



CartiMax™ VCA

Animal Study Whitepaper Summary

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BUILDING OUR DATA

VIABILITY

Viability Characterization of CartiMax

MTF Biologics, Research and Development Department
125 May Street, Edison, NJ 08837

CELL MARKER CHARACTERIZATION

Cellular Characterization of CartiMax using FACS Analysis

MTF Biologics, Research and Development Department
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RETENTION MODEL

CartiMax Retention Model

MTF Biologics, Research and Development Department
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ANIMAL STUDY

Long-term Follow-Up of Focal Cartilage Defects Repair with CartiMax™ Viable Cartilage Allograft in a Goat Model

MTF Biologics, Research and Development Department
125 May Street, Edison, NJ 08837



CLINICAL OUTCOMES Dr. Jones ICRS

Novel Procedure using Viable Allograft for Focal Cartilage Defects

Chase Maloy M.D., Gerard K. Williams Jr., M.D., Lindsey Verdine B.S., Misty Suri M.D., Derya G. Jones M.D.
June 2019 Poster Presentation ICRS One Step Cartilage Repair Focus Meeting

GOALS

The purpose of this retrospective study to assess treatment of focal knee cartilage defects with CartiMax™ Viable Cartilage Allograft (VCA).

METHODS & MATERIALS

CartiMax™ Viable Cartilage Allograft was implanted into 13 patients (5/8 MF), mean age 26.77 (15-56). Symptomatic ICRS grade 3-4A femoral (n=7) or patellar (n=11) lesions from 1.4-9 cm² were treated. International Knee Documentation Committee (IKDC), Knee injury and Osteoarthritis Outcome (KOOS), Lysholm, Short Form-12 and pain severity and frequency were collected. Radiographs and MRIs were performed at 3 and 6 months.

RESULTS

13 patients with average follow-up of 5.7 months (0-9) showed average decreases in VAS and Pain Frequency of .75 and -2 respectively at 3M. Increases in Lysholm (25.25), and KOOS: Pain (12.19), Symptoms (19.64), ADLs (14.55), Sports (13.66), and QOL (24.91) compared to the pre-operative baseline (POB) were seen at 3M. These trends were maintained at 6M with decreases in VAS and Pain Frequency by 2.15 and 2.63 respectively. Large increases in IKDC (33.76), Lysholm (20), and KOOS sub-scores: Pain (18.49), Symptoms (16.96), ADLs (17.45), Sports (40.65), and QOL (25) were found at 6M. MRI imaging at 3 and 6 Months showed viable preliminary cartilage tissue with no significant bone edema or graft delamination. Second look arthroscopy demonstrated complete fill and excellent incorporation (Bristow Score 11/12) in two patients.

DISCUSSION/CONCLUSION

VCA contains viable cartilage fibers demonstrating excellent patient safety and potential earlier return to full function. It avoids limiting the subchondral bone plate removing potential sources of pain and functional limitations. The outcomes measured demonstrate improvement from POB. Clinical results appear to demonstrate that CartiMax™ VCA in the early follow up period is a safe and effective solution for large lesions.

Pre-Clinical Data

In Vivo Data GAP

Clinical Data



KEY QUESTIONS ANSWERED BY THE GOAT STUDY

■ What happens in the body after implantation over time?

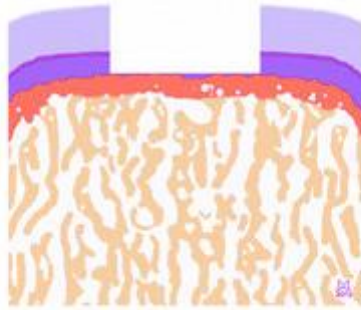
- Can the graft remain in the defect (without fibrin glue)?
- Is the graft safe? Are there any adverse effects in the joint?
- Can the graft support functional chondrogenic activity that leads to remodeling into hyaline cartilage?
- Can the remodeling graft integrate with the adjacent native goat cartilage?
- Can the repaired hyaline cartilage be durable over time (up to 1 year)?
- Can CartiMax VCA be superior to conventional microfracture?



ANIMAL STUDY

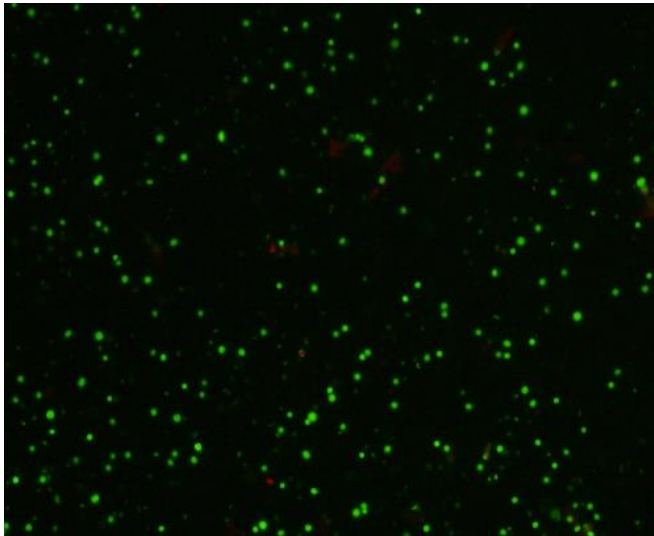
1. **PRE-IMPLANTATION:** Evaluate a given donor lot of CartiMax VCA before implantation
 - Determine cell viability (Live/Dead assay)
 - Explant culture to verify viable cells migrate and expand
2. **IMPLANTATION:** Implant same lot of CartiMax into the chondral goat knee defect

