Urological Materials and Devices

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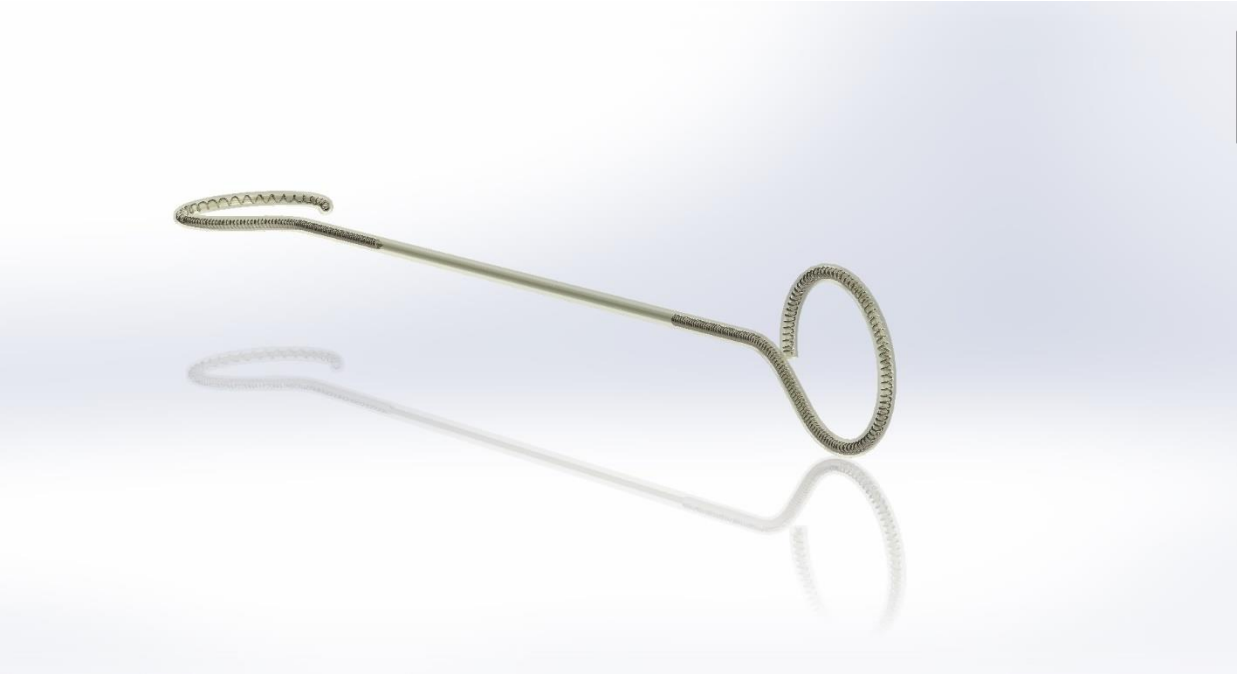
Ureteral Stent and Urethral catheter test methods, how they apply to the state of the art, innovation, end user need and (FDA) approval requirements



When asked, "*What kind of test media would you say urinary devices are tested in"* you would think everyone would respond: **Urine**. However according to ASTM 1828-97 (Standard Specification for Ureteral Stents), test media requirements indicate distilled water **or** artificial urine which corresponds to the FDA device approval guidance document. Think about that, not even saline was suggested; so, market leaders essentially tested their devices in the most benign media: distilled water. That understood, it would seem no one cared to take notice that while establishing equivalence to predicate devices for FDA "approval" embracing the nearly 30-year-old test method, the predominant complication of pain, discomfort and encrustation wasn't being addressed. Essentially "they" continued to make and sell the same thing. And without evidence to the contrary, the same stent without testing in urine was Grandfathered into acceptance for long term use (1 year) while short term implants (< 30 days) typically exhibited complications of about 40%. And while bio-compatibility testing is conducted, these tests make no attempt to characterize stent and catheter materials or address biofilms, the platform for infections and encrustation, which certainly is one cause of urinary catheter and stent complications.

