COLLAGEN SOLUTIONS
MATERIALS FOR LIFE

ChondroMimetic Clinical Study Update

September 20, 2017

ChondroMimetic Clinical Study Update Summary

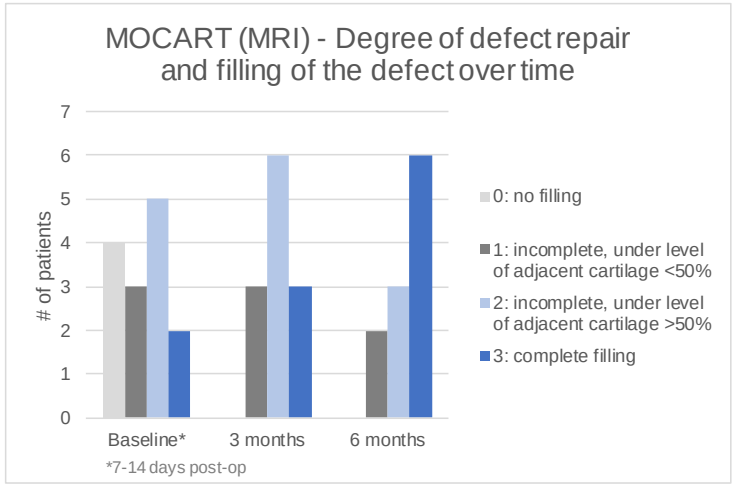
Original Study

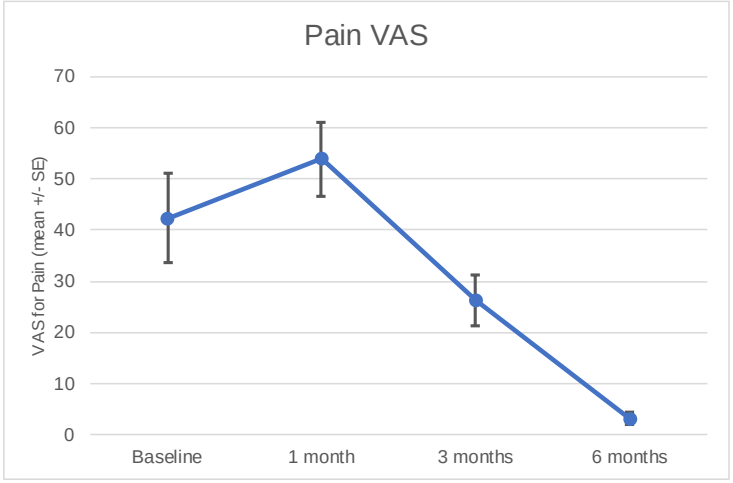
- Single centre study to confirm the safety and early outcomes with ChondroMimetic in the treatment of osteochondral defects of the knee
- 6-Month clinical trial enrolled 17 patients in 2009-2010
- 6-Month results demonstrated safety and improved clinical outcomes
- MRI data analysed in 2017 indicated early improved structural defect repair

