TrueTissue: Allogeneic Tissue Engineered Knee Replacement

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Background

Knee cartilage is one of the most vulnerable parts of the body. As we age, our bodies are subjected to wear and tear. With increasing life expectancy, the risk of developing orthopedic problems is higher than ever before.

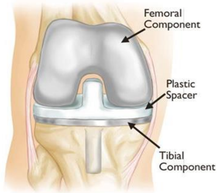

Figure 1: Traditional Knee Replacement

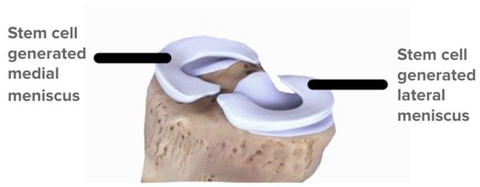

Figure 2: True Tissue Knee Replacement

Traditional knee replacements are made of metal alloys and plastics that require an invasive procedure. Our product, True Tissue, introduces a new solution – live cartilage knee replacements engineered from allogeneic stem cells. TrueTissue is a safe, immune privileged implant that mimics natural knee cartilage. Its integration with the body hastens patient recovery and extends implant lifetime. No drilling or shaping bone is needed for installation, making it a significant breakthrough in orthopedic surgery.

Product Details

Our product has uniform dimensions that are designed based on the upper limits of the average human knee cartilage size. It can be cut later to fit most patients' knees, and then glued in place with cartilage glue.

1. Articular cartilage: in white a disk shape.

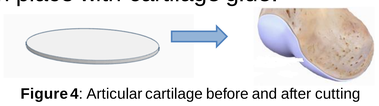

Figure 4: Articular cartilage before and after cutting

2. Meniscus cartilage: in a white rectangular shape.

Figure 5: Meniscus cartilage before and after cutting

Articular cartilage	Meniscus Cartilage
Height: 4 mm	Height: 480,384
Diameter: 160 mm	Length: 30 mm
----------	Width: 12 mm
Volume: 80,384 mm^3	Volume: 1440 mm^3
Exposed surface: 20,000 mm^2	Exposed surface: 360 mm^2

Table 1: Articular and meniscus cartilage product dimensions

Figure 6: packaging and delivery

Cross-Sectional View

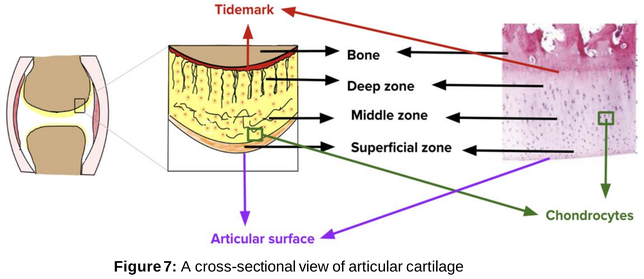

Figure 7: A cross-sectional view of articular cartilage

On the right Figure 7, we showed a real human knee cartilage image and both of our products will mimic the composition and appearance of natural knee cartilage.

Manufacturing Details

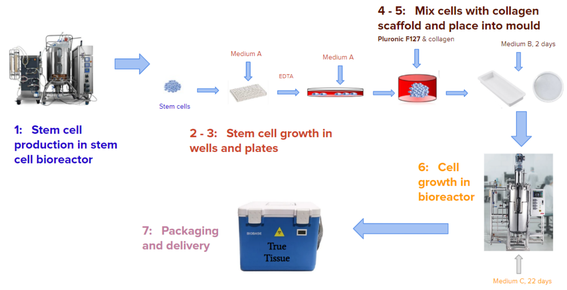

Figure 8: Manufacturing diagram

1. Stem cell (hiPSCs) production and renewal
2. Formation of embryoid bodies in wells
3. Transfer the embryoid bodies to a plate to allow further cell proliferation
4. Transfer cells from the plate into a collagen and pluronic F127 bio-ink
5. Layering the bio-ink in a mold and allowing it to stiffen in the presence of a chondrocyte differentiation medium to create a seeded scaffold
6. Transfer the scaffolds to a bioreactor where chondrocyte differentiation media will be perfused through and then chondrocyte growth media
7. Once grown to proper cell density the scaffolds will be packaged and sent to hospitals as ordered

Modeling with COMSOL

Articular cartilage model

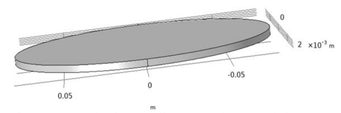

Figure 9: Articular cartilage product model

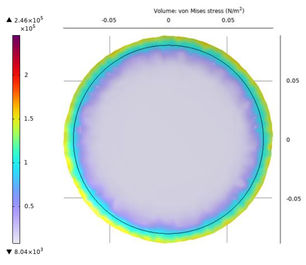

Figure 11: Top view of COMSOL model of von Mises stresses of articular cartilage scaffold under a 2856 N load

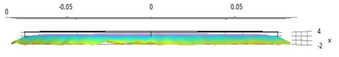

Figure 11: Side view of COMSOL model of von Mises stresses of articular cartilage scaffold under a 2856 N load

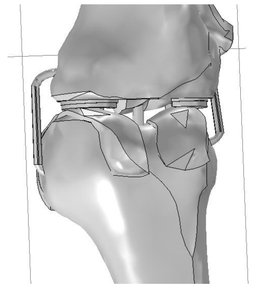

Figure 14: Model of the knee joint with both cartilage

Results from the COMSOL modeling show that our product can resist the same force as a 100 kg person standing on one foot.

