FiberCel™

Viable Bone Matrix (VBM)

Healthier Cells*[1]

Reduced Apoptosis

Increased Cell Proliferation

Demonstrated Osteogenic Potential

HEALTHIER CELLS*

FiberCel is a human tissue allograft comprised of cryopreserved cancelleous and demineralized cortical bone fibers that are aseptically processed to preserve native factors that support bone repair. One of the components of efficient bone regeneration is the presence of viable cells, specifically, cells of the osteoblast lineage (mesenchymal stem cells, osteoprogenitor cells, and osteoblasts). In normal human bone, these cells are concentrated with bone marrow and line the surface of cancellous bone **(Figure 1)**. On average, FiberCel contains over 650,000 viable cells per cc post-thaw comprised of mesenchymal stem cells, osteoprogenitor cells, and osteoblasts.[1]

FiberCel is produced using a proprietary process that preserves more of the inherent properties of the native tissue when compared to traditional processing of cellular bone matrices. This process maintains healthier more viable cells that are able to facilitate bone regeneration.[1]

*Comparisons were made utilizing control samples that were produced using a process similar to existing cellular bone matrices. Samples for the comparison were obtained from identical sources.

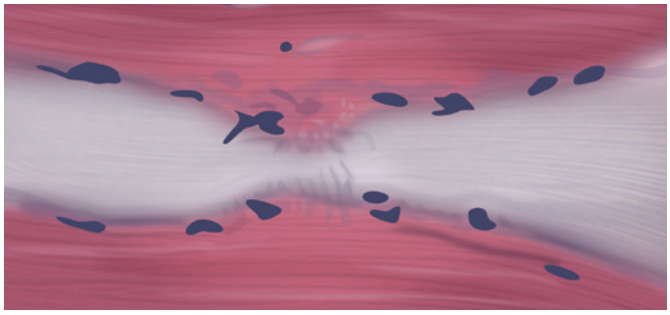
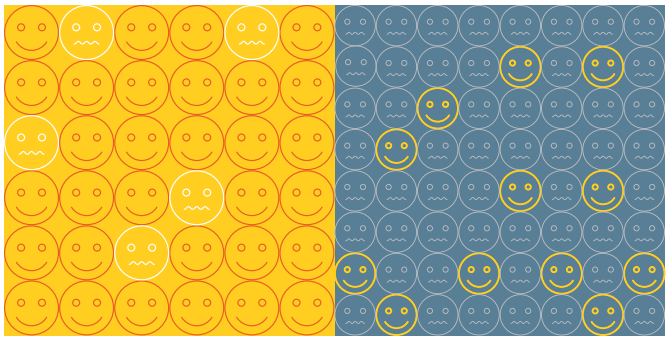


Figure 1. Illustrative histology image of FiberCel. Cells (purple) line the surface of the cancellous bone component (pink) of FiberCel.

Cell Population Illustration



FiberCel Control

FiberCel has a **healthier** cell* population.[1]

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REDUCED APOPTOSIS

Apoptosis is controlled cell death. This process is mediated through a signaling pathway that leads to cell death within a few hours to a few days after initiation.

Although apoptosis is integral for normal bone remodeling, improper stimulation can lead to pathologic bone conditions, such as osteoporosis.[2] Specifically, apoptosis can be prematurely triggered by various stress stimuli including exposure to non-physiological environments, such as excessive heat, oxidative stress and chemical exposure,[3-8] all of which are common on traditionally processed human tissue allografts **(Figure 2)**. For example, removal of bone tissue from its physiologic environment leads to the production of reactive oxygen species which is well established to induce apoptosis of osteoblasts.[3] Furthermore, studies have demonstrated that apoptosis prevents osteogenic differentiation of adult human mesenchymal stem cells and impedes the activity of osteoblasts.[9] Essentially, premature apoptosis results in lower number of healthy cells, leading to decreased osteogenic potential **(Figure 2)** and ultimately poor bone formation. Therefore, minimizing cell exposure to stress that stimulates apoptosis in bone cells is critical for efficient bone regeneration.

FiberCel is optimized to preserve the health of native bone cells

FiberCel is a viable bone matrix that provides all three components critical for bone regeneration: osteoconductivity, osteoinductivity, and osteogenicity.[1] It is a next generation cellular bone matrix that has been optimized to preserve the health of native bone cells and yield more readily available bioactive agents to enhance new bone formation.

