

**Urology Interagency Coordinating Committee Virtual Meeting**  
**June 25, 2021**  
**9 AM- noon ET**  
**Meeting Minutes**

**Meeting Participants:**

Kevin Abbott (NIDDK)	Susan Mendley (NIDDK)
Kathryn Argue (CDMRP)	Melissa Miller (DoD)
Linda Bambrick (NINDS)	Joan Nagel (NCATS)
Julie Barthold (NIDDK)	Deepak Nihalani (NIDDK)
Tyler Best (NIH/OD)	Ralph Nitkin (NICHD)
Joe Bonner (NICHD)	Jenna Norton (NIDDK)
Eric Brunskill (NIDDK)	Matt Oldham (NIDDK)
Gene Civillico (SPARC)	Tracy Rankin (NIDDK)
Theresa Cruz (NICHD)	Jen Rymaruk (NIDDK)
Emily Duggan (NIDDK)	Marcel Salive (NIA)
Bill Elwood (OBSSR)	Victoria Spruance (NIDDK)
Chris Ketchum (NIDDK)	Rob Star (NIDDK)
Ziya Kirkali (NIDDK)	Roger Weiderhorn (FDA)
Kathy Kranzfelder (NIDDK)	Joan Weiss (HRSA)

**Welcome & Introductions**

Dr. Norton opened the meeting and noted that the topic of today's meeting will focus on Neurourology. Participants introduced themselves to the group.

**Setting the Stage**

Dr. Spruance noted that neurourology is multidisciplinary by nature and is covered by a number of other NIH ICs and Initiatives such as the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), National Institute of Neurological Disorders and Stroke (NINDS), and the NIH Common Fund's Stimulating Peripheral Activity to Relieve Conditions (SPARC) Initiative. This remains to be an understudied area and the innervation of urologic organs and tissues has significant implications as it relates to urologic function and dysfunction. Dr. Spruance detailed that neurourology is a highly complex area of study, as urologic tissues have multiple points and sources of innervation. In addition, these circuits are uniquely responsible for coordinating two distinct functions (storage and voiding) that engage multiple muscles and tissues (i.e. bladder, urethra, external sphincter). Dr. Spruance highlighted a few examples of the gaps in knowledge that remain in the neurourology space, including:

- Modulation by non-neural cells
- Modulation by higher brain centers (i.e. amygdala) or spinal interneurons
- Mechanistic links between psychosocial stress and LUT dysfunction
- Response to neural injury (stroke, TBI, spinal cord injury)

- Response to recurrent LUT inflammation, or changes in microbiome
- Role of neural control in organ cross-sensitization
- Across species?

Dr. Spruance noted that in May 2019, NIDDK held a workshop focused on neuroscience and urology and in September 2020, NIDDK held a seven-week series of workshops focused on advancing basic and translational research for genitourinary conditions as it relates to female urethral function and failure.

Dr. Spruance introduced the following guest speakers presenting at today's meeting:

- Capt. Derek Herrera MBA, US Marine Corps (Ret.), will provide a presentation of his personal journey on how using catheters motivated researchers to develop a new method of bladder management for men with chronic urinary retention.
- Charles Hubscher, PhD, University of Louisville School of Medicine, will provide a presentation on targeting neurogenic urinary dysfunctions with activity-based recovery training.
- Margot Damaser, PhD, Cleveland Clinic, will present information regarding new tools and technology for Neurourology.

**Inspired by personal need: how using catheters motivated researchers to develop a new method of bladder management for men with chronic urinary retention**

Capt. Herrera opened his presentation on how using catheters motivated researchers to develop a new method of bladder management for men with chronic urinary retention. Captain Herrera detailed his family military history and noted he pursued a career in the Marine special operations officer. After completing training, he spent time on an infrastructure project within Afghanistan and during an enemy fire attack, he was wounded from the chest down. During his recovery process, he learned about challenges associated with spinal cord injury and emphasized that using catheters was the single largest challenge, and added that he experienced false passage, bladder spasms, UTIs, etc. After his discharge from the military, he attended the University of California at Los Angeles and earned his master's in business administration. After graduating, Capt. Herrera founded UroDev Medical, which focused on the development of disposable catheter using The IntelliFlow™ System and solves issues related to frequent catheterization. He noted this device is under review and close to FDA approval and commented that he is hoping to commercialize this product early next year.

