The In-Flow™ Intraurethral Valve-Pump

29 March 2011
How do you get urine out of the bladder without causing infection?

- 100,000,000 urinary catheters are used globally every year, but they cause infections that kill tens of thousands and cost €billions in medical care.

The In-Flow has been shown to have the lowest infection rate by far of any indwelling device for bladder drainage.

- Active stent-like device replaces passive urinary catheters.

The In-Flow is also the most discrete and dignified solution for female bladder drainage.

- Significantly improves quality of life.
Replaceable urinary prosthesis intended to normalize toileting in women with atonic bladder or other voiding dysfunction resulting in an inability to fully empty the bladder

- A prosthetic device compensates for a specific physiologic deficiency
- The In-Flow compensates for the lack of bladder pressure in women with atonic bladder by providing forceful, virtually complete evacuation of urine on demand
Design and Materials

Female-only Intraurethral Device

- Miniature valve-pump mechanism entirely housed in medical-grade silicone
  - Supplied sterile, 29 day use
  - Sized to length of patient’s urethra (9 lengths)
  - Flexible bladder fixation - simple and safe removal

- Magnetic remote-control (“Activator”)
  - Spins internal magnet at 10,000 RPM, creating turbine pump
  - Engages valve automatically when pump is not in use to maintain continence
Principles of Operation - Insertion

- Device is inserted using disposable introducer
- Flexible silicone “fins” hold it in place
Principles of Operation - Voiding

- Patient normally **sits on a toilet**
- Patient / caregiver presses the button
- Pump is activated and provides **normal flow**, quickly draining the bladder
- Releasing the button automatically engages the valve, stopping further flow
Target Patient Population

- Women with atonic bladder
  - Lack bladder pressure - cannot spontaneously urinate
  - Typically due to neurologic injury or disease (MS, stroke, SCI, diabetic neuropathies, etc.)

- Incurable condition with very limited treatment options
  - Typically requires life-long use of urinary catheters

*The inability to void is one of life’s most discouraging circumstances*
Present Clinical Alternatives

- Urinary catheters may be the simplest and most commonly used medical devices, but they cause serious problems, notably:
  - Low quality of life, and
  - High rates of urinary tract infection (UTI)

- Problems amplified with atonic bladder - must use catheters for life
  - New treatments exist for neurogenic OAB (overactive bladder), but not for atonic (underactive) bladder

- Two types of urinary catheters are most often used for women
  - Intermittent catheters
  - Indwelling (Foley) catheters
Clean Intermittent Catheterization (CIC)

- Current standard of care for long term bladder drainage
  - Known to have substantially lower clinical UTI rate than indwelling (Foley) catheters

- Patient inserts a tube into her urethra 4-8 times per day for voiding

- However, many cannot reliably self-catheterize
  - Lack necessary manual, visual or cognitive ability
    - Particularly true of many women with atonic bladder due to serious nature of their primary medical condition

- Others simply will not perform this procedure
  - Find repeated touching of genital area distressing
    - Elderly women in particular often opt for Foleys despite well understood problems
Indwelling (Foley) Catheters

- Held in place via a water-filled balloon in the bladder
- Typically connected to a urine collection bag
- Medically demanding
  - 5% risk of UTI per day (virtually 100% in 30 days)
  - 50% encrustation, routine skin/tissue problems
Psychologically challenging

- Literally tied to a bag of your own urine
- Many patients consider this an end-stage development
  - Correctly or not
Based on clinical evidence to date, In-Flow compares favorably to both CIC and indwelling (Foley) catheters

- Compared to CIC, improves quality of life with similar safety and effectiveness
- Compared to Foley catheters, improves quality of life with vastly superior safety

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Six clinical studies (total $n=510$), including two long-term studies

Extensive laboratory testing, including independently conducted encrustation study

12 years of patient use in Germany, Canada and Australia
IDE Study Design

- 18-site study (n=273) to compare safety, effectiveness and patient satisfaction of the In-Flow device versus clean intermittent catheterization (CIC)
  - CIC is current standard of care for long-term bladder drainage
  - Study limited to women with atonic bladder who were already using CIC
  - Single-arm crossover design in which each subject acted as her own control

- Relevant clinical endpoints were selected
  - Primary endpoint of PVR objectively indicates how effectively each device drains bladder
    - Required excluding subjects using indwelling (Foley) catheters
  - Secondary endpoint of QoL indicates effects of using these highly personal devices
    - Wagner I-QOL most appropriate instrument available at time of study

- All aspects of study independently monitored
IDE Study Results

- All clinical endpoints were met

1. Primary Endpoint: Post-void residuals (PVRs) - CIC and the In-Flow were equivalent in their ability to fully empty the bladder (98% same)

2. Secondary Endpoint: Quality of life per Wagner I-QOL - Scores were 50% higher for In-Flow than for CIC (clinically & statistically significant superiority)

3. Comparative safety: UTI rates were equivalent, although In-Flow is indwelling and CIC is intermittent (breakthrough technology)
Clinical Role

- The In-Flow distinguished itself in two areas of its IDE study
  - Quality of life scores were significantly higher than for CIC
    - 50% better in the IDE and 80% better in another study
    - In-Flow’s UTI rate was equivalent to CIC – unprecedented for an indwelling device
  - Showing a UTI rate comparable to that for intermittent catheters is a unique and powerful effect
  - Even so, the In-Flow is probably better positioned on basis of its ability to improve quality of life
    - Can be quickly driven by patient demand vs. requiring large-scale studies
    - Exception is that present data re UTI rate are probably adequate to drive adoption by indwelling (Foley) users
Independent Studies

- Five independent (non-company sponsored) clinical studies (total $n=239$) report similar findings to the IDE study
  - Device performed as expected in all instances
  - No serious or lasting adverse events were reported in any study

- Specific findings from the two long-term studies include:
  - In a one-year study of 20 acontractile (atonic) bladder patients, Lynch et al reported 80% improvement in quality of life (QoL) and no negative tissue changes:
    
    "This study shows that the Inflow device provides an effective method of bladder drainage, with few side-effects and significant improvement in QoL."

