(HAuCs) in vivo without impeding the development of elastic cartilage. Herein we fabricate cages to invest chondrocyte-collagen hydrogels with more intricate “anatomic” topographic features.

METHODS: Custom external cages were designed with a geometric element representative of the helical rim using SolidWorks (Dassault Systèmes, Vélizy-Villacoublay, France), then 3D-printed using polylactic acid (PLA) on a 5th generation MakerBot printer (MakerBot, New York, NY). Using auricular cartilage from discarded otoplasty specimens, HAuCs were harvested and expanded to passage 2. The chondrocytes were encapsulated into type I collagen hydrogels at a density of 25 million cells/mL with high fidelity contour matching to the cages. The hydrogels, either protected or unprotected by the PLA cages, were implanted into nude rats and explanted after 3 months.

RESULTS: After 3 months in vivo, all constructs developed a glossy white cartilaginous appearance, similar to native auricular cartilage. Histologic analysis demonstrated development of an organized perichondrium composed of collagen, a rich proteoglycan matrix, cellular lacunae, and a dense elastin fibrin network by safranin-O and Verhoeff’s stain. Biochemical analysis confirmed similar amounts of proteoglycan and hydroxyproline content in the constructs when compared to native auricular cartilage. Cage-protected constructs contracted significantly less than unprotected constructs on base area comparison (14.33% vs. 56%, p=0.0023), retained volume (213.4 mm³ vs. 117.2 mm³ compared to original volume of 280 mm³ and corresponding to 76.2% vs. 41.9% retention, p=0.0290), and maintenance of the topographic “helical rim” feature compared to unprotected constructs. Constructs were imaged via computed tomography with an Inveon Pre-clinical MicroPET/CT/SPECT (CTI/Siemens, Knoxville, TN), then digitally reconstructed with Imaris (Bitplane, Belfast, UK). Preservation of the “helical rim” feature was evaluated subjectively by gross examination and objectively by measuring the angle between the rim and base of the constructs, a measurement that demonstrated a significant difference between protected and unprotected constructs, respectively (151.8° vs. 197.7°, p=0.0445), and that indicated protected constructs better maintain the initial angle (110°) between rim and base.

CONCLUSIONS: We have shown that custom contour matched 3D-printed biocompatible/biodegradable external cages significantly mitigate contraction and maintain the complex topography of HAuC constructs. Furthermore, cages do not impede formation of mature elastic cartilage. This technique can be used to create custom cages that contour to any form, enabling the fabrication of engineered autologous cartilage tailored to individual patient anatomy, without the contraction and loss of topography that has thus far impeded translation to the clinic.

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A Novel Pharmaceutical Therapy Preserves Bone Cellularity in an Irradiated Model of Distraction Osteogenesis

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PURPOSE: The use of distraction osteogenesis (DO) in craniofacial reconstruction is precluded by the deleterious effects of radiotherapy on bone and soft tissue, limiting reconstructive options for head and neck cancer (HNC) patients. Our research has previously demonstrated the individual efficacy of both radioprotective amifostine (AMF) and angiogenic deferoxamine (DFO) in improving healing metrics in irradiated models of mandibular DO. Through histologic evaluation, this study investigates the synergistic effects of AMF and DFO as a novel combination therapy in order to expand the utility of DO as a reconstructive technique for HNC patients following radiotherapy (XRT).

METHODS: 30 male Sprague Dawley rats were divided into five groups: DO, XDO, AMF, DFO, and Combined Therapy (CT). With the exception of the DO group, all rats were administered a fractionated, human-equivalent radiation dose of 35Gy, comparable to 70Gy administered to HNC patients clinically. All groups underwent mandibular osteotomy and placement of an external fixator device. Beginning on post-operative day 4, the left hemi-mandible was distracted over the course of 8 days to a critical-sized defect of 5.1 mm. All rats were sacrificed on post-operative
day 40, and mandibles were dissected and embedded in paraffin. Coronal sections were obtained from the region of interest, defined as the 5.1mm of newly formed bone. Sections were stained using Gomori’s Trichrome and analyzed for osteocyte count, osteoid volume, and bone volume. Statistical analysis was performed using ANOVA, with p values less than 0.05 considered significant.

