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Interview with the Expert

Wireless Bladder Monitor: First in Humans Testing

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In this month's Neuro-Urology News Interview with the Expert, we highlight Dr. Margot Damaser and her work on a novel and wireless ambulatory urodynamics device, which was recently published in Journal of Urology. We discuss her work leading up to the current device, the present study, and its implications. Below is the interview, edited for length and clarity.

Dr. Glenn Werneburg: What are the limitations of urodynamics studies, and what was the impetus for the wireless bladder monitor's development?

Dr. Margot Damaser: My training is as an engineer. My PhD thesis was on bladder biomechanics, and I've been in urology departments my entire career. I even had a urologist on my thesis committee. Early on, it was very kind of a patient and a clinician to allow me to watch urodynamics being performed. I thought "Is this the state of the art?" What made my jaw drop was the use of catheters, the retrograde filling, the discomfort and distress of the patient. The fact that the patient couldn't void around the catheters, or reproduce the symptoms that were bothering her at home. This was in the mid-90's. Ever since then, I've wanted to improve the situation. I've always thought of ambulatory urodynamics as a Holter monitor for the bladder, and have wondered why we don't have such a device. That was the impetus for development.

For years, I'd discuss ideas with companies in industry at the AUA and other meetings. I'd often ask whether they'd consider development of a wireless device. One year, they said "Oh yes we have wireless." But the wireless to which they were referring was a setup wherein the patient remained catheterized, and the wires connected to a transducer that sent the data wirelessly. This was an incremental improvement – indeed it improved patient privacy, but not to the extent of the wireless urodynamics device that I had in mind.

INUS Calendar

INUS International Course of Lower Urinary Tract Dysfunction and Urodynamics
Timisoara, Romania
October 27-28, 2023

INUS Course at EAUN Meeting
Paris, France
April 6-8, 2024

INUS Session at Annual Congress, Urologic Society of India
Hyderabad, India
April 19-20, 2024

INUS Annual Congress 2025
Zermatt, Switzerland
January 16-18, 2025

GW: How many iterations of the device have there been leading up to the current prototype? What challenges have you faced along the way?

MD: There have been a number of iterations. Likely there have been 5 or 6 major, and each of these included many, many minor iterations and designs. Back in Chicago, I started working with a company to add pressure sensing to their device, but this did not pan out. Then, when I came to Cleveland, I connected with electrical engineering partners at Case Western Reserve University. In order to separate ourselves from other companies in the space, our first idea was to put a tiny, more permanent, circuit between the uroepithelium and the detrusor wall. The purpose was not diagnostic, but to provide feedback to a neuromodulation system. The idea was to get it out of the urinary stream, to reduce stone risk. And the thought was that, once healed, infection would also be less of a risk. This didn't work, not because of technology, but because we found that the urothelium would grow out behind the device and push it into the lumen. I call that "Physiology: 1, Margot: 0". We started over. By then, years had passed, and we then changed our design to an intravesical design. To develop this, we worked together in an innovations design program, which consisted of several hours-long intensive design meetings, consisting of brainstorming and prioritization. That's how we arrived at our current design.

GW: What is the current design of the wireless bladder monitor, and what is the design of the present study?

MD: The current design of the device is flexible electronics in a silicone tube. The tube casing is pre-stressed, so it naturally curls, but can be straightened out. So the idea is that it is straightened out for insertion, and once in the bladder lumen where it is not subject to the same straightening force, it curls up. The curl is both to prevent it being voided out, and to prevent it from obstructing the outlet, two of our design criteria. There is a balance between too small and too large – the engineers tell us they can make it smaller, but this may get voided out. The device has an internal battery by design. That is the only stiff component of the device. The battery allows it to continuously transmit data to a radio that is on the outside. The UroMonitor itself does not store data on board, rather it transmits its data via a radio and antenna that is put in a pocket. We chose this design because we wanted a device that could be pulled out by the patient, and not require a second office visit for removal. The device has a string that emanated from the urethra, much like a stent string or tether. This can be pulled out by the patient very easily, and discarded. Because there are no data on the device, this can be safely disposed of by the patient. The radio could then provide communication to either a computer or display, or even to a neuromodulation system for feedback.

