene at the cellular and molecular level. The potential for nanosurgery in future urological practice is appealing. Nanotweezers could have a place in vasectomy reversal or varicocele repair, whereas ‘‘nano-urobots’’ or “nanobots” could have a place in cystoscopy, ureteroscopy, and fulguration of urological tumours. With structured, safe implementation, nanotechnologies have the potential to revolutionise urological practice in our lifetime.[14]

Minimally Invasive Surgery: The next area of excitement in the field of minimally invasive surgery is the implementation of computer-assisted enhancements in manual dexterity for use during both laparoscopic and open surgery. Currently, computer-enhancement techniques allow micrometre-level precision in the performance of operations. The marriage of this technology to three-dimensional imaging will allow the development of even more noninvasive techniques for treatment[1].

Technologies like 3-D video endoscopy, Virtual reality simulation, Telementoring and Image guided surgery will become commonplace in the near future[15]. The future of urology training is expected to undergo a sea change. The present model of learning on animals/patients will soon fade out. With the availability of advanced, high fidelity simulators simulating real life situation including tactile sensation and artificial bleeding; the residents will be able to learn basic skills in a low stress environment that can be later transferred to the operating room[16]. With the advancements in internet and robotic surgery, telementoring will make transatlantic surgery a reality. Medicine will be sans boundaries!

In a futuristic scenario, a 4-cm renal tumour is discovered in a patient. Without undergoing any additional studies, the patient is taken to the operating room for intraoperative MRI, the tumour is biopsied and a molecular phenotype of the tumour determined to guide decisions as to future treatment, e.g. the need for adjunctive chemotherapy. The tumour is then ablated percutaneously with real-time monitoring using three dimensional MRI. Further treatment, consisting of chemotherapy or immunotherapy, based purely upon the results of the molecular phenotyping, is administered after surgery[1].

Urobotics in the 21st century: Urology is among the medical fields with the highest rate of technological advancements, which include the use of medical robots. Urology Robotics, or URobotics, is a new interdisciplinary field for the application of robots in urology and for the development of such systems and novel technologies in this clinical discipline. Robotic devices to assist urologists with Laparoscopy, Percutaneous access to the kidney, T.U.R.P. and Prostate biopsy are currently in development or already in clinical use. Future robotic systems will be capable of replicating the tactile feel and sensation.

There will be a trend toward miniature devices, microbots and eventually nanobots. These microbots will be mobile, controlled remotely to desired locations and will give additional views (360^o) of the surgical field. They will also be capable of tissue retraction, lighting and supplementary visualization.[17]

Disease Susceptibility Testing: What will be the overall effect of these sorts of advances? One may be in the area of identifying and predicting susceptibility to disease. Physicians will be able to identify certain expression patterns in a patient's tissue sample. Once the susceptibility of an individual patient to a disease, e.g. diabetes or prostate cancer, can be identified it will be possible to tailor a screening programme for individual patients. This technology can help to select a preventative therapy for a targeted population and to consider environmental and dietary adjustments for underlying risk factors. In urology, specific potential applications of disease susceptibility testing include the prevention of recurrent stone disease, limitation of progression of BPH, and a variety of applications in the treatment or prevention of urological cancers. The susceptibility can be determined at different stages of life, allowing the timing and frequency of screening studies to be set to the optimal point of intervention for any particular disease.[1]

Predicting Treatment Response: Another application of these discovery efforts in the decades to come is likely to be the prediction of treatment response. Indeed, many people feel that histopathological analysis, as currently understood in terms of examining tissue under the microscope, will become an antiquated science. Applications of these new technologies will allow procedures where a biopsy specimen of e.g. tumour, is characterized by using microarray approaches. The variety of different genes and expression patterns in the cells will be identified. The different receptors involved in signaling pathways will be fingerprinted in a unique expression profile identified for an individual tumour. Bioinformatic approaches will then enable the determination of any specific patterns present in the tumour, and allow the therapy to be tailored for the individual patient.

A future visit to a physician might be imagined as follows: Mr. Sam presents with signs and symptoms of prostate cancer. He is found to have a fully differentiated tumour with invasion beyond the boundary of the prostate. His physician orders a microarray analysis after obtaining a biopsy sample, and hundreds of cell-signaling pathways and receptors are characterized. Then, by using a computerized bioinformatics database, his physician selects a specific type of therapy for him, based upon the gene expression pattern identified in his tissue sample. The patient's response to treatment can also be followed by using this technology, with necessary adjustments made to optimize this individualized treatment[1].

Conclusion: The future of Urology appears bright. Urology will transform into Non-invasive surgery from Minimally Invasive one and this will ultimately translate into better, safer and more comfortable treatment for our patients.

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