  - In a pre-IDE study of 40 patients with voiding dysfunction in which 21 patients were followed for more than a year with a mean follow-up time of 24.6 months, Madjar et al concluded that, although dropout was a problem (due largely to discomfort):
    
    "Women who continue treatment for a prolonged time are satisfied with the device use." In fact, "All patients were satisfied with the device and preferred it to previous treatment modalities used."
A series of pre-clinical bench studies were conducted to characterize the performance of the In-Flow system. The results of these tests demonstrated that the In-Flow device and Activator meet their performance specifications and, where applicable, conform with the requirements of relevant voluntary standards. The tests performed were as follows:

- Device Pull-out Force Testing (as per "Inflated Balloon Response to Traction" test in ASTM F623-89 Standard Performance Specification for Foley Catheters)
- Device Flow Rate Testing (as per "Flow Rate through Drainage Lumen" test in ASTM F623-89)
- High Pressure Test (seal maintained under 200 cm H20 bladder pressure)
- Device Pump and Valve Endurance Test (1,140 voiding cycles = 6 months use)
- Activator Endurance Testing (11,552 operation cycles=5 years)
- Activator Drop Testing (50 cm onto hard surface)
- Activator Battery Endurance Testing (2 months)
- Catheter's DC Magnetic Field Levels (Alpen Committee standards)
- Activator DC Magnetic Field Testing (Alpen Committee standards)
- Activator AC Magnetic Field Testing (IEEE Standard for Safety Levels with Respect to Human Exposure to Radio Frequency Electromagnetic Fields 3 kHz to 300 GHz)
Biocompatibility Testing

A series of biocompatibility tests was conducted to characterize the biocompatibility of the materials used in the In-Flow device, inserter, Activator, and Sizing Device. These tests demonstrated that these components do not cause cytotoxic response, irritation, or sensitization. The device was also shown to be non-mutagenic. The tests were conducted by NAmSA on final, gamma radiation-sterilized devices, in accordance with GLP regulations. The tests conducted are listed below, according to component.

- **In-Flow Device:**
  - Cytotoxicity (MEM elution as per ISO 10993-5)
  - Vaginal irritation in rabbits
  - Sensitization (guinea pig maximization)
  - Genotoxicity (Ames mutagenicity test)
  - Implantation testing (as per ISO 10993-6)
  - Urinary bladder irritation study in rabbit (surgical implantation)
  - Urinary bladder irritation study in rabbit (saline extract)

- **In-Flow Device Magnet Assembly:**
  - Cytotoxicity testing of nickel and parylene coated magnets (MEM elution as per ISO 10993-5)
  - Acute systemic toxicity of nickel and parylene coated magnets (U.S.P. methodology)
  - Acute intracutaneous reactivity of nickel and parylene coated magnets (ISO Tests for Irritation and Sensitization)
  - Corrosion potential of nickel and parylene coated magnets
  - Individual In-Flow Device Materials:
    - Silicone elastomer—Elastosil (Certificate of Compliance with USP Class VI Biological Tests)
    - Polycarbonate—Lexan HF 1140 (USP Class VI)
    - Parylene Coating (USP Class VI)
    - Adhesive—Loctite 3311  (USP Class VI)
    - In-Flow Inserter (Nylon 6,6; transient contact with labia):
      - Cytotoxicity (MEM elution as per ISO 10993-5)
      - Acute intracutaneous reactivity (ISO Tests for Irritation and Sensitization)
      - Sensitization (guinea pig maximization test)
    - In-Flow Activator (Nylon 6,6: brief contact with hands and abdomen):
      - Cytotoxicity (MEM elution as per ISO 10993-5)
Encrustation Study

- Stickler et al\textsuperscript{1} – in vitro study – showed In-Flow encrustation resistance to be at least 8.4x superior to an all-silicone Foley:

  "Under conditions that simulated a heavy infection of P. mirabilis, where a conventional Foley catheter blocked with crystalline biofilm after 25.7 hours, the In-Flow device drained the bladder for at least 9 days… (and its) central lumen appeared to be essentially clear."

\textsuperscript{1}Microbiology Research Group at Cardiff UK (internationally recognized experts on CAUTI)
Transformational Technology

“It can simply, yet absolutely transform the quality of individuals’ lives.”
- Brother of IDE patient

“…the device has been an unqualified success. It is difficult to put into words the effect that (In-Flow) has had on (my daughter’s) life.”
- Father of IDE patient

- The In-Flow allows use of a toilet
  - Psychologically significant as that is the “normal” way to void

- Promotes hygiene, personal dignity
  - Eliminates need to self-cath 4-8 times daily
  - Eliminates tubes, drainage bags
Thank You

CAUTION: Not cleared by the FDA for sale in the USA. Investigational device. Limited by US law to investigational use.

U.S. Patent Nos. 5,762,599 and 6,417,750 and related patents worldwide. Additional patents pending. In-Flow is a trademark of SRS Medical Systems, Inc.

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New: Sizing Device

- In order to improve the accuracy of In-Flow sizing, both the Sizing Device and measurement protocol have been revised.
- A graduated version of the longest In-Flow device (7cm) is now used to measure urethral length.
  - Bladder neck contact is now consistent, minimizing sizing errors.
- The measurement protocol now includes several postures and not just the lithotomy position in order to account for possible prolapse.