We designed the study, which was just published in Journal of Urology, to test acute short term comfort of the patient – during the insertion, the indwelling time, and the removal. The device gently rests on the bladder neck. As a unit, it is neutrally buoyant, but it orients itself right-side-up based on an empty part on its top. It doesn't float, but it gently rests. So there was the question, which we couldn't answer during animal studies: "Given that the bladder trigone is well innervated, would it be irritating to the trigone?" Our other main questions were: "Will it become obstructive to voiding? and "Will it will get voided out?"

This study was in women because insertion was much easier. We've since developed an insertion technique for men, and are about to embark on a similar study in men. The second aim of the study was to assess the wireless bladder monitor data against simultaneous urodynamics. We wanted fully-sensate individuals, so they could report pain or discomfort. We didn't want any confounding pain, so patients with pelvic pain were excluded from the study. We included women who were referred for urodynamics who had suspected overactive bladder, who did not have any diagnosed neurological issues. This is unlikely our final population for the use of this device, but it met the goals and needs of this study.

We obtained participants' baseline urodynamics first, then removed the catheters and inserted the device. We then evaluated the bladder cystoscopically to ensure acceptable device placement. Then we replaced the urodynamics catheters, and performed the urodynamics again with the wireless bladder monitor in place. We next removed the urodynamics catheters, and allowed the participant to walk around while drinking water. Again, there are no catheters or wires in this scenario. I recall the first patient – she was walking around, drinking water, talking, reporting, and finally she needed to void. She walked to the bathroom in privacy, voided, and during this we were looking at the data in real time via Bluetooth from the radio, on the computer. This was a first! No catheters, no wires, just privacy.

GW: What were the main findings in the study?

MD: We found that from the wireless bladder monitor data, we were able to identify just about all of the urodynamic significant events. These including non-voiding contractions, coughs, and Valsalva. We had two urologically-trained individuals to go through the urodynamics and the UroMonitor data to identify events. We analyzed the data in this way, to determine if the UroMonitor was sensitive enough to pick out urodynamics events as detected by traditional urodynamics. There were only two missed events, and they were both missed because of radio transmission dropouts. These issues can be resolved with some funding investment to improve the electronics. The most painful part of the study, by the participants' reports, was the cystoscopy. The placement of the device was adequate every time. Thus, we since have dropped the cystoscopy portion of the protocol based on these data.

GW: Did any participants share their experience regarding their levels of comfort with the wireless bladder monitor device versus their urodynamics catheters?

MD: Several participants noted that if they just had the wireless bladder monitor, they'd be much happier about coming in to get the testing. As they were walking around, especially with the first few – we'd ask
"What does it feel like?" And again, this wasn't blinded, and people were probably hyperfocused on their bladder, but commonly they'd say "Yes, I can feel something – it feels like something inside, but not painful". And I'd say, "Could you imagine yourself going about your daily activities with this?" "Do you think you'd be able to forget about it?" And every one of them would say "Oh, yes."

GW: Do you think the wireless bladder monitor has the potential to replace standard urodynamics?

MD: It could…eventually. The goal of this effort is for people be able to use it at home, even though that was not part of this initial study. Part of the design of the initial study was to keep the risk low with the initial device, given that it was the first-ever instance of this testing. Home is a much less controlled situation. Again, I think of it like a Holter monitor. There are reasons to do an EKG in the hospital, and a Holter monitor often follows the EKG. If there's something suspicious on EKG, then a clinician might send a patient home with a Holter monitor. At least initially, that is how I see the wireless bladder monitor. If the symptoms cannot be reproduced on urodynamics, a clinician may send them home with the wireless bladder monitor device. And then, depending on the quality and usability of the data in the very uncontrolled home environment, the wireless bladder monitor could potentially replace urodynamics.

GW: Can you speak about the implications for research? Teams are making headway with functional MRI to investigate the pathophysiology of voiding dysfunction, and often a practical limitation is the ability to perform urodynamics together with functional MRI in real time given space and wiring issues. Is the device currently compatible with MRI? Could it be modified to become MRI-compatible?

