expression which parallels primary fibroblast expression levels (4.61 ± 1.8-Fold, 0.027 ± 0.03-Fold, and 0.22 ± 0.17-Fold respectively, p<0.05). dFib cells also showed increased RNA expression of healthy ECM marker genes Fibronectin (0.93 ± 0.28-Fold, p<0.05) and Collagen I (4.67 ± 1.4-Fold, p<0.05), and Elastin (0.93 ± 0.63-Fold, p<0.01) compared to primary fibroblasts (0.62 ± 0.16-Fold, 2.21 ± 0.86-Fold, and vs. 0.27 ± 0.08-Fold respectively). Proliferating dFib cells further showed differential expression compared to fibroblasts for the scar tissue markers αSMA (0.011 ± 0.006-Fold vs. 0.024 ± 0.012-Fold, p<0.05), Collagen III (0.72 ± 0.2-Fold vs. 0.26 ± 0.11-Fold, p<0.001), and TIMP-1 (2.33 ± 0.63-Fold vs. 0.6 ± 0.18-Fold, p<0.001). Scratch test assays revealed dFib cells maintain smaller defects throughout the healing time course with more cells migrating into the defect. Finally, dFib cells closed the defects significantly faster than primary fibroblasts (32 ± 12.85 hours vs. 64 ± 13.85 hours, p<0.01). Similarly, Masson’s Trichrome staining demonstrates smaller defects after 3 weeks of recovery using dFib cells compared to primary fibroblast (1.04 ± 0.13mm² vs. 1.29 ± 0.39 mm²) however, this difference did not reach significance (p=0.16).

CONCLUSION: ASCs can be differentiated into fibroblast-like cells. These cells produce a robust ECM more similar to healthy skin as opposed to the scar tissue produced by primary cutaneous fibroblasts. These cells migrate into and close in vitro scratch defects more quickly than primary cutaneous fibroblasts and tend toward smaller long-term wounds. ASC differentiated fibroblasts show initial promise for regenerative medicine applications and should be investigated further for optimization in cutaneous wound healing and other therapeutic applications.

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Multi-Scale Modeling of Tissue Expansion: Genome Expression Patterns in the Acute Stretch Scenario

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PURPOSE: Despite decades of experience, tissue expansion (TE) often has high complication rates. Creating a reliable model of skin growth would allow for data-driven optimization of expansion protocols and decrease complication rates if used to plan the expansion. The changes in signaling pathways observed on the transcriptional level in skin under stretch are not well understood. Therefore, we combined mathematical models of skin under stretch with the biological response measured by gene expression levels and with histological assessment of skin structure with the goal of creating a comprehensive multi-scale model of tissue expansion.

METHODS: Five animal models (Yucatan minipigs) underwent 10 expansion protocols. Each animal was tattooed with 4 grids, 2 of which served as controls. Expanders were placed subcutaneously. The expansion protocols varied regarding volume of fill (60 or 30 cc), timing (1 hour, 24 hours, 3 days, or 7 days prior to expansion), or single versus 2 fills. 3D photography was captured for isogeometric analysis to measure skin growth and stretch. Total RNA from individual biopsies was isolated, gene expression was estimated using RNA-Seq (64 samples), then differences in gene expression were calculated and verified by qRT-PCR.

RESULTS: Statistically significant changes in gene expression levels correlated to the amount of stretch were obtained for each model. Illustrates the amount of stretch and growth attained prior to sacrifice, as measured by isogeometric analysis for model #3. The apex of the expander (orange) represents the highest stretch and was correlated with the largest changes in gene expression. The genes most dramatically activated by stretch include MMP1, SAA3, ILB1. PDLIM and RHOF were two of the most consistently down-regulated genes. The identified genes include well-known responders to the mechanical force (e.g. MMP1 or TNC), as well as completely new genes with no described role in skin adaption to stretch, presenting a new area for further study.

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Represents the change in selected genes’ expression (as fold change) in the same model, showing the level of expression at the apex (i.e. area of maximal stretch), the side, and base of the expander compared to contralateral controls. These data show correlation between the magnitude of stretch and fold change in gene expression. Subsequent isogeometric analysis provides the tools for determination of the proportion of tissue growth attributable to expansion versus elastic stretch or animal growth.

CONCLUSION: We have correlated skin growth with changes in gene expression levels and the mathematically calculated mechanical forces applied to each tissue expansion scenario tested. With the addition of histological analysis, we will attain a multi-scale model of skin expansion. Future translational studies will aim to guide tissue expansion protocols in humans to minimize complications and maximize tissue growth.

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Reflexive Visual Inspection of Cleft Lip Faces - Analysis of Lookzone Focus Over Time

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PURPOSE: Humans reflexively inspect faces. Elucidating facial lookzone focus over time of cleft lip faces may offer insight into the early visual processing of facial normality/abnormality. By delineating the time sequence of visual impression formation, surgeons and their patients may pinpoint the most salient facial features so as to better direct prioritization of surgical reconstruction.

METHODS: 179 experimental and 179 control facial images were obtained from the senior author’s practice. Experimental images included 41 individuals with repaired cleft lip, and a variety of other facial diagnoses. 720 subjects rated the images for attractiveness. Twenty standardized lookzone regions were mapped onto each facial image. A separate group of 402 subjects observed the images while an infrared eye-tracking camera continuously recorded their eye movements for 6 seconds. R console TraMineR was utilized to analyze the time sequence data. The gender and personal history of observer facial deformity was recorded. OUTCOMES MEASURED: Image attractiveness was rated on a 1–7 Likert scale. Total number of eye fixations within different lookzone regions was recorded continuously over the 6 seconds viewing period.

RESULTS: (i) All observers start focusing on the face after 500ms, and on the cleft defect 200ms after facial scanning, but they revert to the control pattern of focusing on the peri-orbital area after 2400ms. (ii) Male maintain their focus on cleft defect much longer than females (3600ms vs 1800ms) (iii) Observers with family history of facial deformity maintain their focus on cleft defect throughout the 6000ms viewing period, while those without facial history lose focus on the cleft defect after 2000ms. (iv) The attractiveness ratings of the cleft images had no discernable impact on the sequence of reflexive inspection of the cleft images, except for the most attractive cleft images, for which the lip was not focused upon at all (but rather the nasal deformity). (v) Laterality of the cleft deformity did not impact the sequence of facial inspection, but bilateral clefts were less of a visual draw, with reversion to a control pattern of inspection early, versus a more continued focus on the cleft defect for unilateral clefts.

CONCLUSION: Observers are reflexively drawn to the abnormal region of cleft faces upon immediate exposure, before reverting to a more natural pattern of facial inspection after about 2.5 seconds. Unilateral clefts - and cleft faces that are considered less attractive overall - induce a more sustained fixation within the perioral region. A personal history of facial deformity in general appeared to heighten sensitivity for cleft deformity. Males focused longer on the cleft defect compared to females.

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Improving Post-Operative Monitoring of Autologous Breast Reconstruction: A Novel, Oxygen-Sensing Liquid Bandage First-in-Human Trial

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