A Markov Analysis of Surgical vs Medical Management of Chronic Migraines
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INTRODUCTION: Refractory chronic migraine (CM) is a common and debilitating neurologic condition affecting more than 8 million people in the US. It is associated with billions of dollars in lost productivity annually. Novel medical (anti-calcitonin gene-related peptide antibodies) and surgical treatment modalities have emerged for CM in recent years. The current study investigated the cost-utility of surgical vs medical management of refractory CM.

METHODS: A Markov cohort analysis using hybrid Monte Carlo patient simulation was performed to compare surgical decompression vs erenumab for the treatment of refractory CM in adults. Both societal and payer perspectives were considered. Primary model outcomes included incremental cost-effectiveness ratio, or cost per quality-adjusted life year gained.

RESULTS: During a 5-year period, migraine operation was associated with a 0.2 increase in quality-adjusted life years per patient compared with erenumab. In terms of costs, the results demonstrated a $19,337 decrease in direct medical costs, a $491 decrease in indirect costs (productivity lost) for the operation cohort compared with erenumab. Because operation improved quality of life and decreased costs compared with erenumab, even when considering revision operation needs, operation was the overall dominant treatment in terms of cost-effectiveness. Sensitivity analyses demonstrated that operation was cost-effective compared with erenumab when patients required therapy for at least 1 year.

CONCLUSION: Surgical deactivation of migraine trigger sites can pose a cost-effective approach to treating refractory CM in adults. This is especially the case when patients are anticipated to require therapy for more than 1 year.

Acellular Dermal Matrix Modulation of the Peri-Prosthetic Breast Microenvironment During Breast Reconstruction
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INTRODUCTION: Capsular contracture complicates 10% to 70% of implant-based breast reconstructions, resulting in deformity, multiple revisionary operations, and a considerable economic burden. Acellular dermal matrix (ADM) has been proposed as a method to reduce capsular contracture and is used in 75% of breast reconstructive operations, despite limited understanding of its mechanism of action. The aim of this study was to determine how the presence of ADM modulates the peri-prosthetic fibrotic microenvironment.

METHODS: At first-stage tissue expander placement, the tissue expander was incompletely covered in ADM (Figs. 1A, 1B). After
informed consent, capsule specimens were obtained from the peri-prosthetic capsule that develops adjacent to the tissue expander ("native capsule"), and from the capsule that develops adjacent to the ADM ("ADM capsule") at the time of tissue expander implant exchange. Capsule specimens then underwent histologic, single-cell RNA sequencing and proteomic analysis.

RESULTS: Eighteen paired capsule specimens were analyzed. Mean age was 51 years and mean time to implant exchange was 7 months. Histologic examination revealed significantly increased density of elastin fibers in the ADM vs native capsule specimens (**p < 0.05) (Fig. 1C). Using single-cell RNA sequencing, we identified heterogeneity among fibroblasts identified from native vs ADM capsule (Figs. 1D, 1E). Proteomic analysis revealed significant increases in cytokine concentration (CCL 8, CXCL13, CCL4, CXCL10, and CXCL12) in ADM relative to native capsule specimens (p < 0.05, data not shown).

CONCLUSION: Our findings support that the presence of ADM induces changes in the connective tissue matrix, fibroblast heterogeneity, and niche signaling of the peri-prosthetic microenvironment relative to native capsule.

**Adipose Precursor Cell-Embedded Collagen Gels Attenuate Inflammation and Improve Tissue Perfusion in Cutaneous Wounds**

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INTRODUCTION: Augmentation of wound tissue with progenitor-cell populations can provide a means to achieve tissue regeneration after injury. Collagen gels present a potential delivery method for biologic therapies such as these. Adipose precursor cells (APCs) have previously been defined by flow-assisted cell sorting and demonstrate the ability to generate adipocytes and potentially other cell types. The use of APCs in wound healing has not been explored previously.

METHODS: CD1 nude mice underwent full-thickness excisional dorsal cutaneous split wounds. APCs were identified and sorted from the harvested homogenized adipose depots of C57Bl/6 mice by flow-assisted cell sorting (Lin–, Sca1+, CD34+, and PDGFRα+). Sorted APCs were embedded into collagen gels in 96-well plates (100,000 cells/well). Gels were placed into wound defects immediately after wounding. Gels without APCs and wounds without gels were used as controls. Monitoring was carried out via photography, dermatoscopy, and scanning laser Doppler flowmetry to assess perfusion between groups. Wounds were harvested for histologic, cytokine, and protein evaluation.

RESULTS: APC-treated wounds exhibited a broadly reduced cytokine profile compared with control wounds (see Fig. for values). Scanning laser Doppler flowmetry perfusion analyses demonstrated that the mean perfusion of healed wounds was 80.40% of baseline in APC gel-treated wounds compared with 62.25% in control gel wounds.

CONCLUSION: APCs represent an intriguing cell type worthy of further investigation in relation to biologic capacity and potential in regenerative medicine. APC-embedded collagen gels can also lend themselves to bioengineering approaches in which chemical or mechanical means to control APC fate can be applied ex vivo or in vivo to alter cell progeny and tissue phenotype.

**Wound Healing Progression, APC-Gel vs. Control Gel:**

![Figure](image_url)

**Increased rate of healing and epithelialization exhibited in APC-Gel treated wounds**

**Denervation During Mandibular Distraction Osteogenesis Results in Impaired Osteogenesis**

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INTRODUCTION: Craniofacial distraction osteogenesis (DO) continues to be marred by complications, necessitating surgical revision. Mandibular DO is mediated by skeletal stem cells (SSCs), which enact bone regeneration via neural crest reactivation. Peripheral nerves are essential to progenitor function during development. We question whether denervation impairs mandibular DO. Harnessing the underlying biology of nerve-dependent DO can aid clinical innovation in craniofacial skeletal regeneration.

METHODS: Eight-week-old C57Bl6 mice were divided into 2 groups: DO with inferior alveolar nerve (IAN) denervation ("DO-Den") and DO with IAN intact ("DO-Inn"). An IAN segmental defect was created in the DO-Den cohort after mandibular osteotomy (Figs. 1A, 1B). The IAN was protected in Do-Inn. After a latency period, all mice underwent gradual DO. Specimens were harvested at postoperative days (PODs) 10, 15, and 23 for analysis of the stem and progenitor cell populations using fluorescence-activated cell sorting and at POD 43 for micro-CT and histologic analysis.

RESULTS: DO-Den demonstrated reduced histologic osteogenesis relative to DO-Inn, which was evident on micro-CT at POD 43 (*p = 0.018) (Fig. 1C). Furthermore, DO-Den regenerate had significantly reduced mSSCs present at PODs 10, 15, and 23 relative to DO-Inn (*p = 0.0032, *p = 0.0099, and *p = 0.0111, respectively) (Fig. 1D, 1E). Transcriptional alterations...