



White Rose HIP Health Technology Bulletins

The White Rose Health Innovation Partnership (WRHIP) aims to accelerate new health-related technologies by facilitating interactions between academia, industry and the NHS using an *open innovation* approach.

The new projects funded as part of this initiative are built upon a foundation of excellence in health innovation by the Partnership's members. This series of Health Technology Bulletins offer an introduction to this research excellence and cover a broad range of clinical and technology areas.

Each bulletin is written to give a general introduction to the topic area along with short case studies of clinical applications of new knowledge. Information is also presented on where to learn more about these new technologies and health challenges, and how to access the network of health innovation professionals established by the Partnership.



Opportunities for innovation in Urology

Urological problems are often a taboo subject for many as the symptoms associated with them can be highly embarrassing. Urology refers not just to urinary incontinence, but also to sensory and emptying abnormalities of the lower urinary tract, pelvic organ prolapse, anal incontinence, defaecatory dysfunction / constipation, sexual dysfunction and chronic pain. It is estimated that as many as 80% of the population will suffer from some sort of urological problem during their lives.

The symptoms of urological disorders are very diverse and difficult to interpret. They are not sex-specific or organ-specific, but they are often age related ^[1]; as an individual gets older, the greater the chances of them suffering from a urological problem. More than 20% of men over 75 have some sort of Lower Urinary Tract Symptom (LUTS), but in the same age group more than 45% of women will suffer from some sort of urological problem, most commonly urinary incontinence. The reason that women suffer more commonly from Urinary Incontinence is that their bladder control mechanisms are different to those of men. Worryingly, the prevalence of urological problems is likely to increase in the future due to the increasing levels of diabetes, obesity, hypertension and dyslipidaemia in the UK population.

There are three types of urinary incontinence

Stress Incontinence:

The complaint of involuntary leakage with effort, exertion, or on sneezing or coughing

Urgency Incontinence:

The complaint of involuntary leakage accompanied by or immediately preceded by urgency

Mixed symptom Incontinence:

The complaint of involuntary leakage associated with urgency and also with exertion, effort, sneezing, or coughing. 40% of all patients present with this.

Overactive bladder syndrome (OBS) is a major source of referral of patients to hospitals by their GPs. However, 20% of all patients referred are just found to be drinking too much. OBS is an empirical diagnosis used as the basis for initial patient management after assessing lower urinary tract symptoms, physical findings, urinalysis and other indicated evaluation. NICE (National Institute for Health and Clinical Excellence) recommend the use of frequency volume charts to help identify this syndrome in women ^[2]. Patient reporting is an important part of both the diagnostic process and treatment regimens with tools such as ePAQ (Electronic Personal Assessment Questionnaire) ^[3] now emerging to aid this. Tools such as this will also help in the future management of patients with urological

problems in a community setting, in-line with current UK healthcare policy. More information on ePAQ can be found in the WRHIP Technology Watch Bulletin "*Innovative Products as Drivers of Efficiency Improvements in the NHS*".

Urological problems are often highly debilitating long-term conditions and so as well as products for diagnostics and treatments, there are products which help people to live day-to-day with their conditions. There is the need for improved products in all these markets and this bulletin will highlight some of the areas where new products are being developed and where there are opportunities for new technologies to be incorporated into urology products.

New treatments in development

Surgery for treatment of urological disorders is becoming increasingly less common. In 1992, more than 1,000 prostectomies were carried out in Sheffield per year. With advances in technology and treatments this number has now dropped to 150 – 200 per year, despite a 3-fold increase in patient numbers. However, according to a number of clinicians, one of the biggest problems is that many new products for use in the treatment of urology are often developed without adequate trials being carried out in humans. This can result in poor product design and patients using poorly designed devices not benefiting from treatment regimes. The importance of proper trials and a good evidence base for new devices is therefore imperative for new products. Some of the new treatments which are in development for urological disorders are outlined below.

Botulinum toxin

Increasingly research evidence is showing that targeting the motor system for the development of new treatment regimens is probably not the most appropriate approach and that the sensory nervous system mechanisms should be considered more closely as targets [4]. Research has shown that within the bladder the urothelium (the bladder lining) has a metabolic rate 3x that of muscle and that stretching of the bladder (through filling) releases nerve transmitters which leads to a stimulation of sensory nerves, influencing bladder behaviour [5]. The use of botulinum toxin, which is a neurotoxic protein produced by the bacterium *Clostridium botulinum*, has real potential to revolutionise the treatment of bladder dysfunction without causing retention. Injections of small amounts of Botox have been shown to have positive effects for 6-9 months post-injection as Botox causes the blockage of the release of the neurotransmitter which causes the bladder muscles to contract [6]. This is the first example of the bladder innervation being directly targeted for treatment of urological disorders and it is likely that further targets will emerge. It must however be emphasised that this therapy is still undergoing detailed evaluation and is not yet approved for clinical use for this indication by the MHRA.

