

Osiris Therapeutics, Inc.

Introduction

Hyaline cartilage contains a type II collagen and proteoglycan-rich matrix, chondrogenic growth factors, and tissue resident viable chondrocytes. The matrix and cells are distributed within three distinct cartilage zones, each with unique tissue architectures; the superficial (top), transitional (middle) and radial (deep) zones. Maintenance of these three layers is essential to support normal cartilage functions.¹ Cartiform is a cryopreserved viable osteochondral allograft designed to treat articular cartilage defects. Cartiform consists of full-thickness hyaline cartilage and a small amount of bone. Pores span the full thickness of the graft for ease of handling and implantation, and cryopreservation allows for prolonged storage. The goal of this study was to confirm preservation of native hyaline cartilage tissue architecture within Cartiform.

Methods

Cartiform was thawed, fixed in paraformaldehyde and embedded in paraffin. Paraffin blocks were cut in five micron thick sections and stained with Hematoxylin and Eosin (H&E). The stained sections were evaluated using light microscopy. A fresh osteochondral plug containing normal full-thickness hyaline cartilage and bone was fixed and stained in the same manner for use as a reference control.

Results

The native tissue architecture of hyaline cartilage is maintained within Cartiform after cryopreservation **Figure 1**. H&E staining demonstrates that the superficial, transitional and radial zones of hyaline cartilage are intact. Specifically, cells within the superficial zone have a rounded morphology while cells in the transitional and radial zones form columns. H&E staining also confirms the presence of a small amount of bone and an intact tidemark spanning the intersection between the cartilage and bone in Cartiform.

Discussion

Histological staining of Cartiform confirms that the tissue processing and cryopreservation methods do not alter the architecture of human articular cartilage, which is optimized for tensile strength and load absorption capabilities. The intact bone portion and tidemark confirm that Cartiform is an osteochondral allograft. Similar to traditional fresh stored osteochondral allografts, the bone portion in Cartiform will serve as an anchor, aiding implantation and integration of the allograft tissue.²

Significance

Cartiform is a viable osteochondral allograft that maintains its structural integrity through processing, cryopreservation and storage at -80°C. Because the structure remains intact, Cartiform is expected to integrate and repair cartilage lesions in a similar manner to traditional fresh stored osteochondral allografts. Cartiform has the added benefits of a long shelf life and graft flexibility due to the reduced bone portion within Cartiform.

References

- Quinn TM, Hunziker EB, Häuselmann HJ. Variation of cell and matrix morphologies in articular cartilage among locations in the adult human knee. *Osteoarthritis Cartilage*. 2005;13(8) 672-678.
- 2. Bugbee WD, Convery FR. Osteochondral allograft transplantation. *Clin Sports Med*.1999;18(1) 67-75.



Figure 1. H&E stains of Cartiform (left) and fresh cartilage (right) reveal that Cartiform maintains the natural tissue architecture, including the superficial, transitional, and radial zones of articular cartilage, the tidemark, and an osseous layer (scale bar = $500 \mu m$).



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