

Clinical Feasibility Study Evaluating Biomaterial Guided Cartilage Repair in the Knee

¹G.H. Albers M.D., ¹L. Taminiau M.D., ²A.B. Stibbe M.D., ³U. Pietzner M.D.,
³L. Völker M.D., ⁴A. Luth M.D., ⁴H. Schmitz M.D., ⁵E. Kon M.D., ⁵M. Marcacci
M.D., ⁶R. Erickson, ⁶N. Marcus M.D., ⁷J.H. Elisseeff Ph.D., ⁶B. Sharma Ph.D.

¹Tergooi Hospital, Orthopaedic Surgery, Hilversum, The Netherlands; ²Meander Medical Center,
Baarn, The Netherlands; ³Dietrich-Bonhöffer Hospital, Altentreptow, Germany; ⁴Orthopedic
Clinic Zähringen, Freiburg, Germany; ⁵Rizzoli Orthopaedic Institute, Bologna, Italy; ⁶Cartilix Inc.,
Foster City, CA, USA; ⁷Johns Hopkins University, Baltimore, MD, USA

The logo for Cartilix, featuring the word "cartilix" in a bold, lowercase, purple sans-serif font. The letter "i" is stylized with a blue circle above it, resembling a joint or a specific anatomical feature.

Articular Cartilage Repair

- Articular cartilage lesions are prevalent.

- Chondral lesions found in 60% of 25,000+ patients undergoing knee arthroscopies

(Widuchowski, et al., The Knee. Feb. 2007)



www.vangnessmd.com

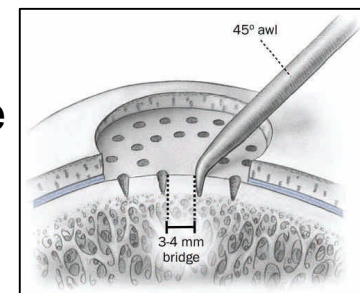
- Microfracture is frequently used as a first-line treatment.

- Good results in young patients, small lesions, low BMI, acute symptoms (Kreutz et al., OA&C 2006; Mithoefer et al., JBJS, 2006).

- Poor outcomes associated with poor defect fill, osseous overgrowth.

- Mithoefer et al. reports 54% microfracture patients had “good” repair tissue fill (>67% of defect) by MRI.

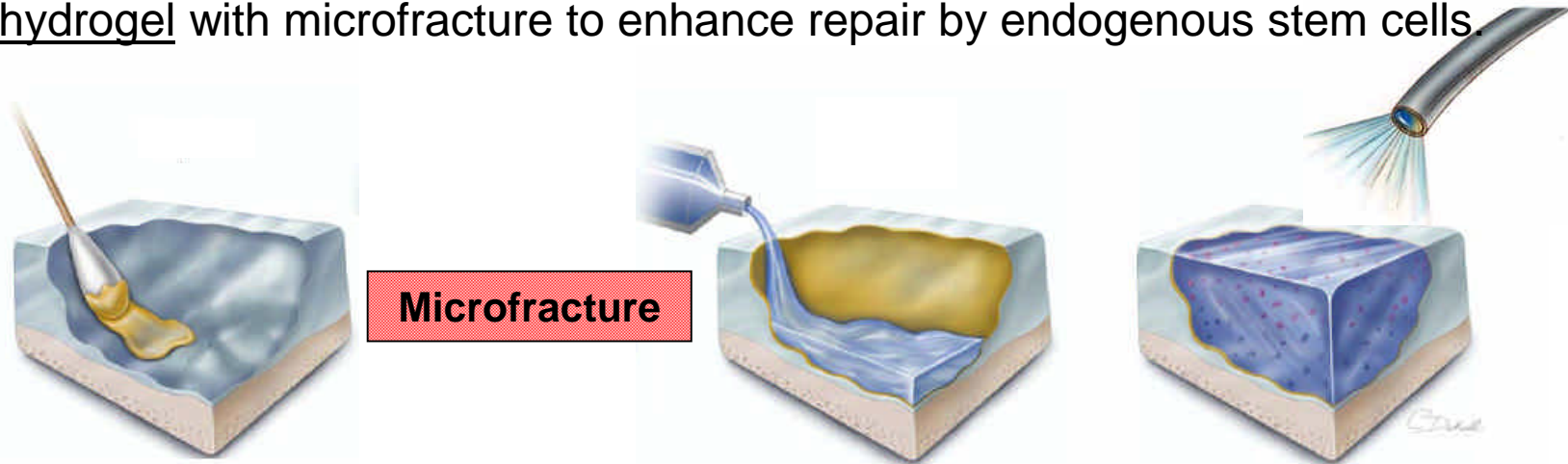
- Other techniques (ACI, OATS, allograft) limited by cost, need for multiple surgeries, donor site morbidity, risk of infection.