Chondral defect, full thickness



1. PRE-IMPLANTATION: VERIFIED CARTIMAX SAMPLES HAVE VIABLE, FUNCTIONAL CELLS

Viable Cells



**(94 ± 3)% Cell Viability
(post-thaw)**

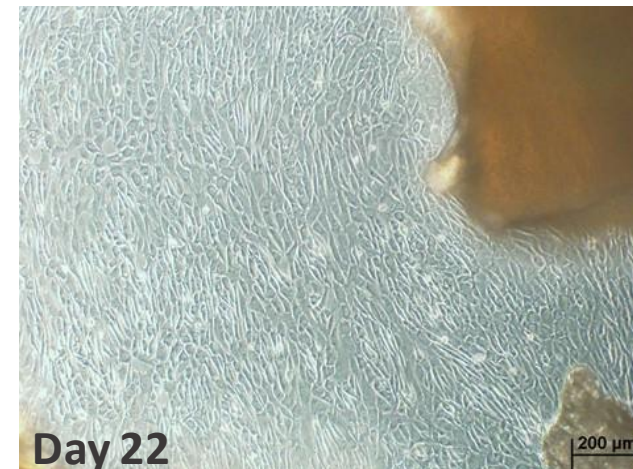
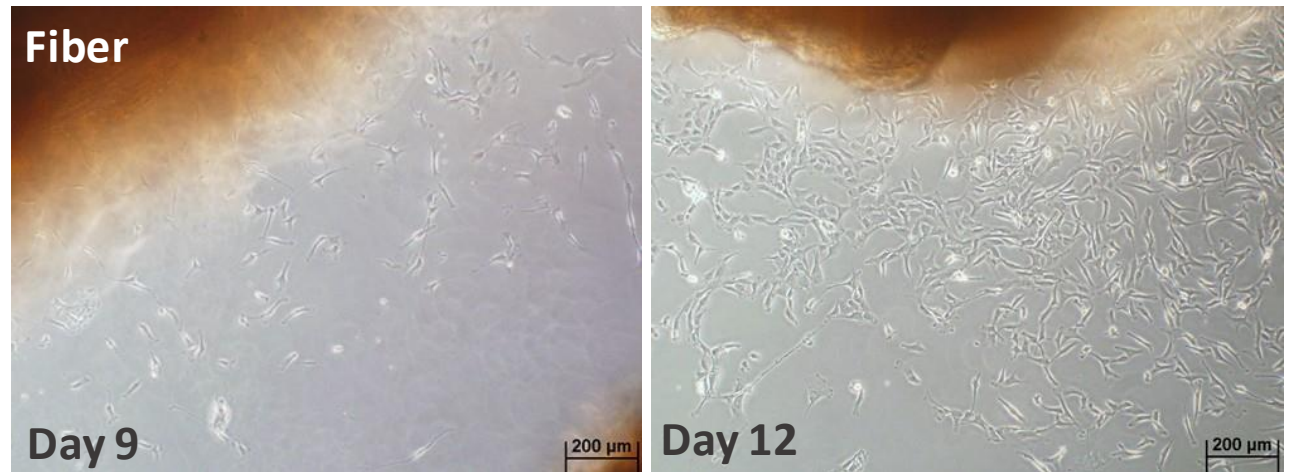
Green = LIVE cells

Red = DEAD cells

Live Dead Staining



Functional Cells (Migrate + Expand)



Cells migrate, gradually expand and cover the entire dish over time

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2. ANIMAL STUDY DESIGN

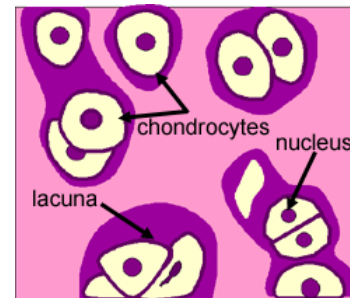
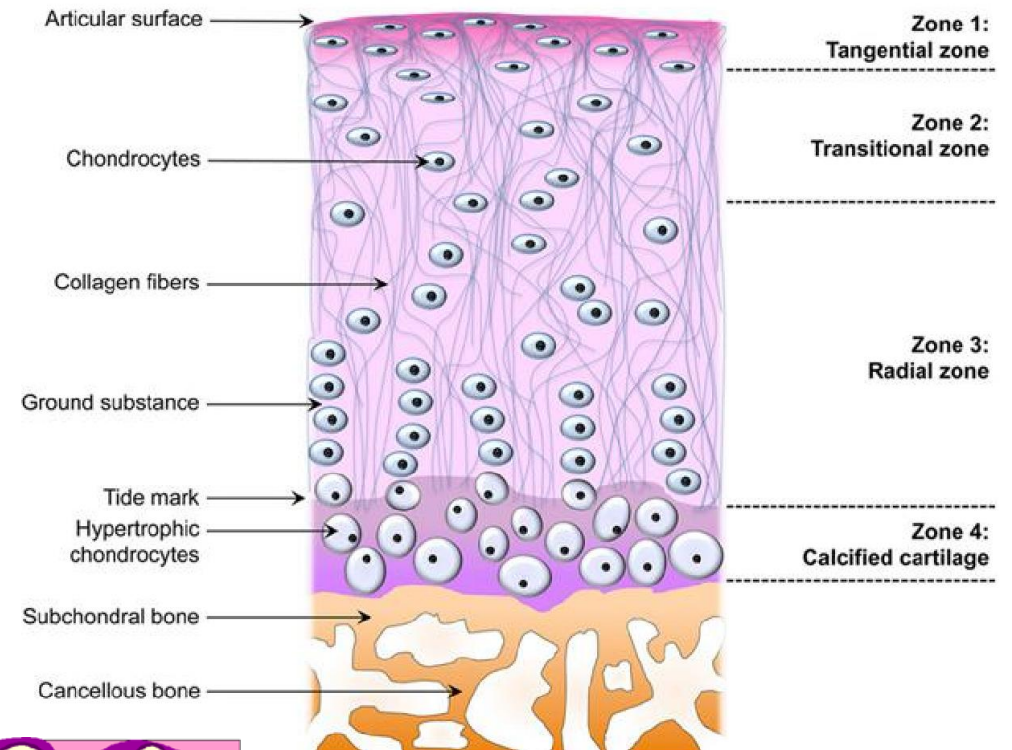
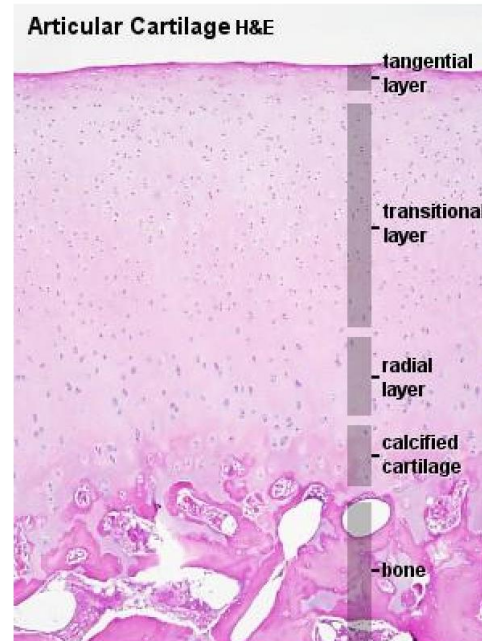
- **IMPLANTATION**: Implant same lot of CartiMax into the chondral goat knee defects
 - **Animal**: Spanish goats (typical large animal model)
 - **Critically-Sized Defect**: 6mm diameter surgically-created
 - **Test Group**: CartiMax VCA (w/o microfracture or fibrin glue) in medial femoral condyle
 - **Control Group**: Microfracture in the trochlear groove
 - **Post-Surgery**: All animals splinted for 6 weeks
 - **Study Time-points**: 12, 24, 52 weeks
 - **Outcome Measures**: Histological staining of explanted tissues

