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**INTRODUCTION:** Despite extensive research efforts, no therapeutic agents are currently clinically indicated for the treatment of peripheral nerve injuries. Insulin-like growth factor 1 (IGF-1) is an ideal therapeutic candidate because it can accelerate axonal regeneration and also minimize the deleterious effects of prolonged denervation on muscle and Schwann cells. However, given its short half-life, a practical delivery system is needed to stabilize the protein and provide sustained release to target tissues. Using a novel encapsulation method, we demonstrated sustained release of bioactive IGF-1 from nanoparticles, in vitro, and improved nerve regeneration and functional recovery, in vivo. An optimized carrier system to maintain the nanoparticles at target tissue sites for the duration of drug release and avoid frequent redosing is now needed. We, therefore, developed a biocompatible nanofiber hydrogel composite that could be loaded with IGF-1 nanoparticles; fine-tuned its drug release kinetics in vitro and in vivo; and applied it in a chronic denervation median nerve model to assess its impact on functional recovery.

**METHODS:** An injectable nanofiber-hydrogel composite system (made of PCL nanofibers covalently bonded to hyaluronic acid) was developed by electrospinning. Its 3-dimensional structure was formulated to mimic that of fat extracellular matrix. The release kinetics of this delivery system were then optimized in vitro and in vivo (using ELISA and immunofluorescent staining) to achieve controlled release of IGF-1 at therapeutic levels (≈10 times EC50) for a prolonged period. Finally, using a chronic median nerve denervation model, we tested the effects of this modality on axonal regeneration, Schwann cell senescence, muscle atrophy, and muscle force.

**RESULTS:** The level of synthetic mimicry between our drug-delivery system and extracellular matrix fat was noted to confer high levels of biocompatibility as evidenced by a minimal inflammatory response 25 days postinjection. The release kinetics of IGF-1 from the nanofiber system were superior to other carriers (fibrin glue and saline). This system kept a significantly higher concentration of the injected IGF-1 nanoparticles next to the nerve and within muscle when compared to fibrin glue and saline. Functional analysis is currently ongoing.

**CONCLUSION:** We introduce a novel drug delivery system in which IGF-1 nanoparticles are combined with a nanofiber hydrogel carrier to provide sustained local concentrations of bioactive IGF-1 within target nerve and muscle. This therapeutic approach has the potential to improve functional outcomes via enhanced axonal regeneration and maintenance of denervated muscle and Schwann cells. IGF-1 and the polymer components of the engineered delivery system are currently used in Food and Drug Administration-approved formulations and devices, which will facilitate clearance of regulatory hurdles.

**REFERENCES:**
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**Self-propagating Autologous Skin Substrate for the Treatment of Cutaneous Defects: Clinical Series of the Utilization of a Novel Therapy for In Vivo Full-thickness Skin Regeneration**

**Presenter: Mark S. Granick, MD**

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**INTRODUCTION:** The rate of incidence of full-thickness chronic and acute dermal wounds is increasing and becoming a significant burden on healthcare systems. Large and complex wounds, which are unable to heal on their own, or reconstruction patient management strategies that have failed to fully close wounds are frequently treated by skin grafting, a procedure that is over 2-millennia old and is still being used as a conventional treatment option. Split-thickness skin grafts (STSGs) have not demonstrated neogeneration of dermal appendages (hair follicles, sweat and sebaceous glands, etc) or full-thickness skin replacement and consequently are prone to contraction, fibrosis, infection, and morbidity. Skin grafting requires surgeons and an operating room, which inherently produces a barrier to patients and the wound care community, including nonsurgical clinicians and midlevel providers. Here we investigate outcomes from a multi-institutional case series of early clinical use of a novel autologous homologous skin construct (AHSC) for complex wounds. A retrospective cohort study at 9 institutions between December 1, 2017, and July 23, 2018, of 15 patients (age range, 7–72 years) with wounds which...
had failed the clinical standard of care or complex wounds where modalities beyond skin grafting would have been required.

METHODS: Biomedical manufacturing of a small full-thickness skin harvest into the AHSC cell-tissue product followed by application into a clean wound bed. Wound closure, AHSC % take, volume restoration, hair-follicle presence, 2-point discrimination, bioimpedance, pigment propagation, Raman spectroscopy, and histomorphologic assessment of regenerated skin were conducted on regenerated skin specimen when possible.