Mithoefer et. al, JBJS, 2006

ChonDux™ Cartilage Repair System

ChonDux™ combines a biological adhesive and photopolymerized hydrogel with microfracture to enhance repair by endogenous stem cells.



Biological Adhesive

- Functionalized chondroitin sulfate
- Bonds hydrogel to cartilage surface
- Supports cartilage tissue formation at interface

(Wang et al., Nature Materials, May 2007)

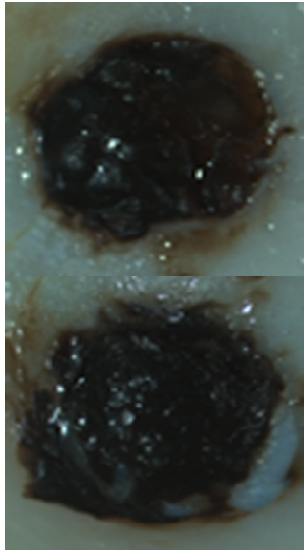
Photopolymerized hydrogel

- PEG and hyaluronic acid
- Reinforces clot
- Retains cells and factors from bone marrow in defect
- Conducive to chondrogenesis

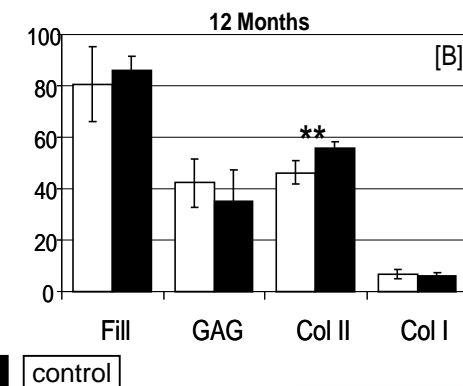
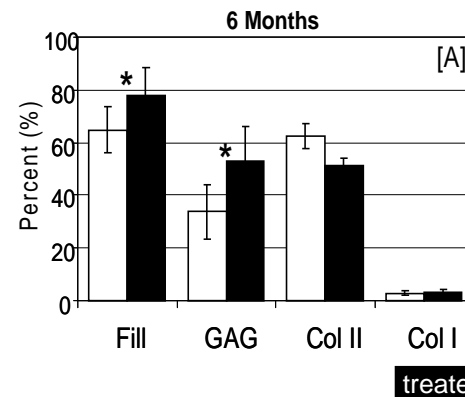
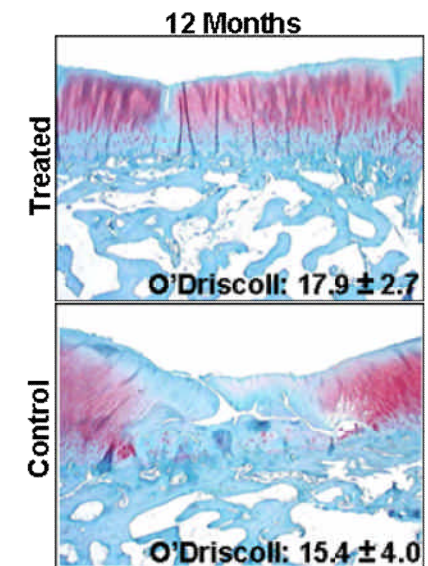
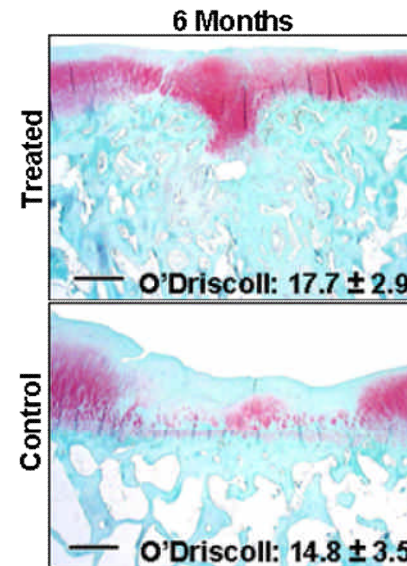
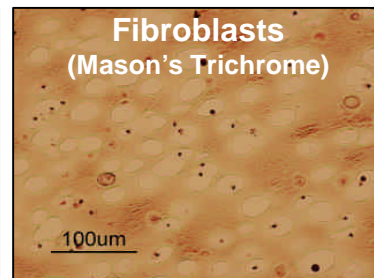
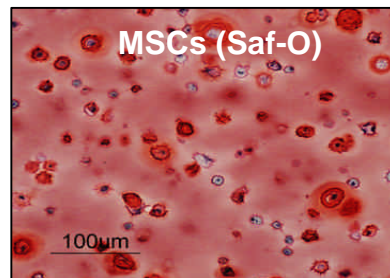
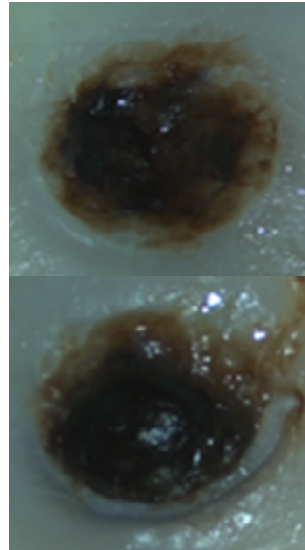
(Williams et al., Tissue Engineering, 2003;
Sharma et al., PRS, Jan 2006)