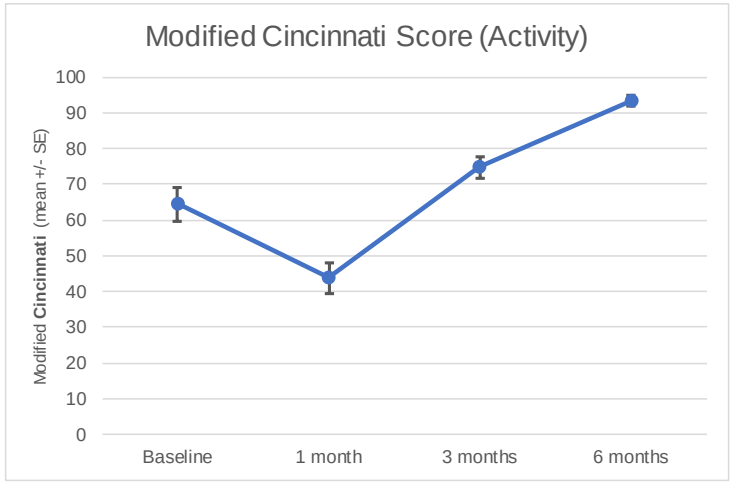
Extension Study

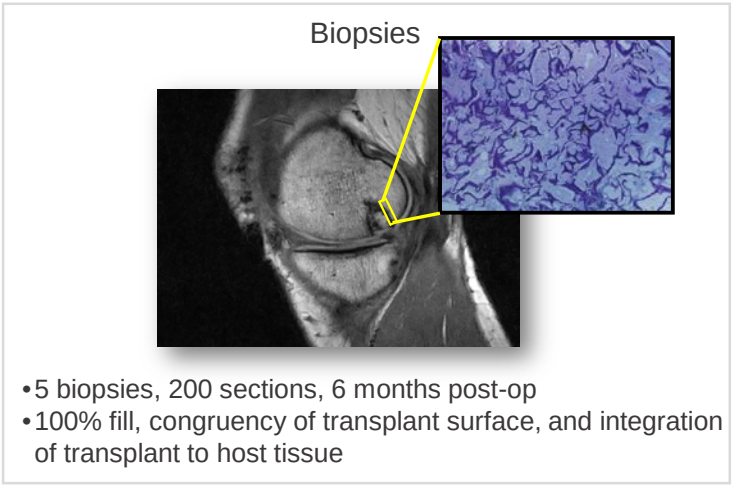
- 15 patients assessed in 2017 for prospective 8-year extension study
- **“Last Patient Out” on September 20, 2017**
- Study to assess long-term sustained cartilage defect repair
- Full clinical and MRI data analysis ongoing

ChondroMimetic 6-Month Clinical Study Summary Results









Summary

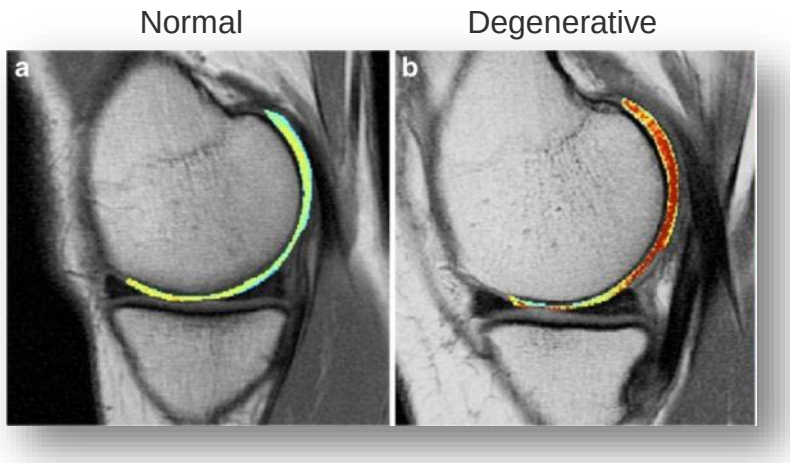
- MRI illustrates performance of defect filling, lateral integration, subchondral bone condition
- Clinically relevant decrease in Pain
- Increase in activity level by Cincinnati score
- Biopsies indicate integration of transplant to the host tissue

Advanced MRI Analysis

To assess sustainability, completeness of bone and cartilage defect filling, and cartilage quality, applied to both 6-Month and 8-Year data sets