RESULTS: The XDO group demonstrated significant decreases in both osteocyte number and bone volume ($p=0.000$) and a significantly increased osteoid volume ($p=0.017$) when compared to DO controls. The AMF, DFO, and CT groups demonstrated a significant increase in osteocyte number in comparison to the XDO group ($p=0.006$, $p=0.000$, and $p=0.000$, respectively), and were not statistically different from DO. Additionally, the CT group had significantly greater bone volume than the AMF, DFO, or Control group ($p=0.001$; $p=0.000$, $p=0.002$), as well as significantly lower osteoid volume ($p=0.001$; $p=0.004$, $p=0.022$).

CONCLUSION: Our combination therapy significantly improved bone cellularity in the context of radiation. While our research has previously demonstrated the efficacy of both AMF and DFO alone, the increased bone volume in comparison to individual therapy and control groups in this study provides preliminary evidence that a complementary effect may be achieved through their use in conjunction. While further investigation surrounding the differing mechanisms through which AMF and DFO promote bone healing and regeneration is necessary, these results corroborate previous work by our laboratory and highlight the potential for pharmaceutical therapies to facilitate the use of DO as a reconstructive technique in HNC patients.

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Conformity of the Actual to Planned Result in Orthognathic Surgery

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PURPOSE: Virtual surgical planning (VSP) has dramatically improved the workflow process for orthognathic surgery. Qualitative evidence suggests improved surgical efficiency, and splint accuracy. However, the translation from the 3D plan to the actual result, has not been adequately examined quantitatively. The purpose of this study was to compare the planned to the actual 3-dimensional result, comparing placement precision of the maxillomandibular complex in space. We hypothesize the greatest conformity exists in the anteroposterior dimensions.

METHODS: This was an HIC-approved retrospective study of patients who underwent Le Fort I maxillary advancement, bilateral sagittal split osteotomies, and genioplasty using VSP. The preoperative planned 3D file (.stl) was imported into Mimics (Materialise, Leuven, Belgium), for manipulation. Postoperative cone beam CT scans were converted, and imported into the same digital platform. Registration between the two-sets was performed using non-changed landmarks (including, mastoid, styloid, and the orbitozygomatic region). Overall bony position was then assessed, as were 3D linear and angular measurements (including: A point, B point, Pg, Me, ANS, SNA, SNB, and ANB). Multiple instances of each measure were taken, and inter-rater reliability measured. Differences were compared using t-tests, with p <0.05 being statistically significant.

RESULTS: Over 200 patients met criteria for evaluation over a 2-year period, who underwent Le Fort I, bilateral sagittal split osteotomies, and genioplasty. A subset of these were examined 3-dimensionally and compared. Three-dimensional analysis showed differences between the plan and outcome for the following landmarks in the x, y, and z dimensions: A point ($x=1.23$mm, $p=0.09$; $y=1.34$mm, $p=0.04$; $z=1.74$, $p=0.04$), B point ($x=1.32$, $p=0.07$; $y=2.15$, $p=0.02$; $z=1.67$, $p=0.02$), Pg ($x=1.24$, $p=0.07$; $y=3.71$, $p=0.04$; $z=2.12$, $p=0.06$), Me ($x=2.64$, $p=0.02$; $y=3.95$, $p=0.008$; $z=2.40$, $p=0.03$), and ANS ($x=1.12$, $p=0.04$; $y=1.20$, $p=0.04$; $z=1.71$, $p=0.005$). The mean difference in angles were as follows: SNA (1.19°, $p=0.06$), SNB (1.29°, $p=0.01$), ANB (1.58°, $p=0.04$).

CONCLUSION: This studied reveals, that despite 3D planning with splint accuracy, there were small deviations in actual bony positioning compared with the planned position. These were more apt to occur in the transverse and vertical planes, but some difference was noted sagittally in all cases. The differences may be due to intraoperative aesthetic judgements pertaining to the vertical position and midline. Additionally, pitch alteration could influence the relative sagittal placement. The relationship of bone to soft-tissue cannot always be predicted during the VSP, and freedom for manipulation should be left to the surgeon’s eye.