Preclinical Studies

Microfracture+
ChonDux



Microfracture



Clinical Feasibility Study Objectives

- Determine human safety
- Evaluate surgical application
- Assess measurement tools for monitoring cartilage repair

Study Design

- **Multicenter study**
 - 5 centers, 15 treated patients
- **Inclusion/Exclusion**
 - Single, symptomatic, full-thickness lesion (Outerbridge II or IV)
 - 2-4 cm²
 - Medial femoral condyle
 - Stable knee
 - No general osteoarthritis
- **Outcome measures**
 - Defect fill and integration (MRI)
 - Pain (Visual Analog Scale)
 - IKDC subjective knee evaluation score
 - Time Points: baseline, 3 mo., 6 mo., 12 mo.
 - Safety (Adverse Events)

Patient and Injury Data

- **Age:** 27-57 yrs., 10/15 patients > 40 yrs. old
- **BMI:** 26.9 ± 3.8 , 3/15 patients > 30
(BMI: normal < 25; overweight > 25; obese > 30)
- **Etiology:** most were unknown causes/gradual onset, ~40% traumatic/sports injury
- **Duration of Symptoms:** 2 to 192 mo., 50% patients had symptoms for > 24 mo.
- **Defect Size:** $2.5 \pm 0.5 \text{ cm}^2$