MD: It is not currently MRI compatible, primarily because of the battery. We'd need to either come up with a non-metallic battery design or power it externally, which are possible. This would take some design modifications. But, I think it has useful research potential even before that goal is achieved. For me, it really gets at this idea of being able to understand what the bladder is doing at home, and opens up many questions that could be asked. One question I want to figure out how to study, is a tough one, which will likely require multiple studies to answer. The ultimate questions are "Outside of urodynamics, what is the real threshold in neurogenic bladder for renal dysfunction? How relevant is a 40 cm H2O threshold at home? Is there a time constraint? Is having vesical pressure above 40 cm H2O for a short period less dangerous than a longer period? Is a period of >40 cm H2O during voiding OK? Or is the 40 cm H2O not relevant at all in the ambulatory or home setting, and only relevant during the standard urodynamics study? A study designed to answer these questions would be difficult to design prospectively, given the need to wait for somebody to develop renal dysfunction. That's why I think we'd need to stage the investigation, and ask an easier to question to answer first.

GW: As an inventor, please take us through the process of development. Starting with an idea, like you had back in the 90s, and taking us through all the way to the clinical implementation of the idea, like the current device prototype.

MD: How long do you have? I'll give you highlights. An important part to keep in mind is the massive number of failures. I told you about the one, "Physiology: 1, Margot: 0". But there have been many other failures. Keep the faith, hang in there, and learn from the failures. Fail soon, learn from it, and move on. Don't be emotionally attached to each design. That's all part of the game. We've made it a point to have clinical input at every iteration of our design from the very beginning. So that's a highlight, and really how we set the design criteria – by having urologists, electrical engineers, and biomedical engineers in the same room. This would be over repeat meetings.

We set some design criteria. For example, being able to remove the device at the end of testing and throw it out. As we discussed, that would be important for the patient to not require a repeat visit. Rather than having them remove a mini-USD card or something from the device that had just been indwelling, they can just throw out the whole device. But the engineers might have said, "Yes we'll just store everything on the USD card and save it when we're done." So it's always been a back and forth between the clinicians and the engineers to find that middle ground. Finally, keeping your eyes on the prize is important – the goal was always this concept of this unobtrusive home monitoring, and identifying the stages to get us there. And then we also had tech-transfer people from Cleveland Clinic Innovations involved very early as well. They were able advise on what is patentable and not patentable, and what it would take to get from this design to a patent. What could they support and not support? This is important because protecting the intellectual property before you publish and present is key to commercialization. With this in mind, we didn't present for a long time. We would present failures, so it looked like we were failing. But no one knew we had picked up and started over with successful subsequent prototypes. Like in any research program, finding the money, finding the research support, finding a way to convey the idea appropriately to secure funding can all be challenges along the way. There were many times that things would need to stop until we could procure more funding to make hires, or start new projects, and then we would start up again.

GW: **What advice do you have for junior INUS members who are interested in embarking on a career with a neuro-urological focus?**

MD: Your ideas are valuable, they have a future. Just because one funding source decides not to fund you, it doesn't mean your ideas are not valuable. Keep the faith, keep your ideas, pick yourself up and try it again. Research is a long-term game. Whether it's basic research, or translatable device development research, it doesn't matter. If you're coming up with something new, it's going to take a long time to get there, so hang in there. Talk to experts who can point you in the right direction. Put in the work and don't let failures get you down.

Meet the Board Member

Dr. Marcio Averbeck, MD, PhD (BR)

INUS Treasurer

Head of Neuro-Urology, Moinhos de Vento Hospital, Porto Alegre, Brazil @marcioaverbeck

Marcio A. Averbeck received his medical degree from the Federal University of Pelotas, Brazil (2003). His specialization in Urology (Medical Residency Program) was obtained in 2008 from the Federal University of Health Sciences of Porto Alegre, Brazil. From 2008 to 2010, he was a member of the kidney and pancreas transplantation team at Santa Casa Hospital Complex, in Porto Alegre. In 2009, he was awarded a scholarship from the European Association of Urology (EAU)/ European Urological Scholarship Program (EUSP) and his Clinical Fellowship in the Neuro-Urology Unit in Innsbruck, Austria, hosted by Prof. Helmut Madersbacher.

