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**“The distinct morphology and structure of tissue engineered bone and cartilage derived from mesenchymal stem cells”**

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**Background:** The production of engineered bone and cartilage from mesenchymal stem cells is a rapidly developing field. Potential applications include the treatment of degenerative joint diseases, as well as the treatment of traumatic and surgical bone injury. As engineered tissue is implanted, pathologists will play a role in evaluating the integration, biocompatibility, ultrastructure and performance of the engineered tissue, especially in explanted specimens. Our purpose is to introduce pathologists to the staining profile and distinctive morphology of engineered bone and cartilage tissue such that it is recognized aptly in clinical practice. There have been extensive publications addressing tissue engineering over the last decade, however very little has been directed at the practicing pathologist.

**Design:** Human mesenchymal stem cells were grown *in vitro* in pellet culture (for chondrocyte differentiation) and monolayer (for osteogenic differentiation) for three weeks in chondrogenic and osteogenic media conditions. The cultures were then harvested, paraffin-embedded, and routine histology with hematoxylin and eosin staining was performed. Additional stains including safranin-O, Masson's trichrome, and von Kossa were performed on the engineered cartilage and bone to highlight matrix production as a surrogate marker for differentiation. The morphology of the engineered tissues was compared both qualitatively and quantitatively to native tissue.

**Results:** The engineered tissue demonstrates similar morphology to native developing cartilage and bone by routine hematoxylin and eosin staining. Of note, the cell to matrix ratio of the engineered cartilage lies between that of native fetal and adult cartilage. Other parameters such as mineralization activity and the formation of extracellular matrix, as demonstrated by trichrome and safranin-O staining, paralleled that of native tissue. The morphology of bone engineered from MSCs resembles early native intramembranous bone formation and the special stains, including a negative safranin-O, support this observation.

**Conclusions:** In the near future human tissue engineered explants will require pathologic evaluation. The engineered cartilage has a characteristic cell to matrix ratio, which lies in between that of fetal and adult native tissues. Engineered bone resembles early intramembranous bone formation. The phenotypic differences are highlighted here with the purpose of introducing surgical pathologists to the histology of a biomaterial that they may soon encounter in practice.