Surgical Application



Mini-open approach



Debride lesion
Apply adhesive



Microfracture



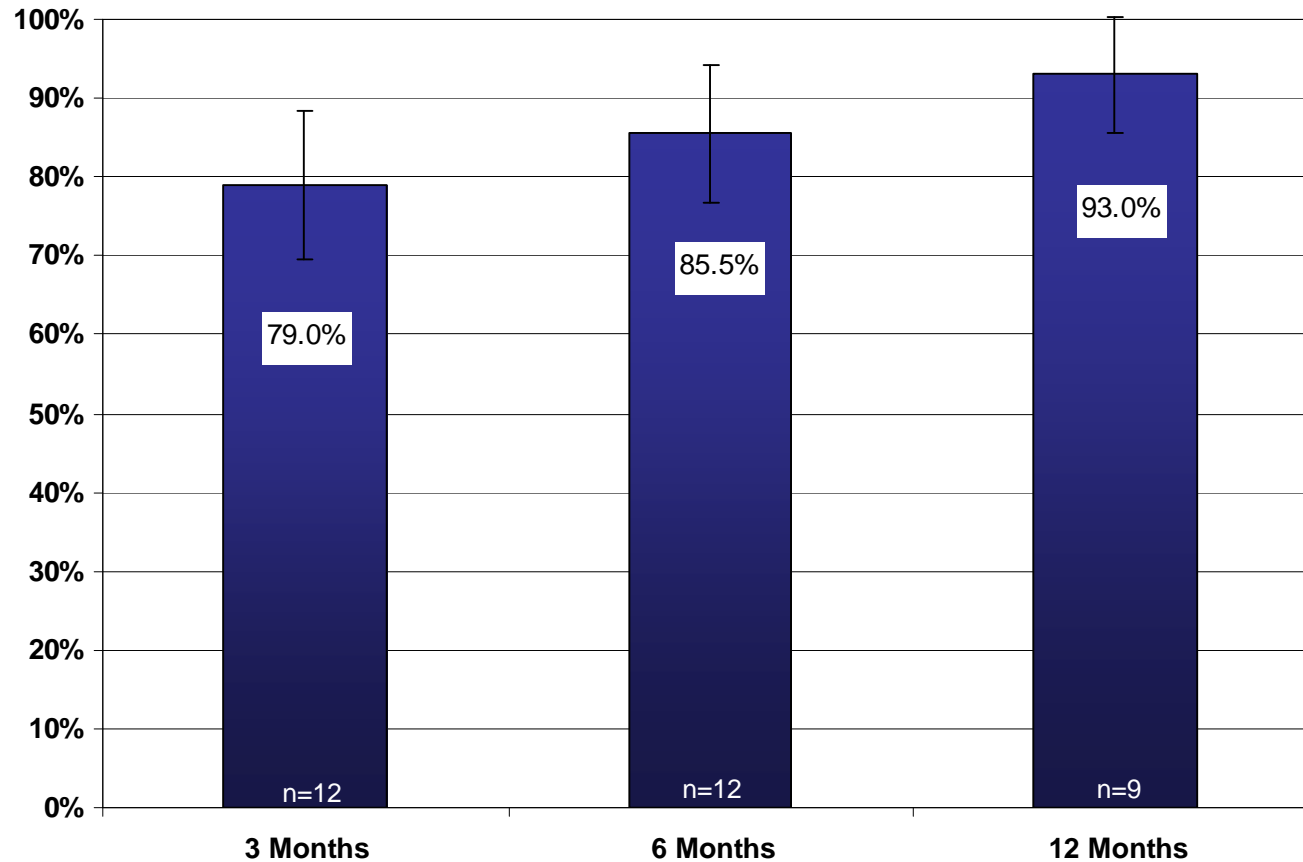
Apply hydrogel and
photopolymerization

Treatment of
irregular lesions



Hydrogel secure
upon release of
tourniquet

Defect Fill (MRI)