Dr. Averbeck with his wife and sons

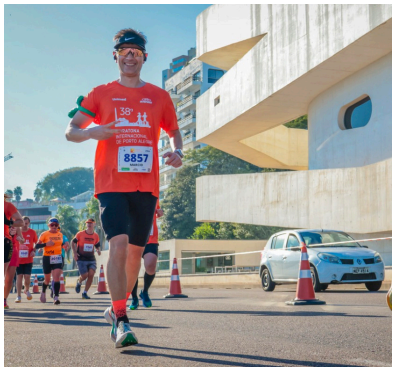
Since he came back to Brazil, Dr. Averbeck has become involved with resident training at Presidente Vargas Women's and Children's Hospital in Porto Alegre. Dr. Averbeck also has an appointment as invited Professor at Unisinos University (Porto Alegre, Brazil). He obtained his Master's Degree and his PhD in Health Sciences from the Federal University of Health Sciences of Porto Alegre (2011/2017). In 2014, he was invited to take over as Head of Neuro-Urology at Moinhos de Vento Hospital (affiliated with Johns Hopkins Medicine International).

Dr. Averbeck is a founding member of the International Neuro-Urology Society (INUS) and worked previously as INUS Secretary. He has been elected INUS Treasurer last year, during the Annual Meeting in Innsbruck. Marcio Averbeck is also an active member of several medical associations/societies, including the American Confederation of Urology (CAU), European Association of Urology (EAU), International Consultation on Incontinence Research Society (ICI-RS), International Continence Society (Deputy-Chair of the ICS Standardization Steering Committee), American Urological Association (AUA) and the Brazilian Urological Society (Head of International Affairs).

Dr. Averbeck has published dozens of articles and several book chapters in the field of neuro-urology. Additionally, he took part as editor of the SBU Urodynamic Atlas (2015) and the SBU-INUS Manual of Neuro-Urology (2017).

His main areas of interest are neuro-urology/neurogenic lower urinary tract dysfunction, BPH-related bladder dysfunction, neuromodulation techniques, and post-prostatectomy urinary incontinence.

Outside of the world of neuro-urology, Dr. Averbeck enjoys playing the guitar and street running. He is married to a television journalist and has two sons.



Dr. Averbeck during a recent road race.

Literature Review

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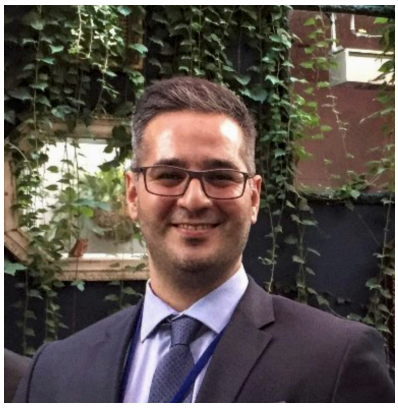
Foreword by Dr. Glenn Werneburg, NUN Editor (US)



Foreword

Neuro-Urology News is interested in featuring trainees in its Literature Review section. The INUS Board is accepting submissions for this section from any basic science or clinical trainee around the world. In this issue, Dr. Aidin Abedi discusses two neuro-urological articles. The first, by Choksi et al., aimed to elucidate the association between white matter tract disruption and the symptomatic profile of patients with neurogenic lower urinary tract dysfunction and multiple sclerosis. In the second article, Krhut et al. sought to characterize the functional brain activation patterns that resulted from motor-threshold peroneal and tibial nerve stimulation techniques.

Introduction

In tandem with the progress in the field of neuroscience, our field of neuro-urology has taken significant strides in understanding the central nervous system (CNS) mechanisms of neurogenic lower urinary tract dysfunction. This progress is attributed not only to advancements in neuroimaging, but also to the efforts of multidisciplinary teams led by neurourologists specializing in these areas.

Until recently, the role of the spinal cord in neurogenic lower urinary tract dysfunction has remained elusive, partially due to the absence of functional imaging techniques. However, one emerging research theme involves evaluating the impact of various neuromodulation methods on functional brain activation patterns and identifying functional and anatomical correlates of urinary dysfunction in specific patient subgroups. The selected articles in the literature review section of this issue focus on two distinct but relevant topics. One explores the structural disruption of CNS tracts to elucidate pathology, while the other is focused on the functional brain activation patterns associated with neuromodulation paradigms. Together, these articles illustrate how neuroimaging can advance our field in different ways.