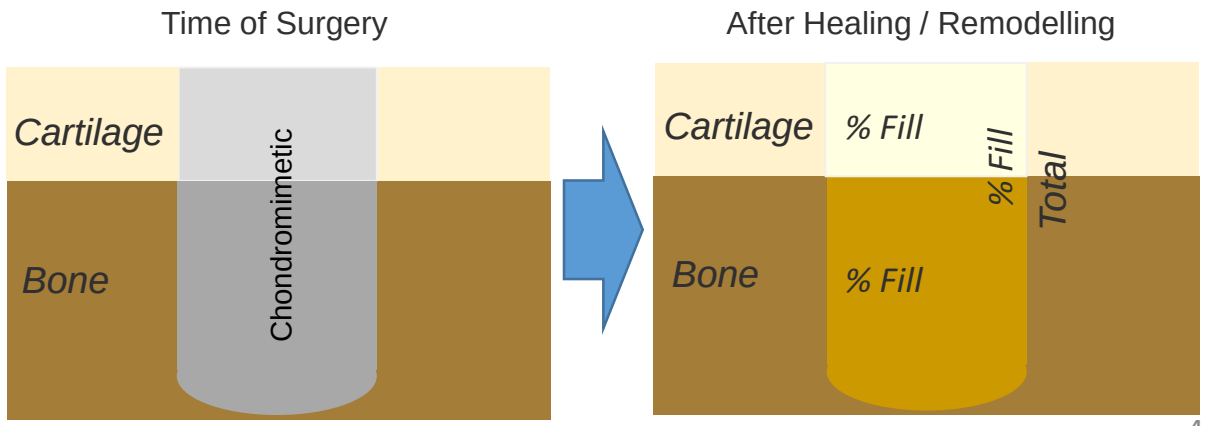
T2 Mapping

- Technique to evaluate knee cartilage
- Assesses the 3D structure of cartilage
- Used in research studies to detect disease- and treatment-related changes to cartilage



3D Quantitative MRI

- Technique to quantify the % fill of both cartilage and bone
- Used to provide quantitative and statistical analysis of completeness of bone and cartilage defect filling

