distinct biomarkers, and relative ease of harvest. Despite the immense potential of ASCs to enhance bone regeneration, the Food and Drug Administration (FDA) remains hesitant to approve ASC-based therapies given the consistent need for scaffolds, onerous processing techniques, and requirement of cell culture. The purpose of this study is to define the optimal method of administration of ASCs that will most readily mitigate the deleterious effect of radiation therapy (XRT) on bone healing during fracture repair while maintaining compliance with FDA guidelines; this will consequently maximize the translational applicability and clinical adoption of such therapies.

METHODS: Forty-four male Lewis rats were randomly divided into four groups: control, XRT, ASC, and minimally processed ASC (MP-ASC). Excluding the control group, all rats received a fractionated dose of 35Gy of radiation, and all groups underwent subsequent mandibular osteotomy. The ASC group was treated with cultured ASCs, while the MP-ASC group received non-cultured ASCs. More specifically, for both groups, ASCs were harvested from the inguinal fat pads of isogenic Lewis rats. Cultured ASCs were processed, plated, and achieved confluence within 10–12 days. These cells were subsequently implanted into the osteotomy site at passage two. In the MP-ASC treated group, ASCs were harvested, centrifuged, and immediately implanted into the osteotomy site without the need for cell culture. After animals were sacrificed on post-operative day 40, gross pathology and MicroCT analysis were utilized to determine union rates and the quality of the bony regenerate within the osteotomy site.

RESULTS: The implantation of MP-ASCs significantly increased union rates compared to XRT alone based on MicroCT results and pathology (60% vs. 15%). Although MP-ASC administration resulted in slightly decreased union rates compared to cultured ASCs (60% vs. 100%), the quality of bone regenerated was similar between the groups based on bone mineral density (687.25 ± 92.02 vs. 619.64 ± 42.5; p=0.17) and bone volume fraction (0.755 ± 0.097 vs. 0.721 ± 0.057; p=0.75). The implantation of cultured ASCs resulted in similar union rates as non-radiated mandible fracture sites (100% vs. 100%).

CONCLUSIONS: Mesenchymal stem cells (MSCs) are adult stem cells with immense potential to enhance bone healing and regeneration following injury. This study identifies the ability of MP-ASCs, a minimally processed type of MSCs, to enhance bone regeneration in the absence of cell culture. With these results in mind, additional studies are required to further maximize the osteogenic potential of ASCs while also maintaining adherence to FDA regulations that mandate the minimal processing of tissues prior to implantation.

K. Ranganathan: None. J.V. Lynn: None. K. Urlaub: None. N.S. Nelson: None. A. Donneys: None. L. Buchman: None. S.R. Buchman: None.

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Changes in Mouse Skeletal Progenitor Cells in a Model of Osteoporosis

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PURPOSE: Osteoporosis is a disease characterized by low bone mass and structural deterioration of bone tissue. People with osteoporosis are more prone to fracture due to the decrease in bone mass with 40% of post-menopausal women developing an osteoporotic fracture. Of those suffering a fracture, 20% will die and only 30% will fully recover indicating that there is also a deficit in fracture healing. Our group recently described mouse skeletal progenitor cells. One sub-population, the mouse skeletal stem cell (mSSC) has been shown to be capable of forming all components of the skeleton. Another sub-population, the bone cartilage skeletal progenitor (BCSP) has been found to be important in fracture healing. We hypothesized that the changes in skeletal anatomy following estrogen depletion will be reflected by alterations in skeletal progenitor cell populations.

METHODS: C57/BL6 mice underwent either sham operation or oophorectomy. Bone mineral density (BMD) was assessed by microCT. For fracture healing, mice underwent femur fracture 10 weeks after oophorectomy. Skeletal progenitor cells were harvested from uninjured bone or fracture callus as previously described and sorted by FACS. For colony forming units (CFUs), sorted cells were placed in growth medium for two weeks prior to colony counting.
RESULTS: We first examined the impact of oophorectomy on BMD. 10 weeks after oophorectomy, mice were examined by microCT and BMD calculated from the femur. As expected, there was a significant decrease in BMD following oophorectomy compared to sham. Analysis of skeletal progenitors from uninjured bone showed significantly fewer mSSCs with decreased CFUs in oophorectomized versus sham. Following fracture, there was visibly less callus formed at the fracture site. Following fracture in oophorectomized mice, there was some increase in BCSPs in response, but it was nearly an order of magnitude less than seen in sham.

CONCLUSIONS: Osteoporosis is a disease that can have devastating consequences for the health of older women. Our aging population will only increase the demand for viable therapies for the consequences of osteoporosis. While the impact of estrogen depletion on bone are well-characterized, it has not been very well understood at the cellular level. Here, we show the impact of oophorectomy on an important cellular component of the skeleton, and propose that therapies targeted at this cell population may be effective in combating the disease. <!--EndFragment-->

T. Andrew: None. D. Struck: None. M. Lopez: None. T. Boyko: None. M. Longaker: None. C. Chan: None. G. Yang: None.

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Graded Balanced Orbital Decompression With Stereotactic Navigation

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PURPOSE: Using a state of the art High Definition video animation we present our technique for orbital decompressions for patients with severe thyroid orbitopathy that minimizes complications while maximizing the amount of decompression. This method involves advancing the lateral orbital wall combined with endoscopic medial wall decompression in such a way as to promote osseous union and minimize cosmetic deformities. Stereotactic intraoperative navigation is utilized in all patients to minimize complications.

METHODS: This paper represents a case series of over 150 orbits where orbital decompression for severe thyroid related orbitopathy was performed in a graded balanced manner. All patients were treated via a graded balanced orbital decompression with advancement of the lateral orbital wall with interpositional bone grafts. Preoperative and postoperative measurements were tabulated and statistically analyzed.

RESULTS: All patients demonstrated significant improvement in proptosis with an average Hertel exophthalmometry reduction of 9mm. The reduction in Hertel readings varied based on preoperative measurements and postoperative goals thereby demonstrating the “graded balanced” nature of our decompression technique. In addition, all patients with preoperative elevation of intraocular pressure demonstrated a reduction to within the normal range. Less than 5 percent of patients required post orbital decompression strabismus surgery. Of all patients, more than 70% demonstrated improvement of visual acuity of greater than 1 line. Postoperative computed tomography scan demonstrated osseous union of the lateral wall after advancement with this new technique.

CONCLUSION: The graded balanced orbital decompression with interpositional bone grafts effectively decompressed the orbit with significant improvement in final visual acuity, exophthalmometry measurements, and final intraocular pressure. In addition, this technique promotes osseous union with minimal cosmetic deformities. This is one of the largest series of a graded balanced orbital decompression with intraoperative navigation and combined orbital and endoscopic orbital decompression. Our customized video animation effectively demonstrates our technique to patients for educational purposes.

C. Gilliland: None. A. Bhatki: None. I. Vrcek: None. G. Gilliland: None.

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Identification of esrp1 as a novel IRF6 Target Gene and Determining its Role in Palate Development

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