specimen \((P < 0.001)\). When controlling for implant volume in our model, fill weight maintained a strong association with NAC necrosis. Rates of NAC necrosis among TE reconstructions using air only were lower at equivalent volumes compared with TE using saline fill and direct to implant reconstructions. Other influential factors included diabetes \((P = 0.005)\), smoking \((P = 0.04)\), and hypertension \((P = 0.03)\). With a prospective cohort of 27 patients, our predictive machine learning model achieved 96% accuracy \((P = 0.02)\) with high positive predictive value and specificity for NAC necrosis. The model correctly predicted 4 of 5 cases of NAC necrosis and all 22 cases without necrosis.

**CONCLUSIONS:** Implant weight is an independent risk factor for NAC necrosis following NSM, indicating that lower implant volumes, or using air-only initial TE fill, may mitigate the risk of NAC necrosis. The findings of our predictive Random Forest machine learning model also provide a basis for utilizing artificial intelligence to predict cases with a high probability of NAC necrosis. We created an easy-to-use interface for our model, which allows a user to input patient characteristics and receive a prediction which includes a binary outcome: “NAC Necrosis” or “No NAC Necrosis” and the predicted probability of necrosis. Such models may be developed using institutional data and utilized to inform patient decision-making prior to mastectomy.

**REFERENCE:**
1. Wapnr I, Dua M, Kieryn A, et al. Intraoperative imaging of nipple perfusion patterns and ischemic complications in nipple-sparing mastectomies. *Ann Surg Oncol*. 2014;21(1):100–106.

**Extended Local Release of Neuromodulators from a Novel Nanoparticle System for Chronic Migraine and Facial Aesthetics**

**Presenter:** Thomas Harris, MBChB

**Co-Authors:** Chenhu Qiu, PhD candidate, Salih Colakoglu, MD, Sami Tuffaha, MD, Hai-Quan Mao, PhD, Sashank K. Reddy, MD PhD

**Affiliation:** Johns Hopkins University School of Medicine, Baltimore, MD

**PURPOSE:** Neuromodulators of the botulinum toxin family (eg, Botox) have been used effectively to treat a wide range of conditions, including chronic migraine, spasticity, hyperhidrosis, and facial rhytids. Despite their broad utility and commercial success, these agents suffer from two significant shortcomings: limited duration of effect, necessitating frequent redosing, and diffusion from target sites leading to unwanted muscle paralysis. To overcome these challenges, we have developed a novel nanoparticle-based botulinum toxin system that prolongs therapeutic effects while preventing off-target activity.

**METHODS:** Botulinum toxin A (BoNTA) and BoNTA toxoid (chemically inactivated form of the toxin) were each encapsulated within polymeric nanoparticles. BoNTA or toxoid was mixed with a carrier molecule and assembled into polyelectrolyte complex nanoparticles using a biodegradable amphiphilic block copolymer using a flash nanocomplexation/nanoprecipitation process. Nanoparticles were characterized by dynamic light scattering for size distribution and zeta potential, and transmission electron microscopy for morphology. In vitro release of BoNTA or toxoid was determined using ELISA and bioactivity of released BoNTA was analyzed using a substrate hydrolysis assay. The in vivo paralytic effect of BoNTA nanoparticles was assessed using a quantitative rodent forepaw model using stimulated grip strength testing.

**RESULTS:** The BoNTA and its toxoid both demonstrated high encapsulation efficiency of 83%–88% of the input protein into NPs; and the average loading level (mass of total protein/mass of NPs) was 13.4–14.2%. Both NPs showed a similar, sustained linear release profile with 30%–35% of protein released within 30 days, ~75% in 98 days, and a projected release duration of about 4 months. Critically, BoNTA released from NPs demonstrated high levels (>80%) of bioactivity retention, confirming that the encapsulation process and release did not impair the bioactivity of BoNTA. Reference protein-loaded NPs showed superior localization when injected in rodent models when compared with unencapsulated proteins. Finally, the NPs stored at ambient temperature \((20°C–25°C)\) for 70 days exhibited a similar release kinetics, demonstrating a good shelf stability.

**CONCLUSIONS:** We demonstrated a novel NP-based neuromodulator system that enables local, linear, long-acting neuromodulator release with strong preservation of bioactivity. Given the high level of potency of BoNTA and the linear release above the EC50 for almost 4 months, we anticipate powerful extended neuromodulatory effect in vivo with this formulation. It is hoped that clinical translation of
this system will yield superior therapeutic outcomes with less frequent dosing and an improved margin of safety.