WHAT IS ARTICULAR CARTILAGE?



Knee Joint - Side View

Shock absorber,
cushioning areas where
bone meets bone



Organized structure
(distinct lacunae)

OVERVIEW OF CARTILAGE HISTOLOGY

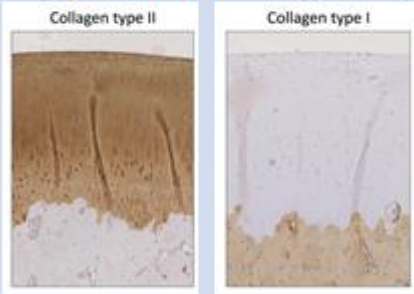
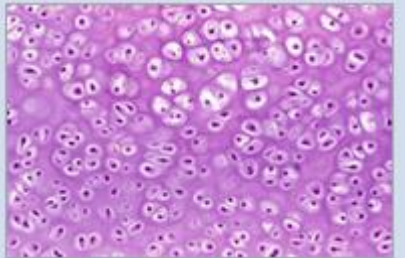
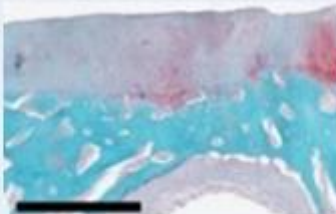
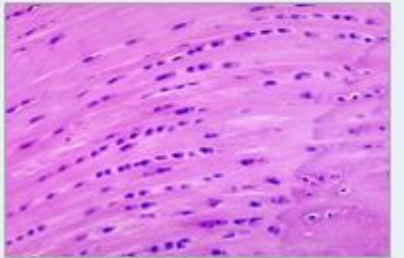
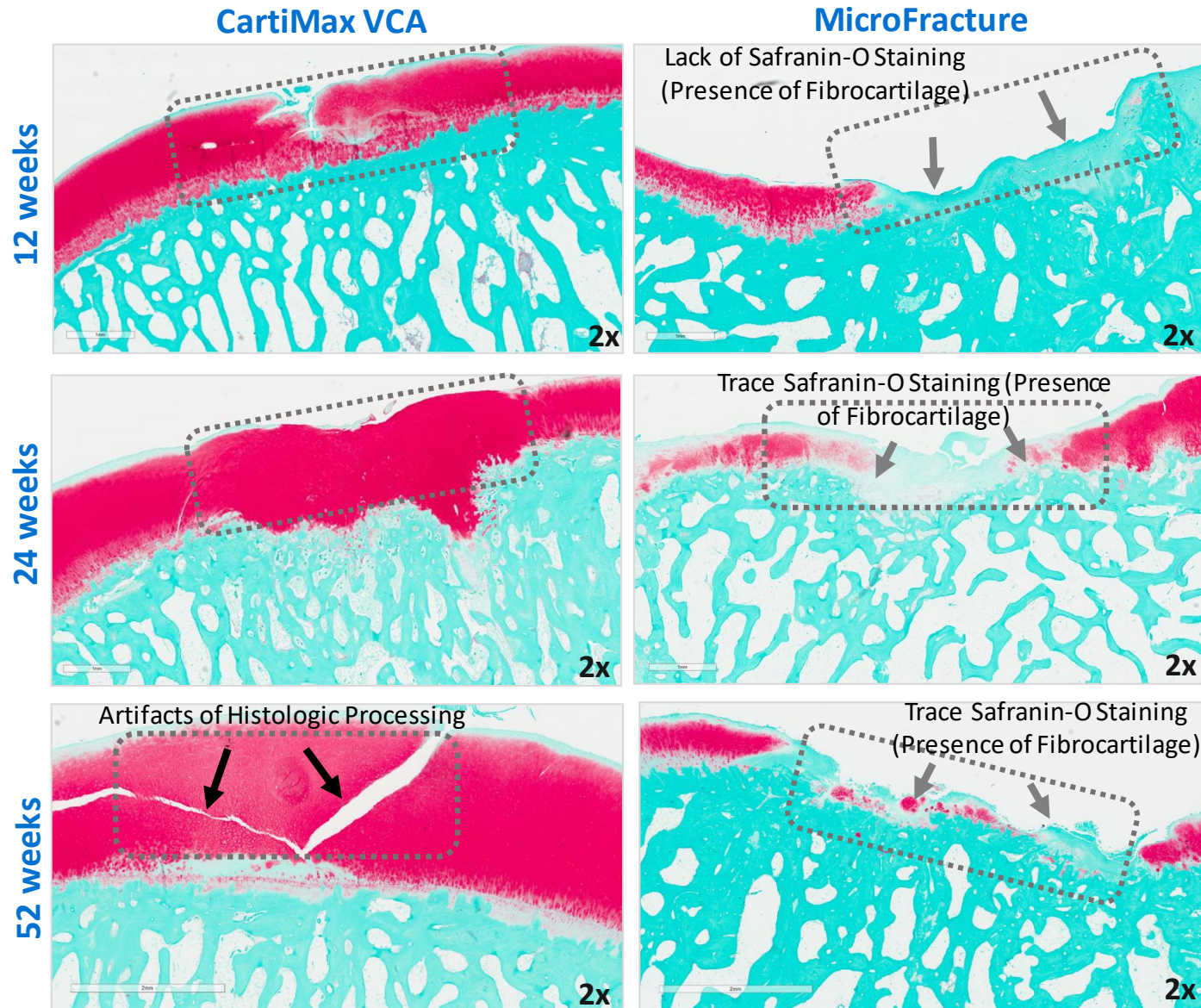
Types of Cartilage & Key Matrix Proteins	Proteoglycans (Safranin-O stain)	Collagen Content (Type)	Architecture
Hyaline Cartilage (Normal articular cartilage)	Red/Pink Staining 	Type II (no Type I) 	Organized Structure  Distinct lacunae
Fibrocartilage (Fibrous, non-articular cartilage)	Lack of Red/Pink Staining 	Reversed Type I (present) Type II (trace)	Fibrous Structure  Fibrous strands