Robot-assisted surgery

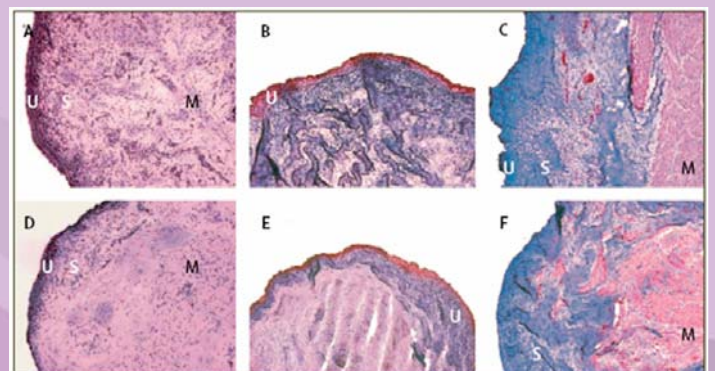
Robot-assisted surgery is becoming more common in the USA, especially for urological procedures. However, the technology is still too expensive for wide scale adoption in the UK, although it will eventually be brought in if the cost comes down and the technology has been developed further. Many see robot-assisted surgery as being very trendy but it is in an early stage of its clinical application and the cost benefits are not proven. Its use still also depends very much on the skill level of the operator. However, robot-assisted surgery may offer potential advantages such as increased dexterity (allowing use of traditional surgical techniques within a minimally invasive environment), more precise movement for complex tasks, advanced viewing capabilities and reduced surgeon fatigue and strain due to ergonomic control stations and potentially less serious side effects of the surgery [7], [8].

Stem-cell therapy

Like robot-assisted surgery, stem-cell therapeutics may offer potential advantages and some initial studies have been carried out in humans to treat female stress incontinence. Stem cells were isolated from the biceps of patients and cultured into myoblasts which were then injected into the urethral wall and the bladder sphincter [9]. The published results of the study showed that 18/20 patients were "cured" 12 months following the procedure. However, debate surrounds how well these studies were carried out as a number of the patients treated both as part of the trial and outside the study, have reported severe side effects, including sealing of the urinary sphincter and ruptured bladders [10]. However, research into stem-cell therapies for urological disorders is continuing.

Tissue Engineering

Tissue Engineering is an area which offers great hope in many areas of medicine. In Urology, tissue-engineered autologous bladders for patients needing cystoplasty were the subject of 16 years of laboratory research before the first clinical study could be undertaken [11]. The implanted engineered bladders showed both muscle and endothelium in histological studies, but only 3 of the patients involved in the studies did well in the short-term follow-up. However, the fact that the first clinical studies have been carried out suggests that this area may have promise in the future and that tissue engineered bladders could be used in patients, although there is a long way to go. Tissue engineering of the urethra is one of the areas of research currently underway in Sheffield.



Morphological analysis of implanted engineered bladders [8] A, B and C show the presence of phenotypically normal urothelium and smooth muscle D, E and F show the presence of native bladder tissue

Opportunities for new technologies

Within the areas of diagnostics, treatments and long-term care products, there are significant opportunities in Urology for a range of existing technologies, especially in the areas of IT, Microelectronics and Nanotechnology. Nanotechnology has been steadily emerging for the last 50 years in a number of areas including designer molecules (pharmaceuticals), smart surfaces (materials science) and integrated electronics. Combining these technological developments with developments in surgical treatments should allow better treatment and management of these conditions. Some examples of what might be possible are suggested in this bulletin.

Diagnostics:

Dipstick test

The miniaturisation and decreased costs of electronic components has vastly improved the availability and accuracy of diagnostics. Real-life, real-time diagnostics now exist and therefore it should be possible to produce an ambulatory diagnostic for bladders. However, whilst the electronics exist for this, the sensors needed for such an in vivo diagnostic are very difficult to make. Such sensors need to be disposable, cheap, robust, very small and bio-compatible. The development of such devices would allow bladder functions to be measured much more accurately and rapidly than they can be currently and such sensors could also be used in other diagnostic applications. They would also contribute to improved patient outcomes since the quality of diagnosis would improve over the current paper-based urology diaries that patients self complete.