RESULTS: The entire cohort of 15 patients had successful wound preparation and application of AHSC following full-thickness skin harvest. No repeat treatment with AHSC or STSG was required for AHSC-treated wounds. No donor site complications were reported. All patients had complete AHSC take and wound coverage at the time of follow-up (average, 4.0 ± 2.9 months). Two-point discrimination, bioimpedance, Raman spectroscopy, and histomorphologic analyses showed that AHSC-regenerated skin was analogous to native skin. Hair follicles were present in healed AHSC-treated wounds and were similar to native skin hair follicles on histomorphologic and Raman spectroscopy analysis.

CONCLUSIONS: This novel treatment method demonstrated regeneration of full-thickness skin with minimal donor site morbidity and was able to cover exposed underlying structures in complex wounds. Due to the observed results, utilization of AHSC can be considered as a therapeutic option for patients suffering from burns, complex wound reconstruction, chronic wounds, and traumatic defects. Therapy utilizing AHSC can be performed by surgical and nonsurgical trained clinicians and midlevel providers across a variety of care settings, including resource-poor areas. AHSC demonstrated safe and efficacious treatment for the complete closure of complex cutaneous wounds refractory to conventional therapies and cases involving open deep structures not amenable to reconstruction with STSGs alone.

A Novel Suture Training Device to Innovate the Surgical Curriculum in Medical School

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PURPOSE: Suture training is a critical component of the medical school curriculum because it serves as the first opportunity to learn proper technique. For those students who enter surgical specialties such as plastic surgery, early and repetitious practice is crucial in developing competence for residency. Currently, the majority of medical schools in the United States utilize suture training tools such as porcine feet or sponges to simulate human tissue. At our institution, satisfaction survey data have indicated dissatisfaction with the accessibility, quality, and longevity of these materials. Herein, the purpose of this project is to devise a novel tool for suture training using medical grade silicone and a 3-dimensional (3D)-printed stencil to create life-like, standardized tissue defects.

METHODS: Our plastic surgery department’s 3D printing laboratory developed a 10 × 5 × 2 cm mold. Using Blender software, tissue defects of varying depths, shapes, and sizes were included in the design. Different textures of silicone were poured into the mold and dyed with pigment to simulate the layers of skin, fat, and muscle. Plastic surgeons were consulted on material textures and layer depths. Study outcomes included a 30-question survey given to fourth year medical students following a 30-minute practice session with the silicone device. Questions measured texture characteristics and similarity of suture material to human tissue on a scale from 1 to 5 (5 being identical to human tissue). Additionally, the survey assessed limitations with current suture training models and impression of this novel device’s educational utility.

RESULTS: Twenty-five fourth year medical students participated in the study. All (n = 25) had sutured on human tissue an average of 46.0 (SD: 66.0) times. Additionally, all participants had sutured on porcine feet and sponges. The most common barriers to self-directed suturing practice were accessibility to material (n = 23) and material longevity (n = 20). The mean score for the silicone pad’s tissue layers (4.20, SD: 0.5) and “feel” (4.36, SD: 0.64) was significantly higher (P < 0.0001) than those for porcine feet (2.52, SD: 1.00; and 2.48, SD: 0.87, respectively) and sponges (1.21, SD: 0.51; and 1.38, SD: 0.65, respectively). Upon assessment of varying suturing techniques on each material, the mean scores for the silicone pad’s interrupted sutures (4.56, SD: 1.411), running sutures (4.30, SD: 0.62), and knot tying (4.44, SD: 0.711) were significantly higher (P < 0.0001) than those for porcine feet (3.08, SD: 1.21; 2.16, SD: 0.85; and 3.36, SD: 0.95, respectively) and sponges (1.75, SD: 0.85; 1.66, SD: 0.816; and 2.04, SD: 1.04; 2.16, SD: 0.85; and 3.36, SD: 0.95, respectively) and sponges (1.75, SD: 0.85; 1.66, SD: 0.816; and 2.04, SD: 1.04; 2.16, SD: 0.85; and 3.36, SD: 0.95, respectively) and sponges (1.75, SD: 0.85; 1.66, SD: 0.816; and 2.04, SD: 1.04; 2.16, SD: 0.85; and 3.36, SD: 0.95, respectively). All (n = 25) participants stated that the silicone suture pad was the best tool to practice suturing, and 92% (n = 23) stated that their suturing skills would be better or much better if the silicone pads replaced porcine feet and sponges during medical school.

CONCLUSION: Preliminary survey data demonstrate that the silicone suture pad generated with a 3D-printed stencil.