SESSION 12 QUICK SHOTS

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Micropatterned Microsphere Scaffolds: Optimizing the Performance of Engineered Dermal Substitutes

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PURPOSE: Current dermal replacement products perform sub-optimally in complex wound beds, such as those that have been irradiated or those with exposed hardware, mostly as a result of insufficient cell invasion and vascularization. We have previously observed more robust endothelial cell invasion of scaffolds containing a micropatterned matrix of differential collagen stiffness in a murine model when compared to collagen controls. Herein we compare the performance of our micropatterned microsphere hydrogels (MSS) to a widely utilized commercially available dermal replacement product in vitro and in vivo.

METHODS: Microspheres composed of 1% type I collagen 50-150um in diameter were created and encased in a 0.3% type I collagen bulk. For our in vitro study, polydimethylsiloxane (PDMS) wells of 4mm diameter and 2mm height were filled with the microsphere scaffolds. 3x2mm Integra® disks were placed inside PDMS wells. Non-microsphere containing 1% and 0.3% collagen scaffolds served as controls. A monolayer of endothelial cells was seeded onto this three-dimensional platform, activated for invasion with 1uM sphingosine-1-phosphate, and cultured for 3 days. The collagen hydrogels were then analyzed using confocal microscopy to quantify cell invasion. For our in vivo study, 8x2mm MSS disks were created, along with 1% and 0.3% collagen controls. 8mm Integra® disks were created, and the unilateral silicone layer was removed. A disk of each type was then implanted subcutaneously in the dorsum of 8-week old wild-type mice. The scaffolds were removed at 7 and 14 days, imaged, and analyzed with ImageJ.

RESULTS: Cells formed a confluent monolayer on the surface of the collagen disks, and migrated at a significantly higher rate into the MSS scaffold during 3 days of culture compared to control cultures as well as Integra® (142um MSS vs 45um Integra®, p<0.0001). Furthermore, in our in vivo study, MSS and Integra® both demonstrated robust cellular invasion spanning the depth of the scaffold at 7 and 14 days. Integra® had a lower cell density within the bulk at all depths with 705 cells per mm2 compared to 1,454 cells per mm2 in MSS at 14 days. Control collagen disks demonstrated minimal cell invasion and notable volumetric contraction.

CONCLUSION: Micropatterned differential stiffness microsphere hydrogels (MSS) promote significantly more cellular invasion both in vivo and in vitro when compared to a commercially available dermal substitute. This enhanced cellular invasion and accelerated neovascularization, which results solely from the unique architecture of the scaffolds, indicates superior efficacy in the rate of integration into the host wound bed and may result in decreased length of time between its application and definitive wound closure. Further, the significantly more robust cellular and vascular invasion and integration of these scaffolds indicates their applicability in the treatment of suboptimal wound beds, which is beyond the capability of currently available dermal substitutes.

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Autologous Fat Transfer for Scar Prevention and Remodeling (AFT-SPAR): Could Saline be as Efficacious as Fat?

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**PURPOSE:** Despite a lack of high-level evidence to support improved skin and scar quality, interest in autologous fat grafting for such continues to grow. This multi-center, double-blinded, randomized, placebo-controlled trial aimed to evaluate the effect of autologous fat grafting in patients with cutaneous scars.

**METHODS:** 17 patients with cutaneous scars affecting quality of life underwent Coleman-type fat grafting, completed with autologous fat/saline at a density of 1mL/cm². Outcomes were measured at baseline, and 6/12 months. Scars were subjectively and objectively evaluated using POSAS, durometer (hardness), cutometer (elasticity), colorimeter (wavelength absorbance), and single-observer histological analyses.

**RESULTS:** POSAS score totals, cutometer and durometer analyses were not significantly different between grafted (fat) and control (saline) scar appearance, elasticity or hardness at 0, 6, or 12 months, respectively. A single significant colorimetric difference in the a* color coordinate at 6 months (p = 0.037) was demonstrated, but was not durable at 12 months (p = 0.49). Single-observer histological 5-point scale ranking revealed no significant differences between AFT-treated and control scar vascularity or inflammation, nor epidermal thickness at baseline, six or twelve months. There was no statistically reliable difference of categorical evaluations, including vascular orientation, collagen organization and remodeling, and inflammation chronicity at the 0.05 level.

**CONCLUSION:** In conclusion, these results suggest that autologous fat transfer can improve the qualitative profile of scar from a patient and observer perspective, consistent with a large body of level-III and -IV scientific work. These qualitative improvements, however, are not corroborated by measurable differences in skin hardness, elasticity, color, or histology. Further rigorous, large volume, randomized-controlled trials are required to elucidate the quantitative effects of autologous fat transfer. Insight into these effects may yield the clinical treatment requisites, and subsequently, the realization autologous fat transfer’s potential for scar prevention and remodeling.

J.C. Brown: None. H. Shang: None. N. Yang: None. A.J. Katz:; The GID Group, Ltd..

**QS33**

**Composite-Mediated Angiogenesis for Soft Tissue Regeneration in a Large Animal Defect Model**

**Michelle Seu, BA, Xiaowei Li, PhD, Zhengbing Zhou, MD, Russell Martin, PhD, Kevin Colbert, MS, Chi Zhang, BS, Hai-Quan Mao, PhD, Justin Sacks, MD, MBA**

**Johns Hopkins School of Medicine, Baltimore, MD, USA**

**PURPOSE:** Soft tissue defects from aging, trauma, or congenital malformation affect millions of people each year. Existing options for soft tissue restoration have significant drawbacks: autologous flaps cause donor-site defects; prosthetics are prone to foreign-body response; and fat grafting and dermal fillers are limited to small volume defects and provide transient volume restoration. To address these limitations, we developed a nanofiber-hydrogel composite to promote angiogenesis and cellular infiltration for soft-tissue regeneration, specifically in a large defect.

**METHODS:** We have developed a novel composite scaffold resembling the architecture and mechanical properties of adipose tissue by interfacial bonding of biodegradable poly (caprolactone) fibers with hyaluronic acid. To examine the superior ability of our composite for soft tissue regeneration, we aim to create a large soft tissue defect model within the inguinal fat pads of female New Zealand White rabbits. Histology, immunohistochemistry, and bromodeoxyuridine (BrdU) assay were performed to investigate the ability of our composite to regenerate soft tissue in this large defect model.

**RESULTS:** We previously demonstrated robust angiogenesis and host cell infiltration within our composite after subcutaneous injection into Lewis rats. We successfully developed a large soft tissue defect model by designing standardized lesions in the rabbit inguinal fat pad. At post-operation day (POD) 7, we found that a large number of macrophages infiltrated our composite, many of which were polarized toward the M2 or “pro-healing” macrophage phenotypes; such macrophages could promote the vascular ingrowth at later timepoints. Now, using our novel inguinal fat pad model, we are testing the long-term effects of our composite for soft tissue regeneration.

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