Choksi, D., Schott, B., Tran, K., Jang, R., Hasan, K. M., Lincoln, J. A., ... & Khavari, R. (2023). Disruption of specific white matter tracts is associated with neurogenic lower urinary tract dysfunction in women with multiple sclerosis. Neurourology and Urodynamics, 42(1), 239-248.

Despite the prevalence of neurogenic lower urinary tract dysfunction (NLUTD) among individuals with multiple sclerosis (MS), its management remains challenging and treatment response is often poor. Due to its sensitivity, magnetic resonance imaging (MRI) plays a well-established role in the diagnosis and monitoring of MS. However, conventional MRI lacks specificity in patients with a confirmed MS diagnosis and may not reveal white matter tract (WMT) changes related to dysfunction or recovery. In contrast, diffusion tensor imaging (DTI) is a specialized technique capable of detecting WMT lesions that may appear normal on conventional MRI despite the presence of focal pathology.

In this study, Choksi et al. aimed to illustrate the correlation between WMT disruption, as determined by DTI, and the symptomatic profile of MS patients with NLUTD. To this end, patients underwent urodynamic assessment, MRI scans, and completed the Urogenital Distress Inventory (UDI-6) and Incontinence Impact Questionnaire (IIQ-7). The study comprised two cohorts of adult women with stable MS and NLUTD, alongside 11 healthy volunteers who served as controls. The researchers utilized mean diffusivity (MD) and fractional anisotropy (FA) to quantify the structural organization of tracts. The analysis revealed significant differences in both FA and MD among all tracts between the first cohort and the control group, both scanned using a 3T MRI. This finding highlighted the limitation of such an analysis for assessing WMT lesions in MS patients, emphasizing the need for a correlative approach. In this context, the researchers identified the tracts with the largest number of robust clinical correlations, such as the left medial lemniscus and left anterior limb of the internal capsule. Subsequently, they validated these findings in a smaller cohort using 7T MRI. While acknowledging certain study limitations, including the inherent complexities of interpreting DTI indices and the variable impact of inflammation on AD over time, the authors have clearly demonstrated that DTI parameters correlate with clinical indicators of bladder dysfunction in MS. These findings suggest that DTI could potentially serve as a biomarker during the management of this chronic condition.

Krhut, J., Tintěra, J., Rejchrt, M., Skugarevská, B., Zachoval, R., Zvara, P., & Blok, B. F. (2023). Differences between brain responses to peroneal electrical transcutaneous neuromodulation and transcutaneous tibial nerve stimulation, two treatments for overactive bladder. Neurourology and Urodynamics.

With the rising number of studies exploring the impact of neuromodulation on lower urinary tract dysfunction, it becomes increasingly important to understand the central mechanisms underlying these treatments. In this study, Krhut and colleagues sought to characterize and compare the functional brain activation patterns resulting from motor-threshold peroneal and tibial nerve stimulation techniques.

Twenty-two healthy adult women participated in this study and underwent functional MRI while receiving neurostimulation or using a sham device. The sequence of stimulation experiments consisted of three blocks, each lasting eight minutes. The first block involved sham stimulation, followed by the second block involving peroneal electrical transcutaneous neuromodulation® (eTNM®), and finally, the third block involved transcutaneous tibial nerve stimulation (TTNS). Each block comprised a sequence of 30 seconds of stimulation followed by 30 seconds of rest.

Through their analysis, they identified commonalities and differences in the activated brain regions among the three experimental conditions. Furthermore, they identified the regions with significant differences in voxel size among the three stimulation modalities, including areas in the brainstem, cerebellum, and putamen that yielded a larger number of activated voxels during peroneal stimulation. Lastly, they performed a functional connectivity analysis, demonstrating that the signal correlation between basal ganglia and the limbic system was more pronounced during peroneal stimulation compared to tibial nerve stimulation. This finding indicated a distinction in connectivity profile between these two stimulation methods. Low enrollment in this study was a limitation. The study sheds light on how alterations in supraspinal activity patterns may play a role in mediating the effects of peripheral nerve stimulation on bladder function.