

# Advances in Ureteral Stent Design

John D. Denstedt

*Division of Urology, Department of Surgery, Schulich School of Medicine and Dentistry,  
The University of Western Ontario, London, Ontario, CANADA*

**Abstract.** Ureteral stents are commonly used in urolithiasis patients for relief of obstruction or in association with stone treatments such as ureteroscopy and extracorporeal shock wave lithotripsy. There are currently many different bulk materials and coatings available for the manufacture of ureteral stents, however the ideal material has yet to be discovered. All potential biomaterials must undergo rigorous physical and biocompatibility testing before commercialization and use in humans. Despite significant advances in basic science research involving biocompatibility issues and biofilm formation, infection and encrustation remain associated with the use of biomaterials in the urinary tract. There have been many significant advances in the design of ureteral stents in recent years and these will be highlighted along with a discussion of future aspects of biomaterials and use of stents in association with urolithiasis.

**Keywords:** ureteral stents, biocompatible materials  
**PACS:** 01.30.Cc; 81.05.Zx

## INTRODUCTION

Ureteral stents have become an important part of contemporary urologic practice since Finney [1] and Hepperlen [2] and colleagues first described the double-J stent and single-pigtail stent [3], respectively. Since that time, there have been many advances in design that have been directed at improving biocompatibility and reducing stent related morbidity. Ureteral stents are very commonly placed in patients with urolithiasis, either to relieve obstruction or in association with interventions, such as extracorporeal shock wave lithotripsy, ureteroscopy or percutaneous surgery. Although significant advances in basic science research involving biocompatibility issues and biofilm formation have been achieved, infection and encrustation remain problems associated with stents in the urinary tract and therefore limit their long-term use. In recent years, different raw biomaterials have made the transition from laboratory research to widespread use in the clinical realm. However, despite ongoing intensive basic science and clinical research, the ideal biomaterial is yet to be discovered. Nonetheless, there have been many significant advances in the design of ureteral stents, and these will be highlighted along with a discussion of the future of biomaterials in the urinary tract.

CP900, *Renal Stone Disease, 1<sup>st</sup> Annual International Urolithiasis Research Symposium*,  
edited by A. P. Evan, J. E. Lingeman, and J. C. Williams, Jr.  
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## **STENT BIOMATERIALS AND COATINGS: WHAT IS AVAILABLE?**

The biomaterials currently placed in the urinary tract are most commonly composed of synthetic polymeric compounds including polyurethane, silicone and other proprietary combinations of “plastic” materials. Silicone, composed of alternating silicone and oxygen atoms, is the current gold standard with respect to tissue compatibility owing to its nontoxic and inert nature [4]. Silitek is a proprietary silicone-based block copolymer. C-Flex is a proprietary silicone-modified styrene/ethylene/butylenes block copolymer and percutflex is a proprietary olefinic block copolymer. Each of these biomaterials has been used widely and successfully in the urinary tract whether it be in the form of urethral catheters or ureteral stents. Hydrogels are the coating most commonly used for urinary tract devices at present. Hydrogels are composed of a hydrophilic polymer that allows water to be trapped in the chemical structure. This reduces the coefficient of friction of the material, which improves biocompatibility by reducing frictional irritation and cell adhesion at the biomaterial— tissue interface. Furthermore there is some evidence that hydrogel coatings result in a reduction of encrustation [5].

## **STENT BIOMATERIALS: WHAT IS NEW?**

Recently, there have been a number of interesting publications assessing new urinary tract biomaterials and coatings. One material that was tested in an study by Laaksovirta and associates [6] is a self-reinforced L-lactide-glycolic acid copolymer, molar ratio 80:20 (80% L-lactide and 20% glycolic acid). In a chronic rabbit implantation model, the authors tested the biocompatibility of this material both in muscle tissue and in the urinary tract. Urethral stents of self-reinforced L-lactide-glycolic acid copolymer or steel were inserted via cystoscopy into the rabbit prostatic urethra and removed as much as 3 months later. The copolymer stents were soft and had been almost completely degraded at 3 months. The material did not encroach into the urethral wall and there was no encrustation.