Participant Discussion:

- Dr. Nitkin (NICHD) queried how the device is inserted. Capt. Herrera noted that patients themselves can remove this catheter; however, he commented that this device does not solve the issue of bladder fullness. Currently, the device has been tested in at least 60 patients with multiple feasibility studies.
- Dr. Cruz (NICHD) asked if there any thoughts on how to adapt this device to female patients. Capt. Herrera noted that a device is already on the market for females, but added that his device can be adapted to use in females.
- Dr. Bambrick (NINDS) queried the timeline for clinical trial. Capt. Herrera noted that a clinical study is being conducted (with 4 to 5 studies conducted thus far) and added that the current

version is designed to be commercialized. He estimated that the study will be completed by the end of the year for market clearance.

- Dr. Rankin queried what types of study participants were recruited in the clinical study. Capt. Herrera noted the inclusion criteria for this device is very broad to include many types of conditions, such as BPH patients and spinal cord injury patients. In addition, this device is non-surgical and low cost, which adds to patient incentives.
- Dr. Damaser queried what factors led to the decision to recommend use for a 7-day duration and queried what would happen if individuals use it longer. Capt. Herrera responded that initially, trials using the device started patients at a 29 day use. However, patients reported that they would like to change the device after a few days.

### **Targeting neurogenic urinary dysfunctions with activity-based recovery training**

Dr. Hubscher opened his presentation by detailing that there are approximately 17,700 new Spinal Cord Injury (SCI) cases per year. The number of people with SCI living in the U.S. is currently estimated to be approximately 288,000 persons and the average age at injury has increased from 29 years during the 1970s to age 43. Also, approximately 78% of new SCI cases are male. Since 2015, the majority of SCI causes are related to vehicular accidents and falls, while a minority of these cases are due to violence (attacks), sports injuries, and medical/surgical reasons.

Dr. Hubscher commented that bladder, bowel, and sexual dysfunctions are among the highest priorities for the SCI population due to their impact on daily living, health, and quality of life. SCI patients experience bladder dysfunction as it relates to incontinence (weakness of the sphincter mechanism, bladder hyperreflexia), lost sensation (bladder fullness, emptying), impaired voiding (over-activity of the sphincters, impaired bladder contraction, concurrent contraction of the bladder and urethral sphincter), and Autonomic Dysreflexia. Ideally, long-term outcomes for SCI would include reasonable urine storage volumes at safe pressures and almost complete voiding of urine, on demand and at safe pressures.

While discussing Autonomic Dysreflexia (AD), Dr. Hubscher noted that AD is characterized by an unregulated sympathetic cascade that is triggered by noxious or innocuous stimuli below the injury level, which leads to focal vasoconstriction and a rise in blood pressure. AD symptoms include increased blood pressure, pounding headache, profuse sweating, nasal congestion, bradycardia, and skin that is flushed or clammy. Causes of AD include bladder symptoms such as distention or a UTI, any pain causing discomfort, and bowel impaction, among other symptoms. AD can present as a clinical emergency if the patient has a SCI above T6 in the spinal column and can be life threatening if not treated immediately. Current bladder management within SCI is focused on use of these catheters for emptying the bladder:

- Straight: 42.6% of patients
- Suprapubic: 11.3% of patients
- Indwelling: 3.2% of patients
- Condom: 11.3% of patients

Dr. Hubscher discussed the use of preclinical studies and clinical studies for SCI and the bladder from the Journal of Spinal Cord Medicine and commented that preclinical studies focused on the Metabolic Cage as well as simultaneous electromyography; Crede (a maneuver which uses a urine voiding facilitatory technique that involves applying manual pressure on the lower abdomen) and reflex measures; Cystometry with Sphincter simultaneous electromyography; and Urinalysis/urine biomarkers. Clinical studies in this research area focus on bladder emptying using a voiding diary; Cystometry with Sphincter simultaneous electromyography, and Urinalysis/Urine Biomarkers.