FIGURE 2: PROMINENT HYALINE CARTILAGE SUSTAINED IN CARTIMAX OVER TIME

CartiMax VCA

Presence of
Hyaline Cartilage =
Prominent
red/pink staining
sustained over
time

Graft is safe
(no animals died)

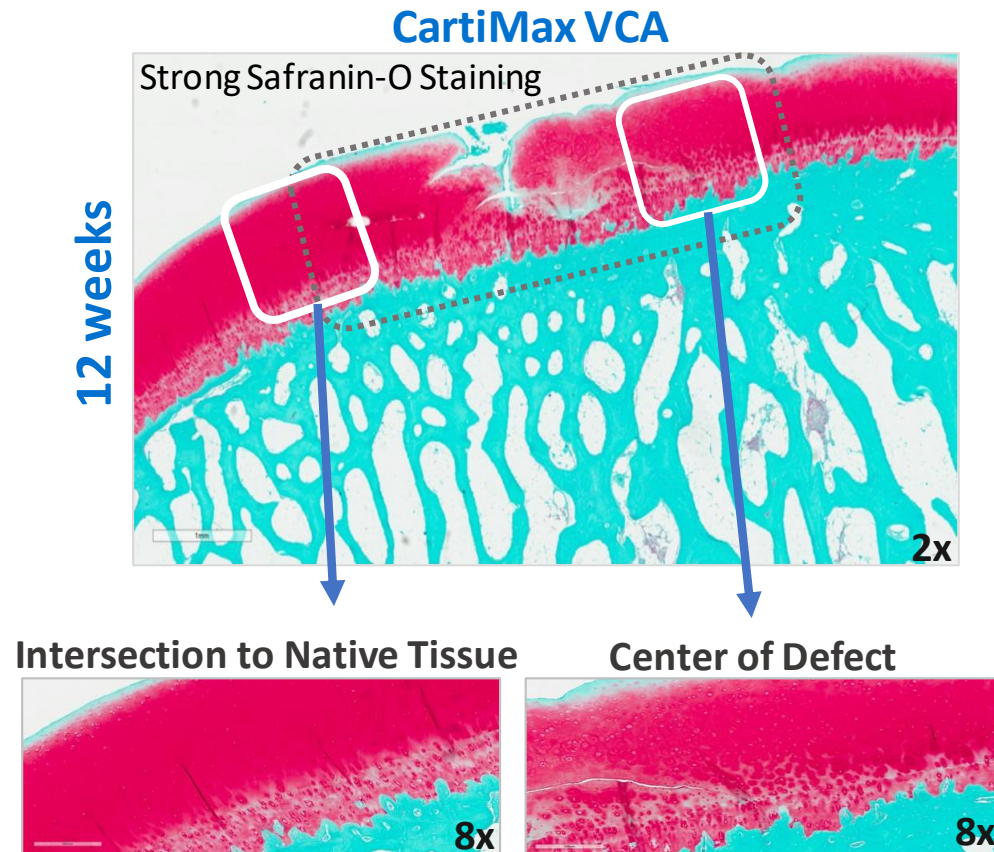


Microfracture

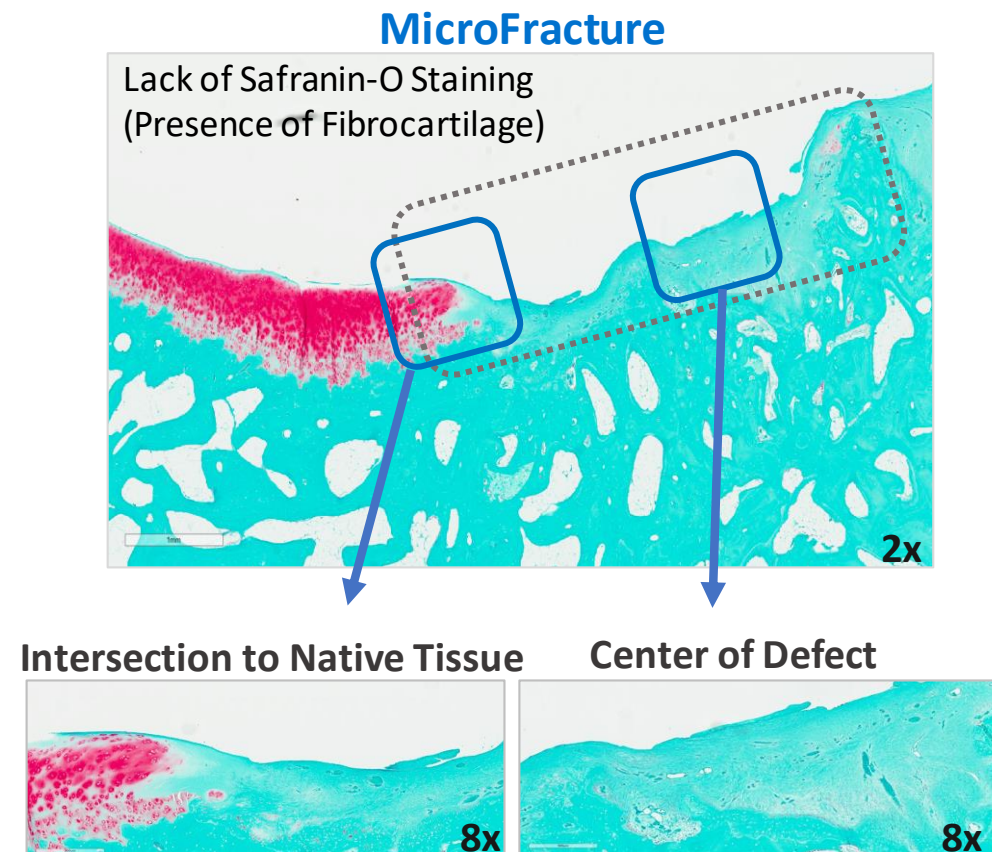
Presence of
Fibrocartilage
Cartilage = Lack of
red/pink staining
over time

Science Driven. Patient Focused.

LET'S ZOOM INTO THE DEFECT AREA

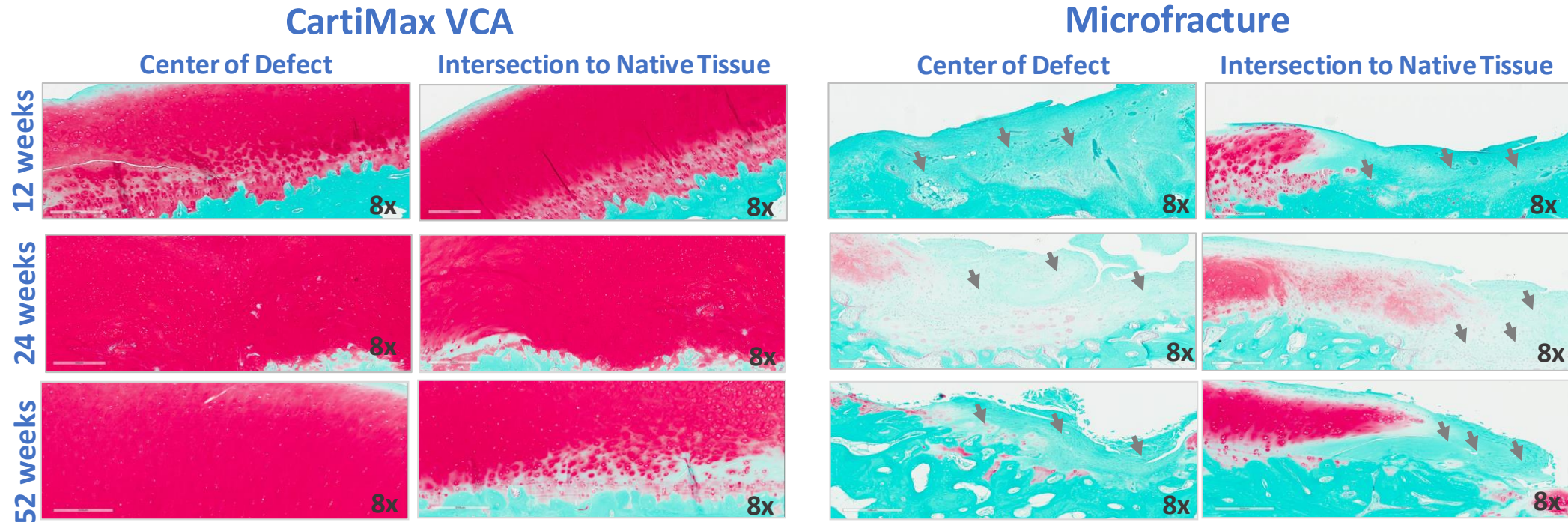


**Robust lateral/vertical integration of
CartiMax to native goat cartilage >
Hyaline Cartilage**



**Incomplete fill and lack of lateral/vertical
integration with microfracture to native
goat cartilage > Fibrocartilage**