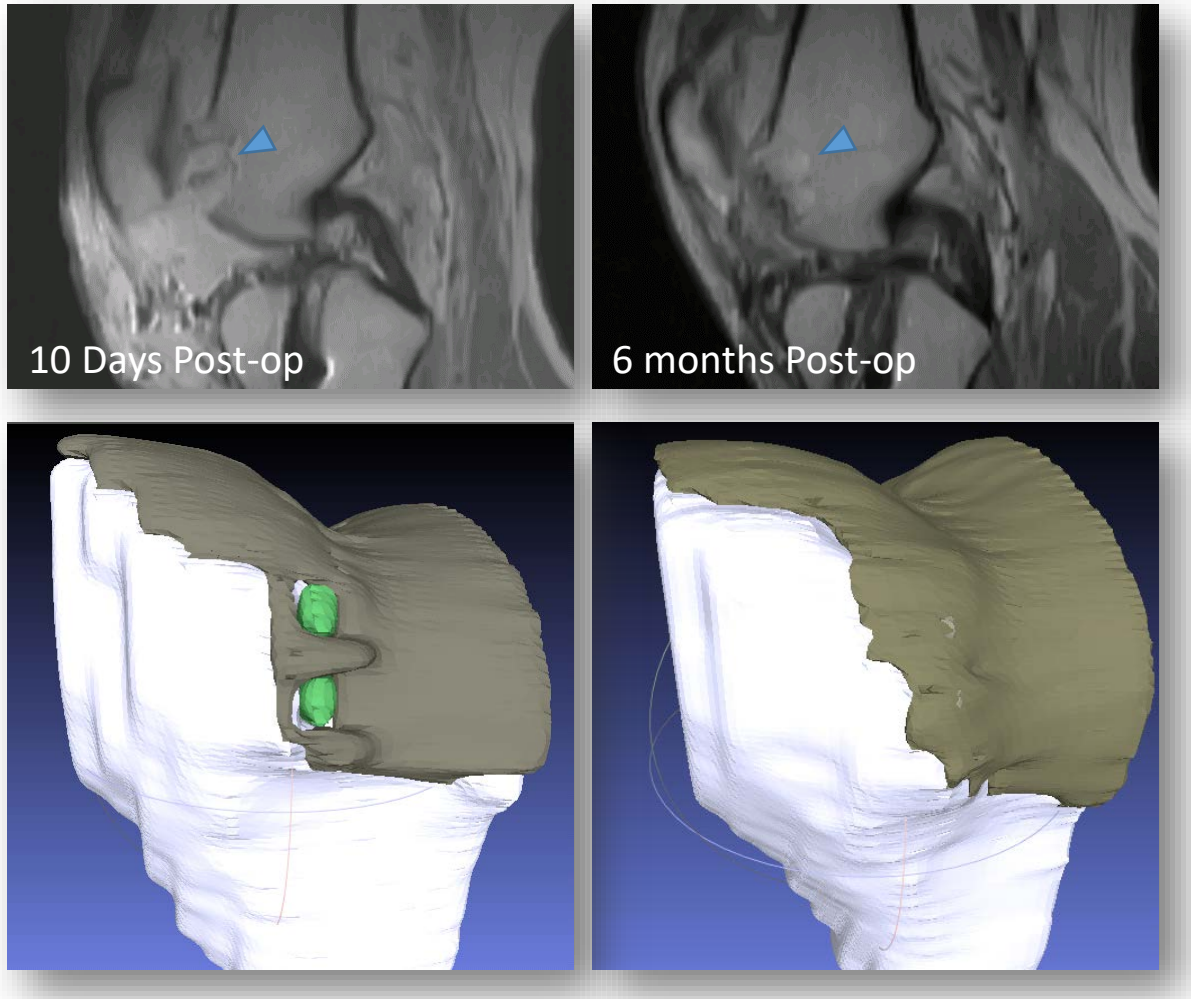


ChondroMimetic 6-Month Clinical Study Case Report

Case Report: Study Subject 02, Female, 39 yrs old, 28 BMI, primary repair (2 implants)

2D MRI

3D MRI Reconstruction



Native Cartilage T2 Signal

Original Scaffold T2 Signal

Summary

- T2 mapping retrospectively applied to original 6-Month MRI data
- Data indicates ChondroMimetic scaffold was virtually indistinguishable from surrounding cartilage at six months following surgery

ChondroMimetic Extension Study 8-Year Follow Up

Status

- Study at Dr. Lazlo Hangody's site in Hungary
- 15 of original 17 patients agreed to participate
- All 15 patients seen and assessed, MRI and other data obtained
- Extension study includes advanced MRI analysis (3D MRI, T2 Mapping)
- Data is being compiled and audited to prepare Clinical Study Report
- Data analysis in collaboration with Qmetrics Technologies and Matt Shive, PhD

Next Steps

- Data to be compiled and audited
- Data analysis to be performed, including MRI, function, and pain
- Completion of the Clinical Study Report
- Submit package to regulatory authorities for re-establishment of CE mark
- Targeting commercialisation outside the US in mid-2018

Appendix

Original ChondroMimetic 6-Month Clinical Study Design

- Open label, prospective study to confirm the safety and early outcomes with ChondroMimetic in the treatment of osteochondral defects of the knee
- February 2009 - October 2010
- GCP-Compliant, single center, Uzsoki Hospital, Traumatology department, Dr. Laszlo Hangody, Budapest, Hungary
- 17 Subjects
  - 15 mosaicplasty backfill defects
  - 2 primary cartilage defects
- Assessments at 6 months
  - Visual Analogue Scale (VAS) for pain
  - Modified Cincinnati Rating System
  - Bandi Score
  - MRI (MOCART)
  - Optional osteochondral biopsy

ChondroMimetic 8-Year Extension Study Design

- Open label post-marketing surveillance study
- Single centre in Hungary with Dr. Lazlo Hangody
- Collaboration with Qmetrics Technologies and Matt Shive, PhD
- 15 of 17 subjects who completed 6 month protocol signed up (2 lost to follow up)
- Assessments at approximately 8 years
  - MRI, including 3D fill assessment and T2 analysis
  - Modified Cincinnati Rating System
  - Knee injury and Osteoarthritis Outcome Score (KOOS)

About Laszlo Hangody MD, PhD, DSc

SPECIALTIES

- László Hangody, MD, PhD, DSc, is a Clinical Professor at the Debrecen Medical School. He is Senior Consultant in the Orthopaedic Department at Uzsoki Hospital and at the Sanitas Private Clinic, also in Budapest.
- Dr. Hangody's research focuses primarily on the cartilage repair, revision surgery of anterior cruciate ligament deficient knees, and minimal invasive total hip and knee replacement.

