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PURPOSE: Peripheral nerve injuries are common and have debilitating effects, including loss of nerve and muscle function, painful neuropathies, and impaired sensation. Current therapies do not address a major challenge of peripheral nerve regeneration: the atrophy or loss of Schwann cells (SC), which are the principal glia cell that support peripheral neurons. Recent interest in peripheral nerve regeneration has focused on using stem-cell derived SC for cellular replacement therapy. Mesenchymal stem cells, including adipose and bone marrow, have been proposed to be a good source of SC. However, bone marrow biopsies are invasive, and adipose-derived stem cells have been shown to rapidly dedifferentiate in the absence of stimulating media. Consequently, there is a pressing need to identify alternative mesenchymal stem cell sources for SC cellular replacement therapy to improve peripheral nerve regeneration. The purpose of this study was to assess the impact of muscle-derived stem cells (MDSCs) in augmenting nerve regeneration and improving muscle function after nerve trauma.

METHODS: Our lab derived SC-like cells from GFP+ muscle-derived stem cells (GFP+ MDSCs) to investigate the potential of SC replacement therapy in the promotion of peripheral nerve regeneration. To assess the in-vivo effects of GFP+ MDSC-derived SC-like cells (GFP+ iMDSC) on peripheral nerve regeneration, we used a median nerve injury model developed in our laboratory. Four groups (n=5 per group) of rats with median nerve injuries were examined: (1) Group-1 animals were treated with intraneural PBS after nerve trauma (negative control); (2) Group-2 were naive controls; (3) Group-3 animals were treated with intraneural GFP+ MDSCs; (3) Group-4 animals were treated with GFP+ iMDSCs. All animals underwent weekly upper extremity functional testing. Five weeks post-treatment, the rats were sacrificed, and the median nerve and extrinsic finger flexor muscles were harvested for nerve histomorphometry, nerve myelination, muscle weight & atrophy, GFP+ MDSC engraftment and proliferation, and neuromuscular re-innervation analyses.

RESULTS: Immunofluorescence studies of the median nerve demonstrate that GFP+ iMDSC remain stably transformed in-vivo 5 weeks post injection, and localize in the endoneurium of the median nerve. GFP+ iMDSC were found to co-express S100 (SC cell surface marker) and Ki-67 (a cellular proliferation marker) in vivo. Median nerve regeneration was higher in iMDSC-treated animals when compared to untreated controls (G-ratio: group 1 [0.47] vs group 4 [0.512], p = 0.2195), though this was not statistically significant. iMDSC therapy improved muscle re-innervation (p = 0.033), and decreased muscle atrophy (p = 0.0143). Lastly, iMDSC-treated animals demonstrated greater functional muscle recovery when compared to untreated control (hand grip: group-1 [0.91 N] vs group-4 [3.38 N], p < 0.0001) at five-weeks post-treatment.

CONCLUSIONS: Schwann-Cell like cells (iMDSCs) derived from muscle mesenchymal stem cells decrease denervation muscle atrophy and improve neuromuscular re-innervation, and subsequent functional outcomes after upper extremity nerve trauma in rodents.

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Wide Propeller Posterior Thigh Flap to Reconstruct Perineal Defects post Abdominoperineal Resection

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PURPOSE: With increasing popularity of laparoscopic and robotic approaches to colectomy during abdominoperineal resection (APR), now thought to account for 40% of all cases (Johnstone et al. 2017), thigh based flaps are becoming the only option for reconstruction of the perineal defect.
Among these the Posterior Thigh Flap (PTF) has historically fallen short of Vertical Rectus Abdominis Muscle (VRAM) flap due to a higher complication rate (43.7% vs 35.8) with wound dehiscence caused by critical distal vascularization being the most common (5–29.9). (Saito et al, 2014; Winterton et al, 2013; Arnold et al, 2012) This study hypothesized that a better understanding of the flap vascularity and consequent modification of the flap design could improve the outcomes.

METHODS: Anatomic dissections were conducted on 14 gluteal and posterior thigh regions of 7 fresh cadavers. Specimens’ popliteal arteries were ligated, and red latex (Carolina Biological, Burlington, NC) was injected from the aorta just above its terminal bifurcation. The course and distribution of Inferior Gluteal Artery (IGA), descending branch of IGA, Profunda Femoris Artery (PFA) and perforators directed to the flap was recorded and mapped. The Y-axis was represented by a vertical line going from the ischial tuberosity to the medial femoral condyle and the X-axis was represented by a perpendicular to the Y-axis passing through the ischial tuberosity. The diameter of each vessel was measured with a caliper and recorded. A normalized map of the perforators was created by averaging the XY measurements after converting them to percentages of the distance between the anatomical landmarks. A Wide Propeller Posterior Thigh Flap (WPTF) including the width of the thigh was designed to increase the reach and survival of the flap. Nine patients underwent reconstruction of the perineal defect following APR with the WPTF.

RESULTS: The descending branch of the IGA was present in 10 specimens (71.4%), with an average caliber of 2.3 ± 0.2mm. In 4 (28.6%) specimens the main arterial axis of the flap derived from PFA with a main caliber of 2 ± 0.5mm. The origin of the descending branch of the IGA was located at 42 ± 6.5mm (X) and 3 ± 15.8mm (Y). The first perforating branch originating from the PFA was 106.6 ± 22.3mm (X) and 56.4 ± 21.2mm (Y); the second PFA perforator originated at 111.6 ± 17.4mm (X) and 102.6 ± 46.2mm (Y). All flaps survived completely. One WPTF was sufficient to reconstruct the defect. In two cases the flap was based on the first PFA perforator. Three patients presented complications: 1 urocutaneous fistula because of residual cancer, 1 delayed wound healing at the lateral gluteal region and 1 coccygeal osteomyelitis, treated with debridement.

CONCLUSIONS: The descending branch of the IGA is absent in a significant number of patients. In these cases, elevation of a narrow flap to allow direct closure of the donor site can cause distal flap necrosis. Implementation of the propeller design and routine harvest of a wide flap that includes the perforators from PFA can increase the survival and versatility of the flap.

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Quantifying Lymphatic Contraction Using ICG Lymphography: A Novel Approach to Lymphedema Assessment

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PURPOSE: Indocyanine Green (ICG) lymphography helps detect superficial lymphatic channels, and has become an instrumental component of lymphedema diagnosis and pre-operative planning. ICG lymphography’s signal intensity can also be used to calculate contraction frequency. This study aims to describe changes in lymphatic contractions in lymphedema using ICG lymphography.

METHODS: ICG lymphography videos were recorded over 3 minutes for both unaffected and affected limb in 4 subjects with upper extremity lymphedema. Videos were then stabilized in ImageJ and then StackReg plug-in. A region of interest was placed on a clear lymphatic vessel in each video and the signal intensity was recorded for the duration of the video. Peaks in signal intensity were used to calculate the contraction frequency per min. This process was performed for lymphatics of the dorsal hand/foot and forearm/calf.

RESULTS: Four subjects with upper extremity lymphedema presented with ILS Stage 1–3 and all underwent axillary lymph node dissection for their treatment of breast cancer. The mean contraction frequency of lymphatics in the dorsum of the hand/foot in the unaffected limb was 0.9 and the affected limb 2.8 (p=0.12). The mean contraction frequency of lymphatics in the forearm/calf in the unaffected limb was 1.3 and the affected limb 0 (p=0.04).

CONCLUSION: This is the first time ICG lymphography was used to measure lymphatic contraction frequency. The