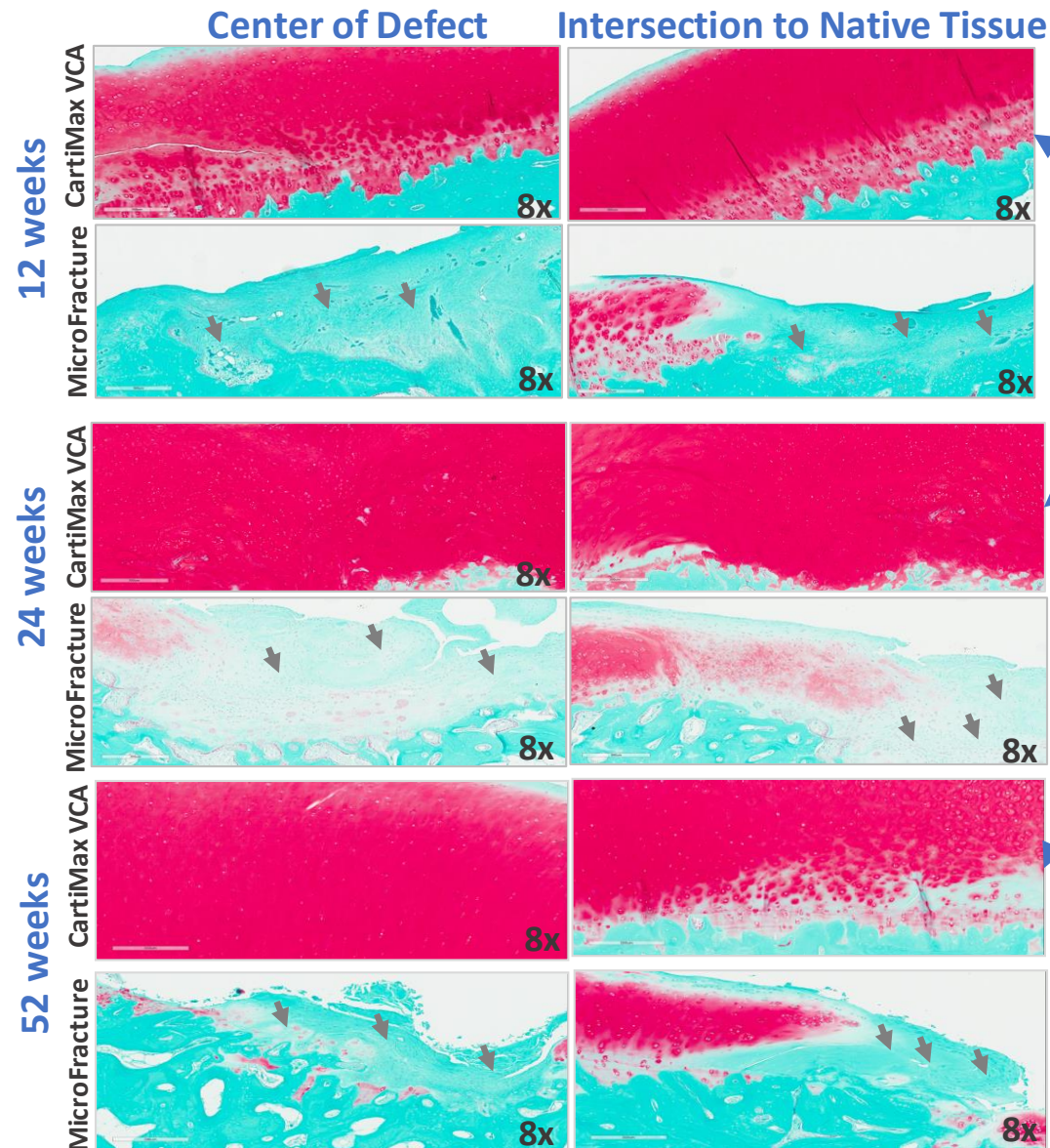
ROBUST LATERAL/VERTICAL INTEGRATION OF CARTIMAX TO ADJACENT NATIVE GOAT CARTILAGE



CartiMax revealed robust lateral/vertical integration to goat cartilage & sub-chondral bone, sustained over time