EXPERIENCE

- Dr. Hangody completed his medical degree (1982) at Semmelweis University of Medicine; received his PhD (1994) and DSc (2000) degrees from the Hungarian Scientific Academy. His specialties are orthopaedics and traumatology.
- He has written a number of chapters and articles for the medical press and has been an invited lecturer at over 300 international scientific meetings.
- He serves on the editorial boards of The Knee; Endoscopy and Minimal Invasive Therapy; Arthrocopy and Joint Surgery; Hungarian Journal of Orhopaedics and Trauma.
- He is an instructor of the PhD program of the Semmelweis Medical School and the Debrecen Medical School.
- Dr. Hangody is the past president of the Hungarian Orthopaedic Association, the elect president of the Hungarian Arthroscopic Society and a Honorary Member of the Arthroscopy Association of North America. He is a member of the SICOT, AAOS, ESSKA, ISAKOS and ICRS.

About Matthew Shive, PhD

SPECIALTIES

- Industry: Bench to bedside development of novel products (preclinical, clinical, regulatory)
- Regulatory: Medical device and pharmaceutical strategic programs
- Clinical: Design and implementation of orthopedic multicenter RCTs
- Research: Biomaterial Science: PhD, Biomedical Engineering (material science focus)

EXPERIENCE

- Current CSO of Arthritis Innovation Corporation
- Former CSO of BioSyntech (BST-CarGel; acquired by Piramal Healthcare)
- Product development consultant for multiple novel orthopedic technologies
- 130+ scientific publications and conference proceedings in the fields of biomaterials, tissue repair and cartilage repair.

SPECIFIC CARTILAGE EXPERIENCE

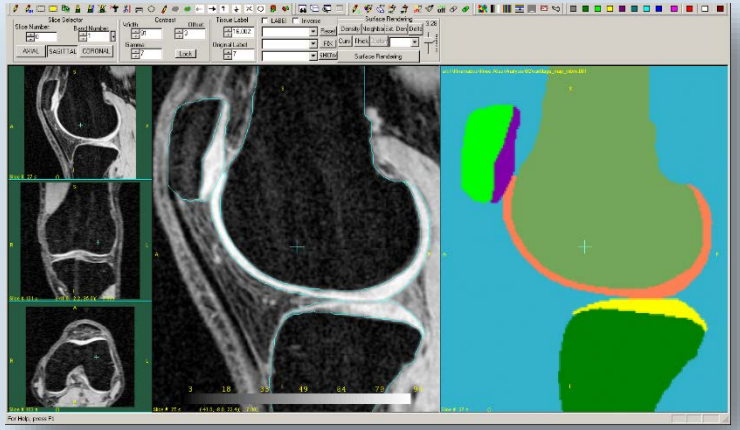
- Designed and implemented phase III RCT for BST-CarGel, approved in Canada, Europe, and Australia.
- Analysis and interpretation of Phase III and Extension study clinical data, Clinical Summary, and all abstracts/publications for cartilage repair product, BST-CarGel.
- Authored of 2 pivotal high impact publications (JBJS, Cartilage) describing both 1 and 5 year outcomes of multicenter clinical trial
- BST-CarGel was acquired by Smith & Nephew in 2016

About Qmetrics Technologies

Qmetrics TECHNOLOGIES

- Specialised imaging service organisation
- Accurate image segmentation, 3D modeling and quantitative analysis
- Quantitative 3-dimensional MRI advanced imaging

Validated Atlas-Based Segmentation and Quantitative Analysis



Semi-automated (radiologist corrected) morphological segmentation using anatomical atlas

3-D Reconstruction from segmentation

Repair tissue quantitatively evaluated as complete 3D object