REFERENCES:
1. Hu H. et al. Flash technology-based self-assembly in nanoformulation: Fabrication to biomedical applications. *Materials Today* doi:10.1016/j.mattod.2020.08.019 (2020).
2. Hanwright PJ, et al. Stimulated grip strength measurement: Validation of a novel method for functional assessment. *Muscle Nerve* 2019;60(4):437–442. doi: 10.1002/mus.26646 (2019).

**Modulation of Surface Topography Increases Multilayer Proliferation of Urothelial Cells within Engineered Vascularized Urothelial Constructs**

**Presenter:** Jason Harris, MPH  
**Co-Authors:** Jason Spector, MD, Xue Dong, MD, PhD, Ryan Bender, BS, Sarah Caughey, BA, Douglas Scherr, MD  
**Affiliation:** Weill Cornell Medicine

**PURPOSE:** There is an increasing need for tissue engineered solutions for urethral repair. While urethral deformations have traditionally resulted from congenital anomalies or from urogenital surgeries, the rapid growth of female-to-male gender affirmation surgeries has led to a more urgent need to improve current approaches to urethral repair. The number of female-to-male procedures increased 289% between 2016 and 2017, with an estimated 7626 procedures in 2019. Phalloplasty uses either pedicled or free flaps to construct a phallus, often using epidermal tissue to extend the urethra. The mismatch of epidermal and urothelial tissue, as well as postoperative inflammation and fibrosis secondary to ischemia, leads to fistula and/or stricture in up to 50% of cases. Tissue-engineered urethral tissues solutions are currently limited by a lack of vascular supply, and creation of multilayer urothelial tissue capable of withstanding urinary flow. Here we present a novel vascularized urethral flap, with a “grooved” topography that fosters increased urothelial cell proliferation.

**METHODS:** A custom-designed 3D negative mold with a urethral channel and a vascular inlet and outlet channel was prototyped in Adobe Fusion 360 and printed on a Prusa i3 MK3S printer in PLA. One version was printed with a smooth urothelial mold, and the other with undulating features on the negative urothelial mold to create 0.4-mm deep triangular grooves in the collagen. A 2-mm diameter pluronic sacrificial macrofiber was used to connect the channels to form a vascular loop, and 1% type-I collagen containing 106 human foreskin fibroblasts per mL collagen was extruded over the mold. After solidifying, the scaffold was molded and seeded with grade I urothelial carcinoma (SW780 cells, at 10 × 106 cells/mL) in the urethral channel, and adenovirus-infected E4 endothelial cells (at 3 × 106 cells/mL) in the vascular channel. The scaffolds were cultured up to 28 days and then fixed for histologic analysis.

**RESULTS:** Collagen scaffolds were fabricated reliably using the custom designed 3D negative molds. Fourteen days after seeding, stable urothelial monolayers were formed in the smooth channels. Multilayers were formed in the smooth channel by 21 days, and the multilayers were maintained up to 28 days. In comparison, the constructs with an undulating lining topography showed robust multilayer urothelial development compared with the smooth lining at 14 days. In addition, the vascular channels supported a healthy endothelial lining at both 7 and 14 days.

**CONCLUSIONS:** We have developed a novel strategy to engineer vascularized urethral tissue. These constructs can be maintained in culture for at least 28 days. Constructs with grooved topography allowed for increased cell-to-cell contact, which led to increased urothelial proliferation into multilayers by the 14-day time point. These constructs allow for rapid prototyping through 3D design and printing and can be used for autologous cell seeding for patient-specific vascularized urethral flaps. Such constructs may have far reaching applications in phalloplasty, congenital defects such as hypospadias repair, and repair of postoperative urethral injury.

**Essential Elements of Surgeon Communication Impacting Patient Satisfaction: A Systematic Review**

**Presenter:** Erin O’Rorke, BS  
**Co-Authors:** Jaclyn Mauch, MD, MBE, Yusha Liu, MD, PhD, Jeffrey Friedrich, MD  
**Affiliation:** Washington State University

**PURPOSE:** Compassionate and effective communication is critical in fostering the patient-physician relationship, with implications for patient satisfaction, clinical outcomes, medical errors, and litigation. Interpersonal and communication