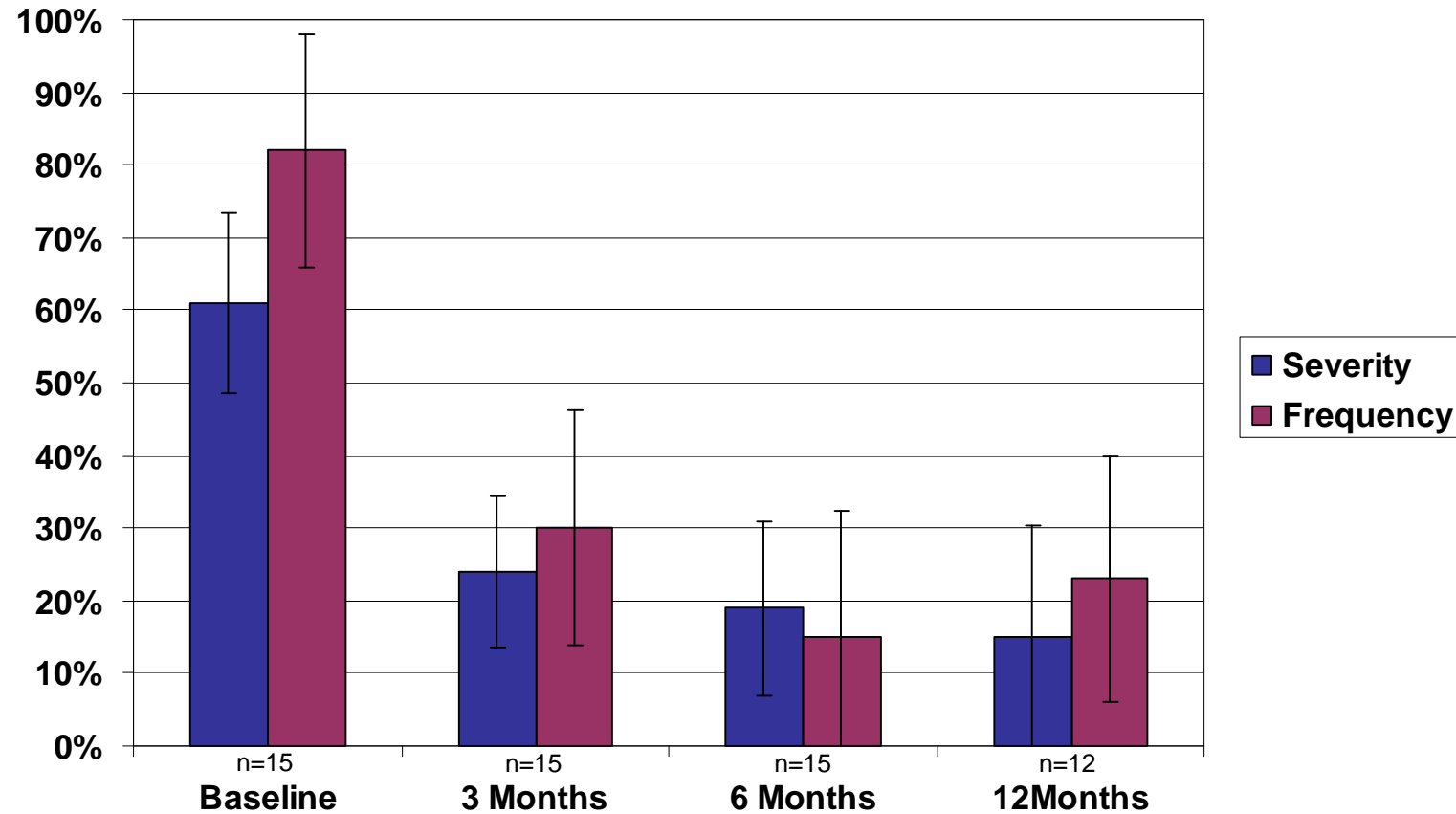
- ~90% of patients have defect fill >75% at 6 and 12 months.

Data reported as median \pm average deviation

MRI Results cont'd

- Repair Tissue Integration
 - 8/12 patients have 100% integration at 6 months (trend continuing at 12 months)
 - 4/12 patients have gap < 2 mm
- No osseous overgrowth into cartilage region in any patients

