patient demographic factors and intraoperative parameters, were included in a multivariate analysis for outcomes of fat necrosis, abdominal wounds, and abdominal bulge or hernia. These results were reported as Odds Ratios (OR) with 95% Confidence Intervals. Univariate analyses were utilized to confirm that potentially confounding pre-surgical and intraoperative factors amongst each of the three primary outcome variables were sufficiently equivalent. Any wound requiring local wound care after 2 weeks was characterized as a minor abdominal wound, whereas major abdominal wounds were defined as wounds requiring return to the operating room.

RESULTS: 409 total DIEAP flaps were included with an average 18.5-month follow-up: 14.4% had fat necrosis, 21.2% had a minor or major abdominal wound, and 6% had an abdominal bulge or hernia. Analysis showed increased odds of fat necrosis with increasing flap weight (OR 1.002 per 1g increase, p<.001), and earlier year of surgery (OR 2.324 for 2010–2013 vs. 2014–2016, p=.02), and decreased odds of fat necrosis with lateral or both-row perforators vs. medial row (OR 0.303, .0229, p-value=.0013), and neoadjuvant chemotherapy (OR 0.384, p=.016). Perforator flow rate/caliber and number of perforators did not affect fat necrosis. However, upon subgroup analysis on flaps with fat necrosis, we found that there was a significant difference in weight between single perforator flaps and multi-perforator flaps (789g vs. 983g respectively, p=.048). There was an increased odds of having abdominal wounds with smoking (OR 1.869, p=.02), hypertension (OR 1.720, p=.04), and increasing flap weight (OR 1.001 per 1g increase, p<.01). BMI was not a significant factor for abdominal wounds when controlled by flap weight in the multivariate analysis. Increased odds of abdominal bulge/hernia were seen with a return to the OR same hospital stay (OR 5.922, p<.01), and with lateral/both row perforators vs. medial row (OR 3.01, p=.058).

CONCLUSIONS: Our analysis of DIEP flaps shows surgeon experience reduced the odds of fat necrosis, while heavier flap weights increased these odds. Moreover, adding lateral row perforators may decrease fat necrosis at the potential cost of increasing abdominal bulges. While perforator number was not a significant predictor of fat necrosis in the multivariate analysis, the subgroup analysis may indicate that there is a higher allowable threshold of flap weight before fat necrosis occurs with multi-perforator versus single perforator DIEP flaps.

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Corneal Neurotization Improves Ocular Surface Health And Prevents Corneal Scarring In A Rat Model Of Neurotrophic Keratopathy

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PURPOSE: Neurotrophic keratopathy (NK) is a degenerative corneal disease that develops in patients with absent corneal sensation and innervation. In the absence of innervation, the corneal epithelium is susceptible to breakdown resulting in persistent corneal ulcerations, scarring and progressive vision loss. In severe cases, patients develop corneal perforation and blindness. Standard ophthalmic therapy fails to address the underlying loss of nerve-derived trophic support, and thus many patients continue to develop vision loss despite optimal ophthalmic management. Clinical studies have suggested that reinnervation of the cornea with corneal neurotization improves corneal sensation, ocular surface health and maintains vision in patients with NK. While promising, clinical studies are limited by the rarity and heterogeneity of NK and the inability to harvest tissue. The purpose of this study was to use a novel rat model of NK and corneal neurotization to determine whether corneal reinnervation prevents breakdown of the corneal epithelium and decreases corneal scarring.

METHODS: Using a novel rat model of NK, the corneal innervation of the left cornea was ablated in ten rats; five were randomized to receive treatment with corneal neurotization after ablation. Tarsorrhaphy of the left cornea was performed in all rats to protect the corneal surface. Four weeks after ablation, the tarsorrhaphy was removed. Each rat was assessed daily with standardized photographs under normal light and with a Wood’s lamp/fluorescein staining to assess corneal scarring and epithelial breakdown respectively. Area of corneal ulceration was analyzed as a percentage of the entire cornea. Data was analyzed using a Fisher’s exact test or Student’s t test where appropriate.

RESULTS: Seven days after removal of the tarsorrhaphy and exposure of the left cornea, a significantly larger percentage of the corneal surface in rats without corneal neurotization treatment was ulcerated in comparison to rats.
with corneal neurotization (30.1 % ± 12.7 vs. 0.0 % ± 0.0, p < 0.001). All rats without corneal neurotization treatment developed progressive corneal epithelial breakdown, while only one rat with corneal neurotization developed a corneal ulceration that healed within one week (p = 0.047). Eighty percent of rats without corneal neurotization developed a corneal perforation after tarsorrhaphy removal, in comparison to no rats with corneal neurotization (p = 0.008). Corneal neurotization treatment also significantly decreased corneal scarring. Contains representative images demonstrating significant corneal scarring, perforation (A) and ulceration (B) in a rat without corneal neurotization seven days after tarsorrhaphy removal and improved ocular surface health in a rat treated with corneal neurotization (C/D).

CONCLUSION: Corneal neurotization decreases breakdown of the corneal epithelium in rats with NK and prevents perforation and scarring. This data demonstrates that axons reinnervating the cornea improve corneal epithelial maintenance and repair, although further research using this model is required to investigate the underlying mechanism. These findings support clinical studies showing that corneal neurotization improves ocular surface health and preserves vision in patients with NK.

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FK506 Binding Protein Expression Within the Injured Peripheral Nerve

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PURPOSE: The mechanism of action of FK506 on peripheral nerve is still unknown despite the growing interest in local FK506 delivery for enhancing axon regeneration. In this study, we analyzed the expression of FK506-binding proteins (FKBPs), a family of immunophilins that act as receptors for FK506, within the injured peripheral nerve and following local FK506 administration. We investigated the expression of FKBP-12 and FKBP-52 which have been shown to mediate immunosuppressive and neurotrophic properties of FK506 within the central nervous system, respectively.

METHODS: Using transgenic Thy1-GFP+ rats expressing green fluorescent protein (GFP) to visualize peripheral axons, the sciatic nerve was transected and repaired either with or without local FK506 delivery using a particulated FK506 delivery system. In a sham group, the sciatic nerve was not injured. Seven days post repair, immunostaining for FKBP-12 and FKBP-52 proteins, Schwann cells (S100), and macrophages (ED-1) was performed to determine the localization and/or co-expression of the proteins within the longitudinal sections of injured and intact sciatic nerve.

RESULTS: With and without FK506 local delivery, FKBP-52 was specifically expressed in Schwann cells in both the proximal and distal stumps adjacent to the site of sciatic nerve injury, 7 days post-repair, as seen in longitudinal nerve sections. FK506 delivery promoted an obvious elevation of Schwann cell proliferation in the distal nerve stump as compared to the nerves without FK506 delivery. FKBP-52 expression was minimal in the regions of the proximal and distal nerve stumps not adjacent to the injury. FKBP-12 was mainly expressed in the vacuoles of the degenerated nerve fibers in the distal nerve stump, with minimal expression in the proximal nerve and at the site of nerve injury. Both FKBP-12 and FKBP52 expression were not detectable within the intact nerves.

CONCLUSION: The mechanism of action of FK506 on nerve regeneration has not been completely characterized. Our findings suggest that FK506 acts on the Schwann cells at the site of injury, accounting, at least in part, for the profound enhancement of nerve regeneration when applied locally. FKBP-52 expression within the injured peripheral nerve. FKBP-12 expression within the injured peripheral nerve.

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Successful Control of Virtual and Robotic Hands using Neuroprosthetic Signals from Regenerative Peripheral Nerve Interfaces in a Human Subject

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