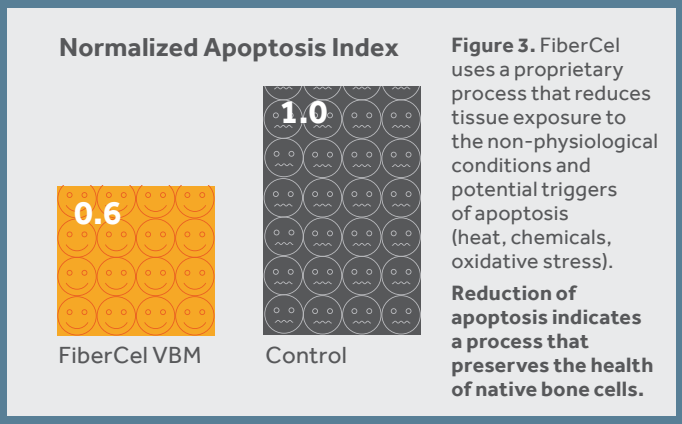

Figure 3. FiberCel uses a proprietary process that reduces tissue exposure to the non-physiological conditions and potential triggers of apoptosis (heat, chemicals, oxidative stress).

Reduction of apoptosis indicates a process that preserves the health of native bone cells.

FiberCel has been developed using a proprietary process that reduces tissue exposure to non-physiological conditions and potential triggers of apoptosis to preserve and optimize the native biological and structural elements beneficial to bone repair. These methods include minimizing tissue contact and the time outside of a physiologic environment. Furthermore, exposure to potentially harmful chemicals frequently used during allograft manufacturing is minimized.

FiberCel has fewer apoptotic cells

Apoptosis inhibits osteogenic differentiation and osteoblast function and can be prematurely triggered by non-physiological stimuli. To assess the impact of FiberCel's proprietary processing on apoptosis, activated caspase levels (indicator for apoptotic cells) were measured from FiberCel versus allografts produced using traditional control methods. As indicated by the higher apoptotic index (ratio of apoptotic cells to viable cells), allografts produced from control processing methods resulted in a significantly greater population of apoptotic cells compare to FiberCel. Specifically, FiberCel exhibited more than 40% reduction of apoptotic population compared to control tissue **(Figure 3)**.