ASTM Ureteral Stent test method F1828 and FDA guidance documents focus on flow, anchorage, radiopacity and tensile strength; all certainly important. However, there is **no acceptance criteria** for any result, only an effort to establish equivalence to approved devices where the basis of acceptance has been based on recommendations once proposed as a starting point in 1989. For example, when considering flow, the ureteral stent test method references urethral catheter flow test methods, which isn't representative. That is to say, the model doesn't differentiate between annular flow and luminal flow; an important differentiation when looking at ureteral stent flow. That understood, the ureteral stent lumen is not necessarily the path of least resistance although it might be constrained circumferentially, testing according to ASTMF1828 indicates some stents exhibit an unnecessary luminal flow rates of 35 L / 24 hours.

Similarly, there is vague understanding regarding anchorage profile design as it relates to flow, migration and comfort when testing according to ASTM F1828. For example, a conventional thermoplastic pigtail anchorage profile is essentially unwinding and winding with changes in axial load not always fully in the kidney. And perhaps more important, testing that profile doesn't consider the placement of the loop in a kidney model nor has there been a focus on the conditioning of samples which should be submerged in human urine at body temperature for an extended period of time. To that end, addressing claims that conventional stents soften when implanted should be limited because in time the same mechanisms that contribute to softening of conventional thermoplastic ureteral stents also begin the oxidation of the stent polymer which eventually results in a cleaved polymer architecture exhibiting rigid characteristics providing a platform for encrustation and patient discomfort. However no matter how soft a thermoplastic stent is claimed to be it still isn't as flexible as the ureter, no matter how much it softens, key characteristics not at all taken into consideration within the scope of approval.

Not adequately represented by testing	**Ureteral stent test method input process**
Migration / anchorage Dynamic vs static, the effect on peristalsis, lubricity and flexibility	**1989** Dr Mardis paper outlining requirements
Flow Annular / luminal, regarding fixturing of anchorage profile	**1990** Dr Mardis proposal to AUA
Lubricity Hydrophilic coatings performance, inner and outside surfaces	**1990** Goldberg / Mardis ASTM proposal
End user need Comfort, quality of life	**1991** Goldberg Surgitek to COOK
Reduced health care cost	**1993 Mardis / Journal Endourology**
Embrittlement / fracture	**05/1993** roster (industry and FDA)
Encrustation / Bio-film	**07/1996** Bard to Goldberg
Occlusion / annular / luminal flow	**2009** Atala / Denstedt / Biomaterials and tissue engineering in urology CRC Press
Test media	**04/2010** Epstein / Meilkerson / FDA
Hydrophilic coatings	
Bladder anchorage	**06/2010** Epstein / ASTM
Guidewire, lumen OD	
Push-ability delivery	**2017 issuance ASTM1828-17**

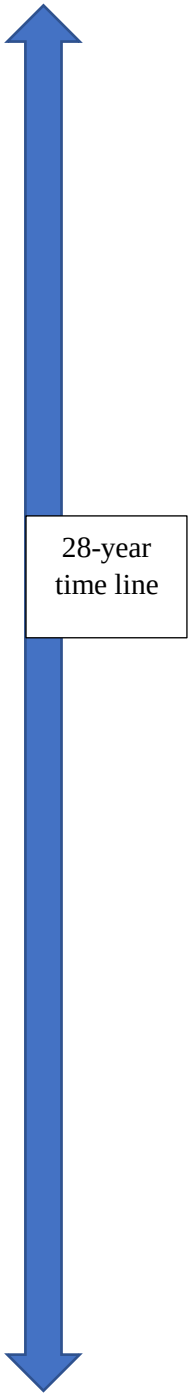


Table 1.0

Brief history of stent approval process and corresponding evolution of test method

So, what's new, what will it take to increase patient comfort, what are the band aides, what hasn't worked, what is leveraged technology and what are the new standards that will embrace real changes leading towards test methods and standards that address the real need?

