METHODS: One hundred fifty-eight patients with 277 expanded skin cases during 2010 to 2014 were reviewed and photograph-evaluated for the expanded skin texture and regenerative condition. Overall texture of the expanded skin flaps (Good, Fair, Poor) were evaluated and documented by senior attending surgeons. The occurrence of five indications of skin regeneration limitation, including skin thickness, skin color, stretch mark, vessel varicose and skin lesion, during skin expansion were recorded. The correlation of indications to overall skin regeneration condition was statistically analyzed.

RESULTS: Among the 277 retrospective reviewed expansion cases, the ratio of skin deterioration showed significant differences between expansion sites (p<0.01). The scalp and forehead expanded skin had best skin condition. Skin deterioration cases was most commonly seen in neck and back expansion cases. The occurrence of each indication was different in different locations. The odds ratio (OR) of skin color, stretch marks, varicose vessels, thickness and skin lesion between Good and Poor was 44.97, 5.09, 22.26, 89.79, 4.61 respectively (all p<0.001).

CONCLUSION: The results from this retrospective study showed that skin color, stretch marks, varicose vessels, thickness and skin lesion were tightly related to the skin regeneration capacity. Integrated evaluating could help predict the regeneration capacity of expanded skin.

46.

MODULATING TAK1 SIGNALING TO ENHANCE SCAFFOLD AND CELL-FREE CALVARIAL HEALING

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PURPOSE: Bone tissue engineering remains hampered by inadequate scaffold design and regulatory limitations on autologous cell use. We developed a novel system to silence and reactivate TGF-β1, which mediates TGF-β1 and BMP2. We hypothesize that Tak1 can be initially silenced to increase local cell proliferation followed by Tak1 reactivation to stimulate bone differentiation, providing scaffold and cell-free bone healing.

METHODS: We developed a novel dual-recombinase system (Cre/lox; FLP/FRT) to allow silencing and reactivation of Tak1. Critical sized-calvarial defects were performed and mice received: 1. Ad.LacZ (control) 2. Ad.Cre (knockout) or 3. Ten days Ad.Cre (knockout) followed by Ad.FLP (reactivation) to modulate Tak1 expression. Cellular proliferation and differentiation were quantified histologically. MicroCT was used to quantify bone healing. In vitro studies with calvarial osteoblasts confirmed these findings.

RESULTS: Loss of Tak1 with Ad.Cre increased cellular proliferation (Ki67 immunostaining; Fig. 1A) while suppressing osteogenesis (Osterix immunostaining) within the defect. Ad.Cre followed by Ad.FLP stimulated increased cell proliferation followed by enhanced osteogenic differentiation. Timed Tak1 suppression followed by Tak1 activation improved bone healing compared to controls by microCT quantification. In vitro results (Fig. 1B, 1C) with calvarial osteoblasts were consistent with in vivo findings.

CONCLUSION: These results validate that TAK1 can be mediated therapeutically to first potentiate cellular proliferation and then stimulate osteogenic differentiation to maximize bone healing without introducing exogenous scaffolds or cells.

47.

DIPYRIDAMOLE-CONTAINING 3D-PRINTED BIOACTIVE CERAMIC SCAFFOLDS FOR THE TREATMENT OF CALVARIAL DEFECTS: AN EXPERIMENTAL STUDY IN SHEEP

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PURPOSE: Previous studies have demonstrated the efficacy of 3D-printed bioactive ceramic (3DBC) scaffolds in the restoration of long bone defects. The objective of this study is to test the efficacy of the osteogenic agent dipyridamole on 3DBC scaffold-mediated healing of calvarial defects using a sheep model.

METHODS: Custom 3DBC scaffolds were either coated with collagen (control) or coated with collagen and immersed in 100 μM dipyridamole (DIPY). Sheep (n=5) were subjected to 4 trephine-induced (12 mm diameter) calvarial defects with immediate scaffold placement via two separate operations: anteriorly (control) and posteriorly (DIPY) on the right (3 weeks healing) and left (6 weeks healing) sides of the calvarium. Following sacrifice, defects were evaluated through microcomputed tomography and histologic analysis for bone, scaffold, and soft tissue quantification as a function of time in vivo. Statistical analysis was performed by a mixed model and significance was defined by p<0.05.

RESULTS: Histologic evaluation demonstrated no signs of inflammation within the defects. Significantly higher percentage of bone formation (p=0.02) was observed for the DIPY-containing scaffolds. A significant increase in bone percentage was observed from 3 to 6 weeks in vivo irrespective of scaffold group (p<0.01). Differences between groups were more pronounced at 6 weeks in vivo (~90% more for DIPY). No exuberant or ectopic bone formation was observed in either experimental group.

CONCLUSION: Defects treated with dipyridamole-containing 3DBC scaffolds demonstrated significantly improved bone generation without histologic evidence of inflammation or ectopic bone formation.

48.

STEM CELLS HARVESTED FROM BONE MARROW AND ADIPOSE TISSUE DEMONSTRATE DIFFERENTIAL HEALING MECHANISMS AND UNION RATES IN A MURINE MODEL OF IRRADIATED MANDIBULAR FRACTURE REPAIR

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PURPOSE: The accessibility of adipose-derived stromal cells (ASCs) over bone marrow stromal cells (BMSCs) warrants investigation into their utility for bone healing. The goal of this study was to compare the mechanisms through which ASCs and BMSCs exert their effect on fracture healing. We hypothesize that ASCs will enhance fracture healing by improving vasculogenesis, while BSMCs will directly affect osteogenesis.

METHODS: Lewis rats were radiated (35Gy) and underwent mandibular osteotomy with implantation of BMSCs (n=12) or ASCs (n=16) marked with Green fluorescent protein (GFP). MicroCT and Confocal microscopy evaluated 40-day union rates and the contribution of ASCs/BMSCs to the bone regenerate. Quantitative PCR of ASCs/BMSCs compared expression of osteogenic and vasculogenic genes. Co-culture of ASCs (n=3) or BMSCs (n=3) with human umbilical vein endothelial cells (HUVECs) was performed to measure tubule formation/vasculogenesis.

RESULTS: ASC-implantation resulted in higher union rates than BMSC-implantation (94% vs. 66%), and contributed indirectly to fracture healing, as GFP was not visualized. (Fig. 1A) BMSCs expressed osteogenic genes to a significantly greater degree than did ASCs. (1B) ASCs expressed greater levels of VEGF, translating into greater tubule formation among co-cultured HUVECs (64.3 ± 7.3 vs. 23.3 ± 2.6; p=0.0008). (1C)

CONCLUSION: ASCs heal fractures better than BMSCs, likely through indirect modulation of vasculogenesis, rather than osteogenesis. ASCs may be a promising clinical option for radiation-induced fracture repair, given their accessibility and improved fracture healing.