In another recent study, Nitinol was evaluated as a urinary stent material in an animal model [7]. Nitinol is a nickel-titanium alloy that has gained widespread use for many disposable devices for urology, including guidewires, stone graspers, and stone baskets. In an in vivo canine model, a novel application was evaluated in the form of a polyurethane-covered retrievable, expandable urethral Nitinol stent. Unfortunately, the study was complicated by stent migration, failed stent removal, and accumulation of granulation tissue at both ends of the stent, leading the authors to conclude that some design modifications were necessary.

Bioabsorbable or dissolvable biomaterials have recently been developed for ureteral drainage stents to eliminate the need for cystoscopic removal. Moreover, such a biodegradable stent would shorten the period of suffering for the patient and possibly eliminate the problem of forgotten or neglected stents. To this end, Olweny and colleagues [8] evaluated the use of poly-L-lactide-co-glycolide (PLGA) bioabsorbable

ureteral stent following Acucise (Applied Medical Resources, Rancho Santa Margarita, CA) balloon incision endopyelotomy in a porcine model. This self-reinforced stent was similar to a standard ureteral stent with respect to fluid flow results and postoperative appearance on retrograde pyelography. However, the PLGA stent was found to have less favorable biocompatibility than a standard stent, as indicated by inferior healing of the ureteral musculature.

The development of tissue-engineered stents is in its infancy, but this area has the potential to revolutionize biomaterial science and clinical applications of biomaterials. The use of autologous tissue would be advantageous because of its inherent biocompatibility. Using a novel approach in a very interesting study, Amiel and colleagues [9] investigated the feasibility of stents created from chondrocytes using *in vitro* and *in vivo* models. Remarkably, they were successful in creating cartilaginous stents *in vitro* and *in vivo* using chondrocyte-seeded polymer matrices. They proposed that this technology might one day become clinically useful in the treatment of urethral or ureteral strictures.

## STENT COATINGS: WHAT IS NEW?

The goals of coating ureteral stents are to facilitate passage over a guidewire beyond an obstruction (i.e., to decrease friction) and to reduce, or eliminate biofilm formation and encrustation. To this end, Tunney and colleagues [10] reported on a new hydrophilic coating, polyvinylpyrrolidone, applied to polyurethane. In an *in vitro* model, the coating resulted in a decrease in both hydroxyapatite encrustation and adherence of a hydrophobic *Enterococcus faecalis* isolate. On the basis of these results, the authors concluded that coatings of polyvinylpyrrolidone might prevent bacterial biofilm formation and encrustation on biomaterials in the urinary tract and therefore warrant further evaluation.

Another coating that has potential for reducing encrustation is the phosphorylcholine group of compounds. In a recent human clinical trial, uncoated and phosphorylcholine-coated ureteral stents were examined by scanning electron microscopy 12 weeks after implantation. The phosphorylcholine-coated stents were less vulnerable to encrustation and colonization by bacterial biofilm than were the uncoated stents [11].

A novel approach to reducing biomaterial-related urinary tract encrustation involves coating biomaterials with oxalate-degrading enzymes derived from *Oxalobacter formigenes*. This anaerobic bacterium is capable of degrading oxalate through its production of several enzymes including oxalyl coenzyme A decarboxylase (OXC) and formyl coenzyme A transferase (FRC). Watterson and coworkers demonstrated incubation-based coating of OXY and FRC on silicone disks. In an *in vivo* rabbit bladder implantation model, they found a reduction in the amount of encrustation on the enzyme-coated disks versus control disks after a 30-day implantation [12].

In another recent publication, Multanen and associates, [13] assessed the biocompatibility, encrustation and biodegradation properties of silver nitrate and ofloxacin-blended caprolactone-L-lactide copolymer-coated self-reinforced poly-L-

lactic acid (SR-PLLA) urospiral urethral stents in a rabbit model. The silver nitrate and ofloxacin-blended copolymer-coated urospiral stents had good biocompatibility properties and caused less tissue reaction than stents with a pure copolymer coating. Furthermore, the silver nitrate coating was effective in preventing biofilm formation and stent encrustation.

## **RECENT ADVANCES IN STENT DESIGN**

Changes in ureteral stent design have been aimed at reducing the morbidity, namely discomfort, bladder irritability, migration, infection, encrustation, and the need for an additional cystoscopic procedure to remove the stent. There are many novel stent designs that have been introduced over the past few years, each of which is discussed below.