Mencius cartilage model

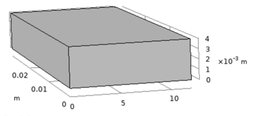

Figure 10: Meniscus cartilage product model

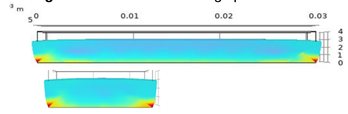

Figure 12: Side views of COMSOL model of von Mises stresses of meniscus cartilage scaffold under a 1000 N load

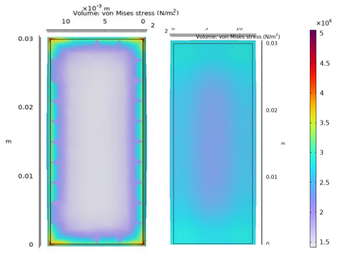

Figure 13: Top and bottom views of COMSOL model of von Mises stresses of meniscus cartilage scaffold under a 1000 N load

$Q_m = 15.5 * 10^{-15} \frac{g}{cell*s}$ (Max Glucose Uptake Rate / Cell)

Max Cell # = 800,000,00

$Total\ Glucose\ Uptake\ Rate = 1.25 * 10^{-5} \frac{g}{s}$

Flow in of Glucose: $1.8 \frac{g}{L} * 0.05787 \frac{L}{s} = 0.105 \frac{g}{s}$

$Glucose\ in\ Rate\ >>>\ Glucose\ Uptake\ Rate\ \therefore c_g = Constant$

Cell Growth Rate: $\mu_{cell} = \frac{\mu_{max} c_i}{\rho_c * k_{sg} + c_i}$

Cell Growth WRT: $\frac{d\rho_{cell}}{dt} = \left(\frac{\mu_{max} c_i}{\rho_c * k_{sg} + c_i} - k_d\right) \rho_{cell}$

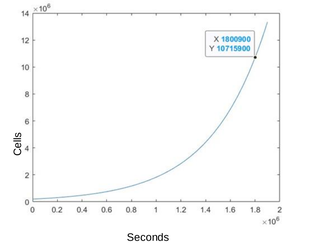

Figure 15: Cell growth modeling. It takes about 21 days to grow the product

Market Prediction

The U.S. knee implant market is currently valued at roughly 4.8B with 800,000 knee replacements performed across 6100 hospitals. The market continues to grow with a 4.9% CAGR due to longer life expectancy.

The advantages of True Tissue over its competitors in several areas justify its higher price point. True Tissue provides better outcomes for patients, a less invasive procedure for surgeons, and lower costs for hospitals.

Total Knee Replacement Model	Affiliation	Materials	Wear & Tear	Avg Femoral ROM (degrees)	Recovery Time (months)	Bone Invasive Procedure	Price (USD)
Triathlon Total Knee System	Stryker	Ti, UHMWPE	Yes	126	6	Yes	3,400
Attune Knee System	DePuy Synthes	Ti, Al, V, UHMWPE	Yes	123	6	Yes	3,800
NexGen Complete Knee Solution	Zimmer Biomet	Ta, UHMWPE	Yes	132	6	Yes	3,400
Legion Total Knee System	Smith & Nephew	Ti, Zr, Nb, UHMWPE	Yes	128	6	Yes	3,900
True Tissue Knee Replacement	True Tissue	Allogenic cartilage, collagen Scaffold	Slight	Full (135-150)	3	No	**14,000**

Table 2: Merit table for True Tissue and current knee replacements

Financials

True Tissue will have an aggressive R&D and clinical trial period in the first 5 years to achieve FDA approval. Year 6 marks the first year of production, capturing 1.35% of the market by selling 10800 implants at $14K/implant. Every following year will have a linear production ramp up to sell an additional 2.7K implants/year, selling 21.6K implants and capturing 2.7% of the US market by year 10.

According to our cash flow analysis with TVM, True Tissue breaks even by year 8 with a NPV of 83M by year 10. Without TVM, our product breaks even by year 7 with a NPV of 232M by year 10.

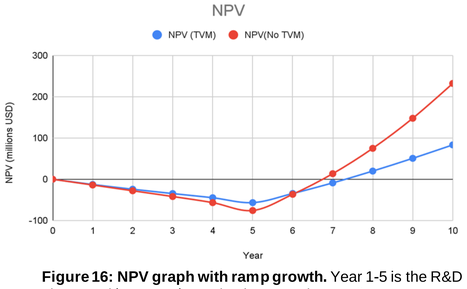

Figure 16: NPV graph with ramp growth. Year 1-5 is the R&D phase and large-scale production starts in year 6.

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