When discussing blood pressure effects from bladder distention, Dr. Hubscher also cited the following study, which focused on improving bladder function using activity-based recovery training using epidural stimulation of the spinal cord (scES) after chronic SCI. Activity-based recovery training included both Locomotor Training, which showed significant improvements in multiple aspects of bladder function, and scES. The study showed that scES, combined with intense activity-based recovery training, has been shown to produce volitional lower extremity movement, standing, as well as improve the regulation of cardiovascular function. For more information about this study, please visit the full article at:

Herrity AN, Aslan SC, Ugiliweneza B, Mohamed AZ, Hubscher CH, Harkema SJ. Improvements in Bladder Function Following Activity-Based Recovery Training With Epidural Stimulation After Chronic Spinal Cord Injury. *Front Syst Neurosci*. 2021 Jan 5;14:614691.  
(<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7813989/>)

Dr. Hubscher also discussed how funding from the NIH Common Fund's Stimulating Peripheral Activity to Relieve Conditions (SPARC) program is used for mapping efforts in this area of research and displayed effective configurations for bladder storage versus non-effective configurations for bladder storage. Dr. Hubscher concluded his presentation with a description of the "Sim4Life" technology, a simulation platform using finite element modeling for directly analyzing biological phenomena and complex neuromodulation devices in validated biological and anatomical models. Dr. Norton thanked Dr. Hubscher for his informative presentation and introduced Dr. Damaser, whose biomedical engineering research program is at the Cleveland Clinic.

### **Tour of new tools and technology for neurourology**

Dr. Damaser provided an overview of new tools and technology for neurourology including:

- New Tools for Diagnosis
- New Tools for Management
- New Technologies to Treat Neurourologic Conditions
- New Tools & Technologies for Scientific Investigation
- New Tools & Technologies for Tissue Engineering & Regeneration

Dr. Damaser commented that, while urodynamics are the primary tool used to diagnose lower urinary tract dysfunction, the use of catheters continues to be problematic in human and animal studies. The development of a wireless catheter-free monitoring, called the UroMonitor, uses an antenna and radio to transmit bladder pressure wirelessly and without the use of a catheter. The flexible device, shaped like a coil, is inserted into a patient's bladder lumen. It tracks physiological data over a four- to seven-day monitoring period and wirelessly transmits the information to a nearby computer for investigational use.

In the future this data could be used to inform a physician's diagnosis and clinical management. The patient can remove the device by a string and dispose of it completely. Initial testing of the UroMonitor in human clinical trials demonstrated significant results when used alone or in conjunction with urodynamic testing and showed that urodynamic events can be identified from the UroMonitor 98% of the time.

Additionally, the UroMonitor can be used for the management of neurourologic conditions such as diabetics and spinal cord injury patients. In this capacity, the UroMonitor could wirelessly communicate with a phone app to warn of increasing frequency of bladder contractions as the bladder fills. With the addition of volume sensing, the UroMonitor could warn patients of bladder fullness near capacity. With respect to the treatment of neurourologic conditions, the UroMonitor could wirelessly trigger stimulation only when needed. As a result, this would save battery usage of the device, reduce habituation, and enable feedback on efficacy.

Dr. Damaser noted that, in terms of scientific investigation, the UroMonitor could be used to obtain bladder function data at home during activities of daily living without the use of catheters and would enable researchers to investigate scientific questions, such as what bladder pressures could result in renal dysfunction at home and how bowel management affects bladder function.

Dr. Damaser concluded her presentation with tools and technologies for tissue engineering and regeneration:

#### Noncellular Regenerative Therapies

- Treating with secretions of stem cells in the absence of cells (Secretome)
- Regenerative Pharmacology
- Regenerative Electrical Stimulation
- Regenerative Materials

The advantages to using this technology include fewer side effects and complications, ability to be used in tandem with other treatments, and the capability to personalize these therapies to the patient. Dr. Damaser thanked Drs. Barthold and Norton for the invitation to present information on this topic.

#### Discussion

Meeting participants offered the following feedback:

- Dr. Nitkin commented that each technology is simple to use and to find the right settings for each patient. Dr. Hubscher noted he is building a database where the information could be used from past patients to help establish a more precise spot for mapping. He noted that mapping is necessary, as every individual is different.
- Capt. Herrera noted he is establishing a training program to teach people how to use the device.
- Dr. Star queried presenters if we can envision a day where all three of these concepts are working together in the same person. Capt. Herrera responded that all systems could be integrated and added that the products have shown to be viable in the long term. Participants commented that an integrated approach could have a real impact on patient quality of life (QoL).

- Capt. Herrera noted patients provided feedback that wearable devices are not comfortable.

**Adjourn**