Microfracture resulted in fibrous tissue and lack of integration over time

FIGURE 2: ROBUST LATERAL/VERTICAL INTEGRATION OF GRAFT TO ADJACENT NATIVE GOAT CARTILAGE

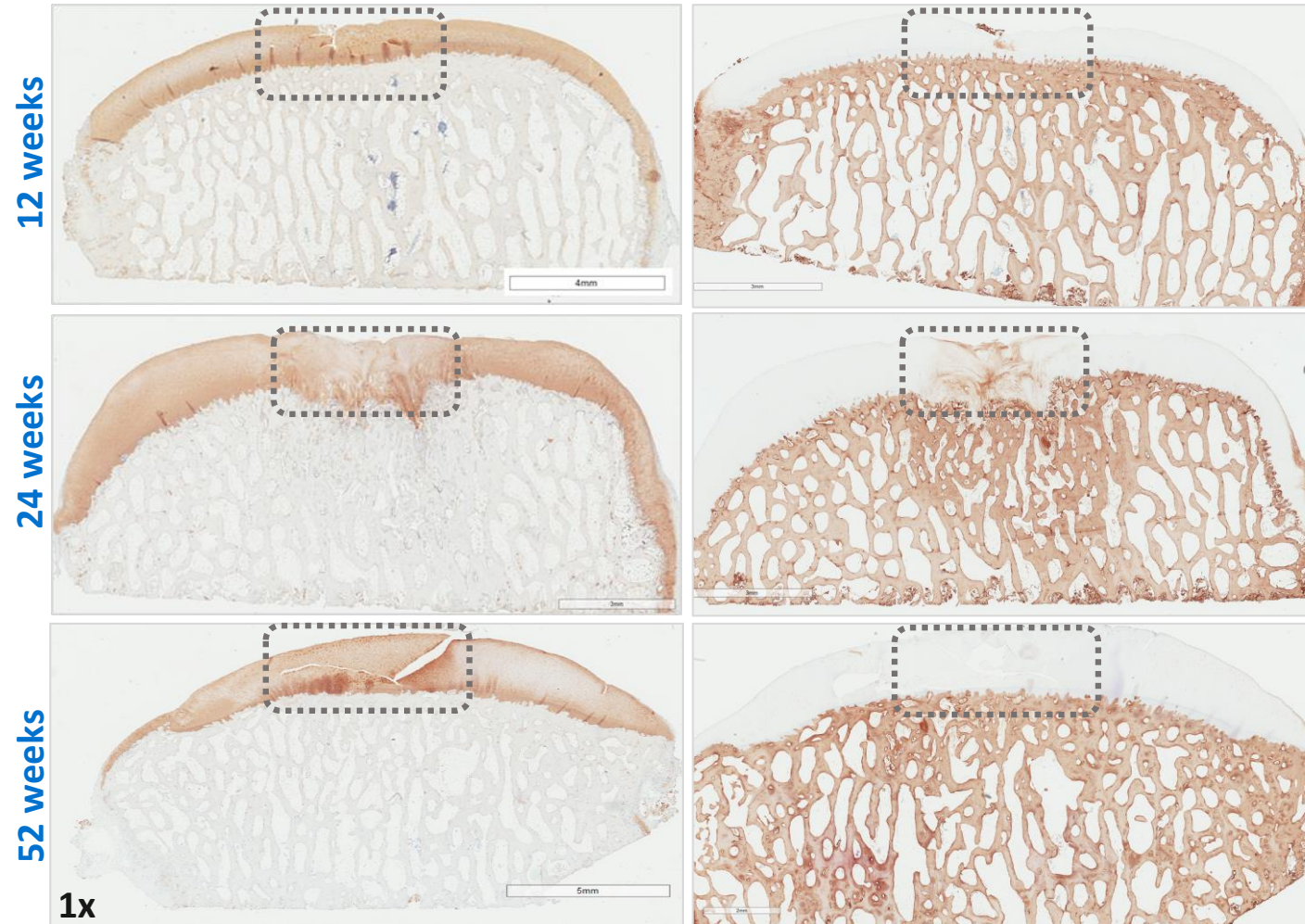


CartiMax revealed robust lateral/vertical integration to goat cartilage & sub-chondral bone, sustained over time

Microfracture treatment resulted in fibrous tissue and lack of integration over time