First: include updated ASTM Ureteral Stent Test Method **F1828-17** mandatory information. For example, requirements for characterization of human urine and statements that di-water or saline as a test media does not contain the chemical composition associated with the degradation of stent materials that is contained in human urine. Additionally, artificial urines are not consistent in pH and other characteristics and thus not an optimal test media unless a urinalysis accompanies report. **Accordingly, test media especially for long term implants should be human urine** and devise should be labeled accordingly.

Second: acknowledge emphasis on quality of life and the corresponding decrease in healthcare costs using a better stent. This objective would have an immediate impact, decreasing expensive ER visits, follow up secondary expense and impact due to remove and replacing stents. And while the primary objective of the ureteral stent market is addressing pain and discomfort, addressing encrustation will establish a platform suggesting decreased UTI's are linked to decreased bio-film. Leveraging this performance for urethral catheters based on same / similar technology will bring into focus that new materials, not reworked legacy technologies and coating are what is really necessary.

Third: Focus on **better testing of stents and catheters comprised of better materials** that will exhibit better results. The corresponding cost savings, especially in long term and chronic care applications, will be realized immediately making current technologies obsolete. For example, coating, whether lubricous or bio-chemical exhibit varying results only maintaining the status quos use of current materials and process. Accordingly, it is time to agree that materials used to date just are not adequate.

Fourth: Look back at all ureteral stents and urethral catheters on the market and label based on their exhibited complication rates. Otherwise enforce a standard providing acceptance criteria associated with the FDA guidance document regarding device performance, patient quality of life and decreased healthcare cost.

Complication Rate Clinical Expense / ER Treatment / Replacement Cost / Morbidly	
Urethral catheter	**Ureteral stent**
Reduce complication rates	**Reduce complication rates**
As tested and approved using water as a test media label for no more than 7 days use	**As tested and approved using water as a test media label for no more than 7 days use**
Tested in human urine, maintain current labeling	**Tested in human urine, maintain current labeling**
	Focus on (>40%) complication rate (< 30 day) use and label with warning accordingly

Table 2.0

As patient quality of life increases health care cost decreases

Urethral catheter

ASTM F623-99 (2006) focuses on device size, balloon design and performance related to anchorage (pull out force). Addressing general conventional requirements and while revision is underway, it focuses on **flow rate and anchorage withdrawal load acceptance criteria, unlike the ureteral stent test method which provides no specifications**. However, ASTMF623-99 also **does not recommend human urine** as test media which perhaps for short term applications is less critical, but then should perhaps indicate exclusion for long term indwelling usage (> 7 days). That is to say like predicate ureteral stents, relabeling of urethral catheters currently in use not subjected to appropriate testing might greatly benefit the end user if warnings were properly identified. And those warning in the absence of appropriate testing, new materials and novel designs that exhibit acceptable results could indicate "**not tested in urine**" and/or "**not for long term use (> 7 days)"**.

Summary:

In 1989 Dr Madris proposed, presented and ultimately championed a Test Method that was adopted by the FDA for Ureteral Stent approval. However, almost 30 years later the same level of focus in an effort to establish technology, acceptance criteria and test methods will support the development of new and innovative devices. Otherwise the leveraging of legacy technology, with a focus on equivalence, will continue be the strategy of risk adverse market leaders that occupy majority market share with little incentive to change. In addressing those changes, test methods need to be flexible with forethought as not to restrict innovations. Only then can true benefits lead to real changes that improve quality of life and reduce healthcare costs.

Footnote

Q Urological (FDA approved) Persistent Aguamedicina structural hydrogel ureteral stent and catheter technology are tested in human urine, have been incubated in various bacterium and tested accordingly. This highly aqueous bio-material is soft, flexible and unlike any thermoplastic catheter or stent appears to according to early results **not exhibit biofilm** and or encrustation after various duration implant time.