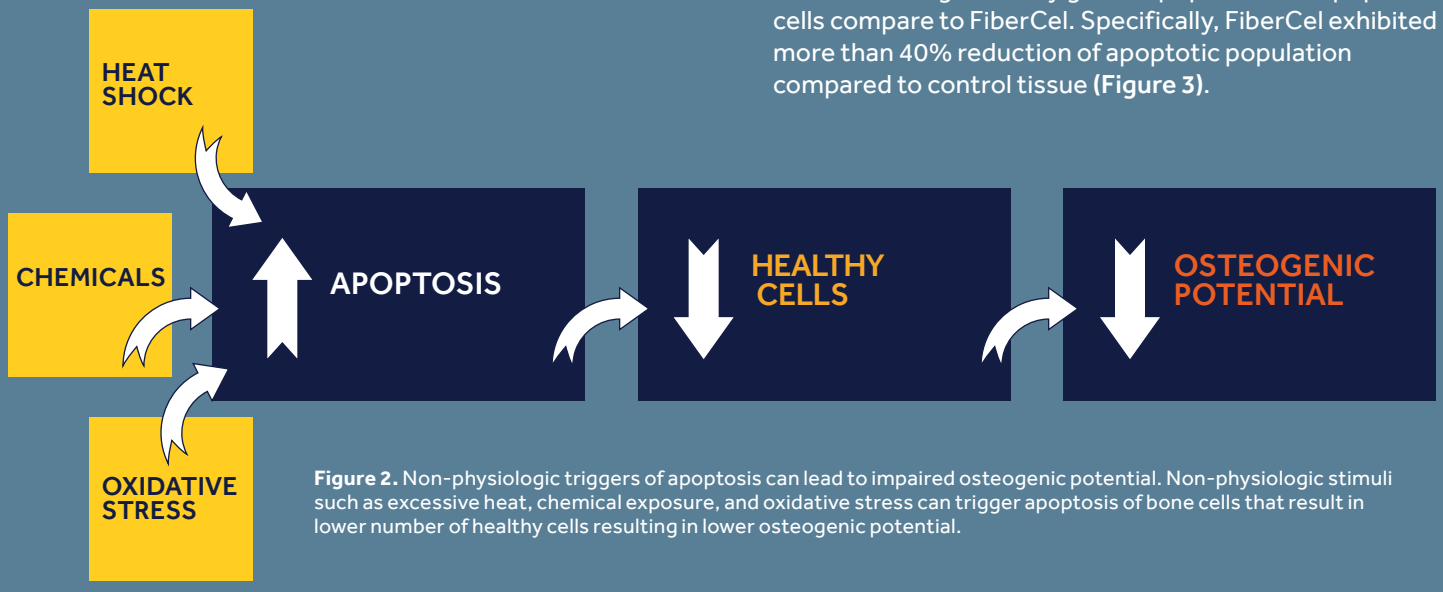

Figure 2. Non-physiologic triggers of apoptosis can lead to impaired osteogenic potential. Non-physiologic stimuli such as excessive heat, chemical exposure, and oxidative stress can trigger apoptosis of bone cells that result in lower number of healthy cells resulting in lower osteogenic potential.

INCREASED CELL PROLIFERATION

The ability of cells to increase in number (cell proliferation) is an indicator of good cellular health.

Cells from FiberCel proliferated at a faster rate than cells isolated from the control.

MINIMIZING APOPTOSIS AND MAINTAINING CELLS WITH HIGH PROLIFERATIVE CAPACITY RESULTS IN A BONE GRAFT THAT PROVIDES THE BASIS FOR BETTER BONE REGENERATION.

DEMONSTRATED OSTEOGENIC POTENTIAL

To further confirm cellular health in FiberCel, osteogenic potential was examined by quantifying production of osteoblast markers:

- **Osteocalcin** – Protein produced by mature osteoblasts
- **Osteopontin** – Protein produced by mature osteoblasts involved in bone mineralization
- **Collagen Type I** – Primary extracellular matrix component of bone

Osteogenic potential and preservation of cell health were confirmed by the production of these 3 osteoblast markers.

Proliferation rate (fold increase) vs days in culture

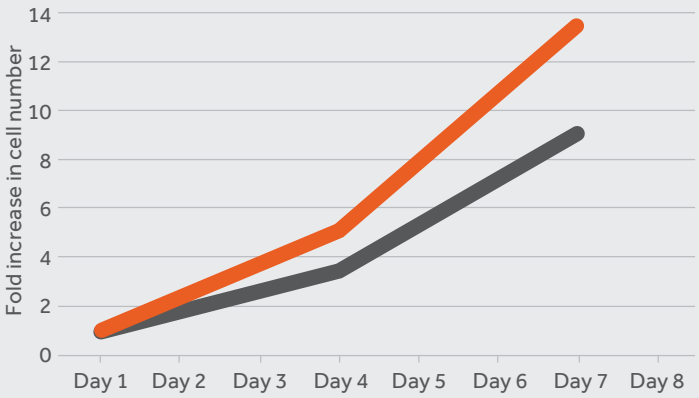

Figure 4. Cells isolated from FiberCel and the control tissue prepared using traditional processing methods were cultured and quantified over seven days. **Cells isolated from FiberCel proliferated at a faster rate than the cells isolated from control tissue.**

FiberCel Standard deviation Day 1 = 0.3, Day 4 = 2.4, Day 7 = 7.4
Control Standard deviation Day 1 = 0.1, Day 4 = 1.0, Day 7 = 7.0

These data sets confirm that the fewer apoptotic cells and more healthy cells in FiberCel result in greater production of bone forming components, which ultimately contributes to better bone regeneration.[10,11]

DESCRIPTION AND INTENDED USE

FiberCel is a human tissue allograft consisting of cryopreserved cancellous and corticocancellous bone matrix that is aseptically processed to preserve native factors that support bone repair. FiberCel is a Human Cellular and Tissue Based Product (HCT/P) per 21 CFR Part 1271. Each allograft is restricted to homologous use for transplant in procedures for repair, replacement or reconstruction on a single occasion by a licensed physician or surgeon. FiberCel can be used in orthopedic or reconstructive bone grafting procedures in combination with autologous bone or other forms of allograft bone, or alone as a bone graft.

CONTRAINDICATIONS

The presence of infection at the transplant site is a contraindication for the use of this allograft.

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