FIGURE 3: CARTIMAX SUPPORTS REMODELING INTO HYALINE CARTILAGE OVER TIME

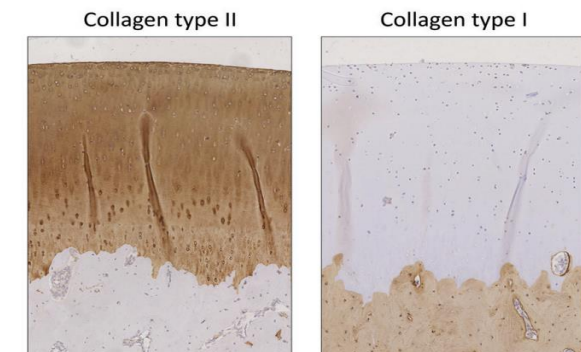
CartiMax VCA



Strong Collagen Type II
(Confirms Presence of Hyaline Cartilage)

Lack of Collagen Type I
(Confirms Lack of Fibrocartilage)

- ✓ Strong collagen type II staining over time
- ✗ No collagen type I staining over time
- Confirms presence of hyaline cartilage



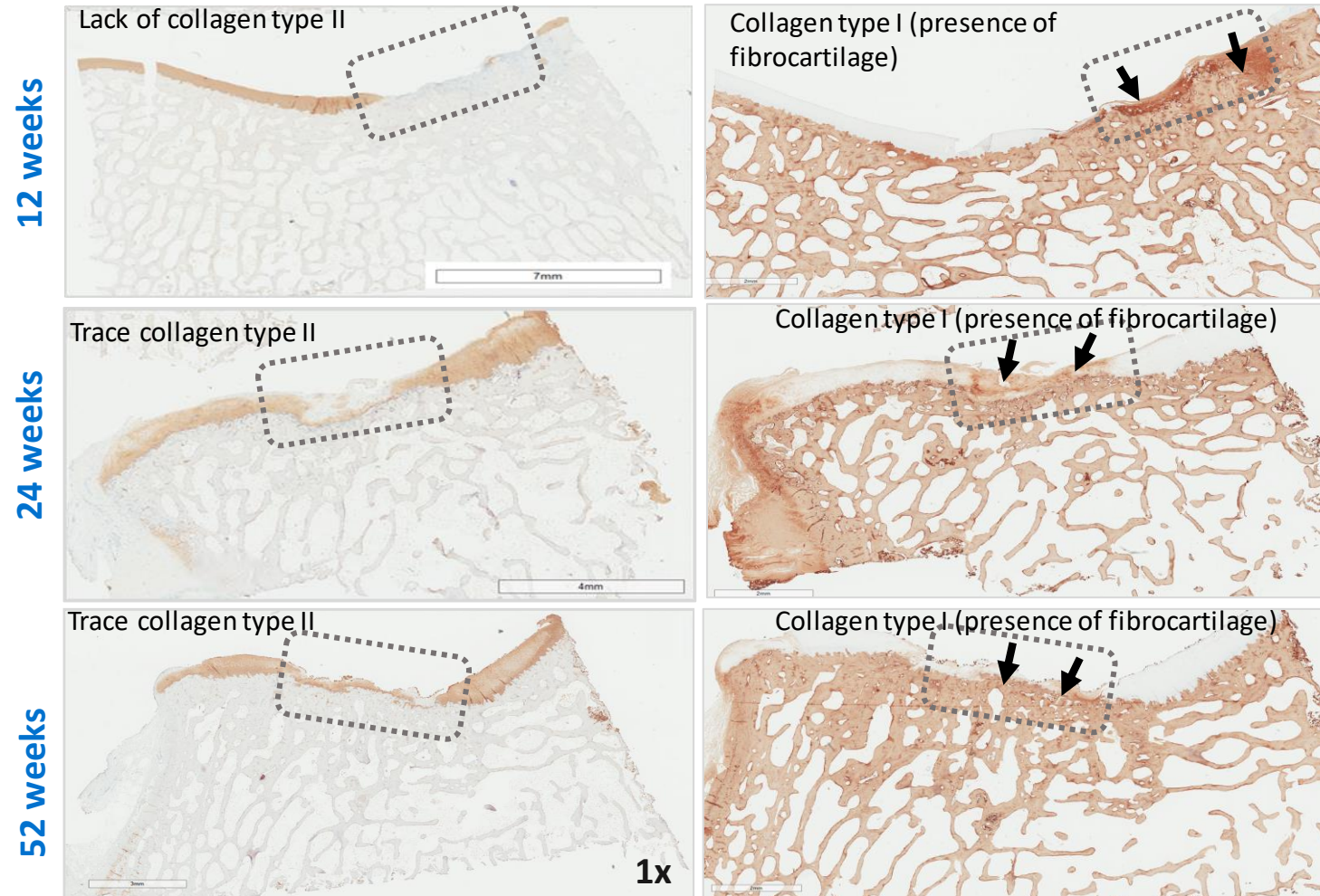
CartiMax Staining is Typical to
Hyaline Cartilage