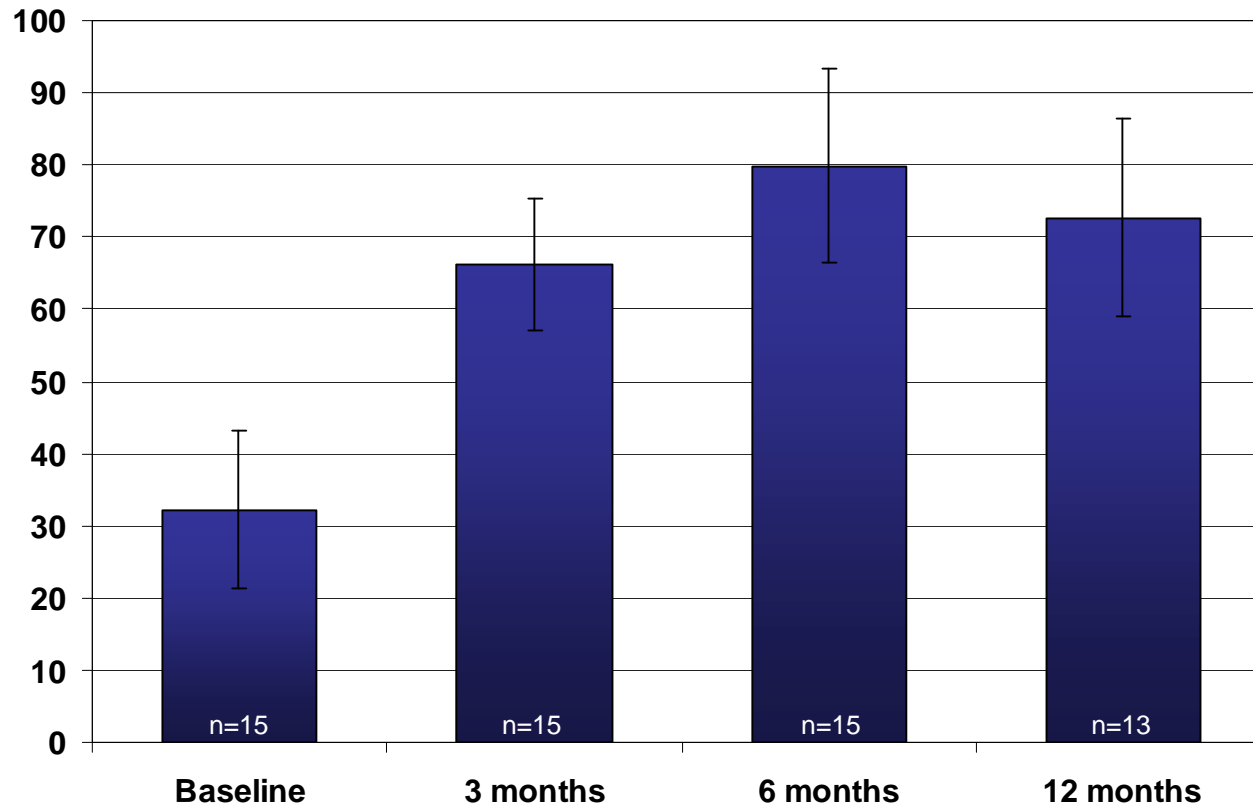
Pain Scores



- 12/13 ChonDux patients have reduced pain at 12 months
- One patient has continued pain, but defect fill of 94%

Data reported as median \pm average deviation

IKDC Scores



- 14/15 patients at 6 months and 12/13 patients at 12 months have improved knee function.

Data reported as median \pm average deviation

Safety

- No unanticipated adverse events.
 - One patient reported a post-surgical hemarthrosis which resolved without treatment.

Conclusions

- ChonDux is safe and clinically applicable.
- Demonstrated significant defect fill, reduction in pain, and improvement in knee function.
- Provides basis for an expanded, controlled study against microfracture.
- ChonDux may offer an effective, single surgery, off-the-shelf treatment for repair of cartilage lesions.

Acknowledgements

Investigators

G.H Albers, M.D.
L. Taminiau, M.D.
A.B. Stibbe, M.D.
U. Pietzner, M.D.
L. Volker, M.D.
A. Luth, M.D.
H. Schmitz, M.D.
E. Kon, M.D.
M. Marcacci, M.D.

Cartilix

Ross Erickson
Norm Marcus, M.D.
Sara Fermanian
Lu Liu
Jayne Prentice
Frank Huerta

MRI

Garry Gold, M.D. (Stanford University)
Virtualscopics, Rochester, NY

Johns Hopkins University

Jennifer Elisseeff, Ph.D.

The logo for Cartilix, featuring the word "cartilix" in a bold, lowercase, sans-serif font. The letter "i" is stylized with a blue circle above it, resembling a dot or a lens.