Capsule Endoscopy

Capsule Endoscopy is an existing diagnostic procedure which involves a patient swallowing a small "pill" containing a colour camera, battery, light source and transmitter. The camera within the pill takes two pictures per second for 8 hours and transmits the data to a data recorder worn by the patient. The capsule moves through the digestive system of the patient naturally and is used to diagnose gastrointestinal tract problems. However, technology advances could allow a much smaller "pill" to be developed (<2mm in diameter) containing sensors for pressure, flow rate, pH and a camera which could be used to view the urinary tract better than current imaging technologies allow, reducing the risk and discomfort to patients.

Treatments:

Functional Electrical Stimulation (FES)

FES is where electrical impulses are used to activate nerves and control muscle function. For use in urology, FES devices have to be implanted, but more robust and biochemically stable electrodes are required. The technique is well accepted clinically and devices are rapidly evolving through miniaturisation, the employment of better materials and an increased understanding of bladder function. Coupled with advances in diagnostic technology, better targets for stimulation should be identified along with information on what stimulus is needed for these targets.

Stents

Stents currently used in urology to bypass obstructions in the urinary tract are associated with very high levels of chronic infection. Advances have been made recently in the cardiovascular area with stents made of polymers and biocompatible materials. Technologies such as these could be used in urology and if such stents could also be seeded with a patient's own cells, the structures could be incorporated into the body.

Long-term care products:

Adhesives

Good adhesives for urology products are essential so that highly sensitive skin is not damaged. However, adhesives for use on long-term care products must also grab instantly to form a seal, withstand high hydraulic pressures and immediately peel off when required and only when required without leaving any residue. Adhesive failures are very common and a real problem and some people still paint liquid latex onto themselves. Given the advances in materials science could it be possible to develop an adhesive which relies on the structure of the skin for sticking, a sort of "molecular Velcro"? Such an adhesive would potentially allow devices to stay in place for much longer.

Absorbent Products

For all the drawbacks associated with the current range of absorbent products, they remain one of the main products used by incontinence sufferers. Modern pads rely on super-absorbent polymers to hold urine, and they are capable of holding quite large volumes of liquid. Once used, pads are simply thrown away and taken to landfill. However, many modern super-absorbent polymers can be very easily regenerated so perhaps the next generation of pads could be designed to be "green" recyclable products which are not thrown away post use. However, modern super-absorbent polymers don't have to be granular – they are highly malleable and so can be any shape / form. Elutable compounds could also be incorporated into these polymers which are gradually released as they absorb liquid.



Urinary Tract X-ray showing the Kidneys, Bladder and the Uterers which connect them.

Founding partners in the Programme include:

University of Leeds
University of Sheffield
University of York
University of Bradford
Medipex
Medilink Yorkshire & the Humber
The Leeds Teaching Hospitals NHS Trust
Sheffield Teaching Hospitals NHS Foundation Trust
Bradford Teaching Hospitals NHS Foundation Trust
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International ARI Institute, University of Toledo, Ohio
Polymer Centre for Industrial Collaboration
Biomaterials and Tissue Engineering Centre for Industrial Collaboration
Pharmaceutical Innovation Centre for Industrial Collaboration
Wireless Technologies Centre for Industrial Collaboration
Particles Centre for Industrial Collaboration

Regional Centres of Expertise

This technology watch bulletin has been informed by a Urology "Open Innovation" workshop which took place in Sheffield in November 2008 and this bulletin has been informed by presentations given at that event. Sheffield is one of the UK's leading centres for Urology research, with an internationally-renowned research group based in Sheffield Teaching Hospitals NHS Foundation Trust. The group at Sheffield is part of the "Devices for Dignity" Health Technology Co-operative (HTC) (for more information see <http://www.devicesfordignity.org.uk>). Urology research in the UK is highly collaborative with speciality practice nurses, physiotherapists and consultants all collaborating with technologists to further the field. Other UK centres include Bristol, Newcastle and Manchester and this "open-innovation" style approach is very different from how research is carried out in mainland Europe. A number of charitable organisations such as Disabled Living and the Bladder and Bowel Foundation also exist to support both patients and the development of new products.

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