Mouser et al.
2017

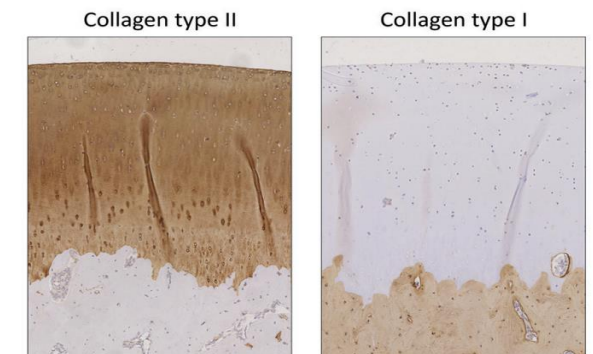
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FIGURE 3: MICROFRACTURE RESULTS IN FIBROCARILAGE FORMATION OVER TIME

MicroFracture



- x Trace collagen type II over time
- ✓ Strong collagen type I staining over time
- Confirms presence of fibrocartilage



Mouser et al.
2017

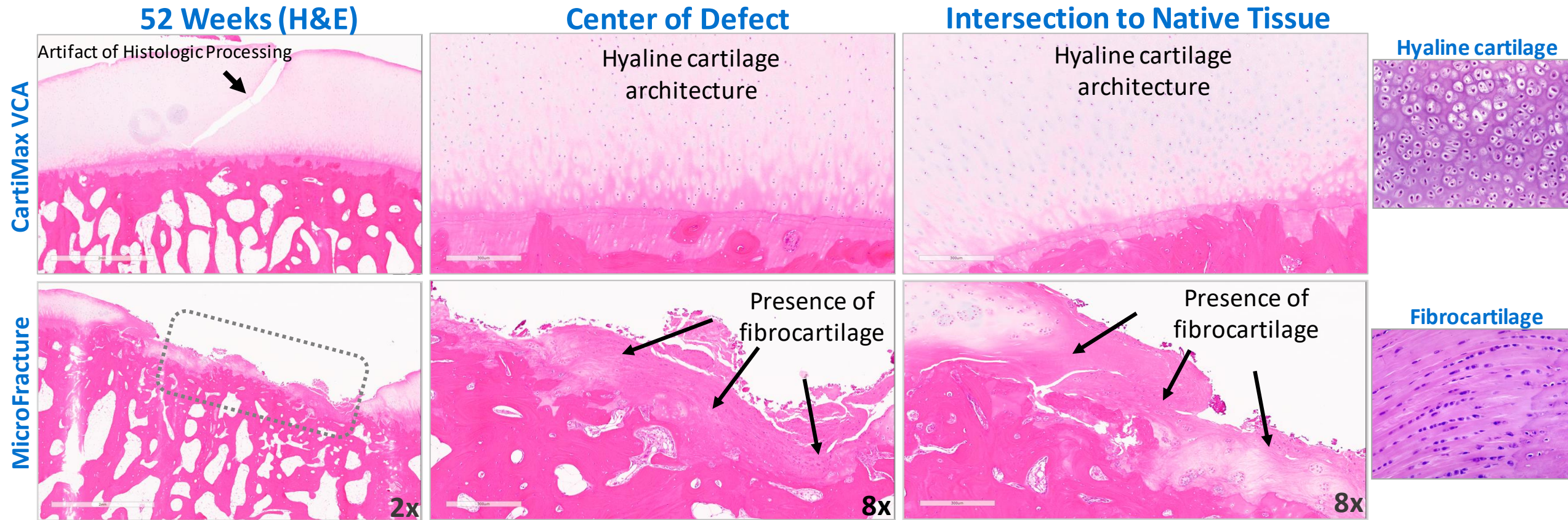
Trace Collagen Type II
(Confirms Trace Level of Hyaline Cartilage)

Strong Collagen Type I
(Confirms Presence of Fibrocartilage)

Microfracture Staining is Opposite to Hyaline Cartilage

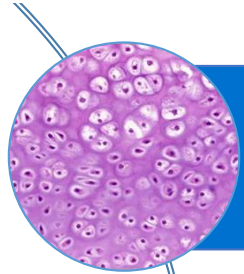
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FIGURE 4: HYALINE ARCHITECTURE IN CARTIMAX VCA TREATMENT

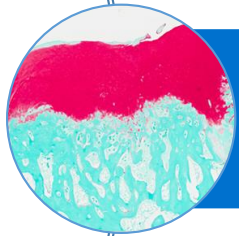


- At 52 weeks (1yr later), CartiMax VCA supports remodeling into hyaline architecture

CartiMax VCA is a safe and efficacious treatment for cartilage defects yielding durable hyaline cartilage unlike microfracture



CartiMax fills and remains in defect without fibrin glue



CartiMax supports rapid integration and remodeling of hyaline cartilage



CartiMax does not require subchondral bone microfracture (drilling)

Take Home Messages

IF YOU HAVE ANY QUESTIONS....

- **We are here to help!**

- MTF Scientists & Engineers
- MTF & ConMed Marketing

- **Channel requests through ConMed Marketing**

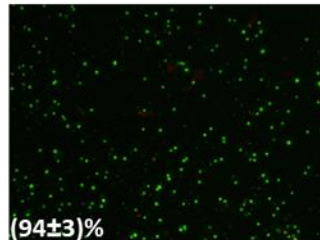
- Conference calls
- Webinars
- Visits





ANY QUESTIONS & THANK YOU?

VIABILITY



FUNCTIONAL CELLS



FORMS HYALINE CARTILAGE