### **Mesh Stents**

One effort to preserve drainage while minimizing irritative symptoms was the development of a lightweight, self-expanding mesh stent. In an established porcine animal model, Olweny and coworkers [14] compared tissue reaction and flow characteristics of a mesh stent with those of a standard 7F double-pigtail polyurethane stent. Although the difference was not statistically significant, the mesh stent tended to result in less inflammation along the urinary tract at 1 week. Furthermore, the flow rate through the mesh stent tended to be greater than that through the standard stent at both 1 and 6 weeks.

The flow characteristics of the mesh stent were compared with those of other stents in a separate porcine animal study. The greatest flow was seen with the mesh stent.

### **Tail Stents**

Attempts to decrease ureteral stent-related bladder irritability have led to the development of a specialty device known as the Tail Stent (Microvasive Urology/Boston Scientific). This stent has a 7F proximal pigtail and a shaft that tapers to a lumenless straight 3F distal tail that resides in the bladder. To date, this stent has been assessed in two randomized clinical studies. The first was a single-blind trial in 60 patients, in which Tail Stents produced significantly fewer irritative voiding symptoms than standard 7F double-pigtail stents [15]. The second study assessed outcomes following percutaneous nephrolithotomy in 40 patients, comparing a Tail Stent with a 18F Councill nephrostomy tube for postoperative drainage versus a 24F re-entry Malecot nephrostomy tube [16]. The results were favorable for the group with the Tail Stents, as marked by a statistically significant reduction in postoperative flank pain.

## Dual-durometer Stents

There is some evidence that ureteral stents that are composed of softer biomaterials are better tolerated than harder stents [17]. However, softer stents have a weaker renal coil strength and are therefore more likely to migrate and also are more difficult to push past an obstructing stone. Attempts at addressing these issues, namely, to facilitate stent placement, reduce migration, and minimize patient discomfort, have led to the development of dual-durometer stents. These stents incorporate a smooth transition from a firm biomaterial at the renal end to a soft biomaterial at the bladder end. Two such devices are the Sof-Curl (ACMI) and the Polaris (Microvasive Urology/Boston Scientific) stents, which have long tapered tips at the renal end and are coated with a hydrophilic-bonded hydrogel that decreases their coefficients of friction [18]. Their firm proximal end and hydrophilic coating allow for ease of access through the ureteral orifice and facilitate negotiation past obstruction, and the soft distal end results in decreased patient discomfort. In a study comparing six ureteral stents, the Polaris was shown to have superior lubricity (which eases stent passage) and lower flexural strength (which minimizes bladder discomfort). Unfortunately, not all contemporary hydrophilic-coated stents were assessed in this study.

## FUTURE OF URETERAL STENTING

### Drug-coated and drug-eluting stents

It is very likely that a variety of pharmacologically active agents will be incorporated into ureteral stents, similar to the stents in final testing stages for treating diseased coronary arteries [19]. These drugs could be applied directly to the polymeric surface of the biomaterial (surface coating) and be pharmacologically active at the surface, preventing infection or encrustation. Alternatively, drugs could be incorporated into the core of the polymeric structure of the biomaterial, being delivered into the local environment in a sustained-release fashion (drug-eluting) and consequently have potential activity at the level of the urothelium.

An interesting approach to achieving controlled release of a drug in the ureter has been reported recently [20]. In this study, large multilamellar liposomes that entrapped dexamethasone were prepared, and in an *in vitro* setting, 51% of the drug was released from the biomaterial in artificial urine over a 48-hour period. Although early in their development, techniques such as this one hold promise for controlled release of drugs from ureteral stents into the local urinary environment.

## CONCLUSION

Ureteral stents will continue to be an essential tool in the practicing urologist's armamentarium. Ongoing research is essential to optimize biocompatibility and decrease stent-related complications such as pain, bladder irritability, infection, and encrustation within the urinary tract. There has been great interest in this field of

research, as marked by the introduction of new biomaterials, coatings and ureteral stent designs. The future of biomaterial research is promising with continued insights into biomaterial science, further improvements in clinically available ureteral stents and a significant reduction in stent-related morbidity.

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