Time Matters: Knee Cartilage Defect Expansion and High-Grade Lesion Formation while Awaiting Autologous Chondrocyte Implantation

Robert J. Pettit, Joshua S. Everhart, Alex C. DiBartola, Ryan E. Blackwell, and David C. Flanigan
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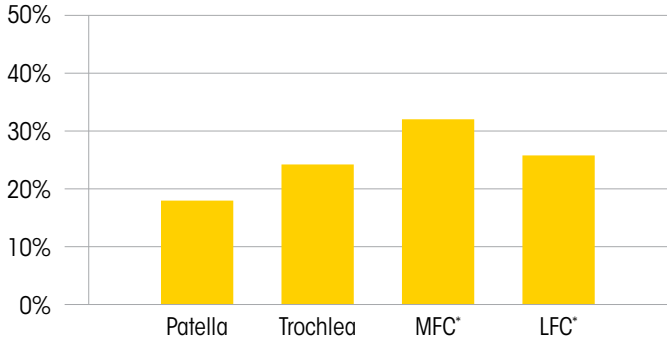
Delays in treatment—Risk factors for patients awaiting autologous chondrocyte implantation

Objective	Study design	Methods
The objective of this study was to assess potential risk factors, including time delay until implantation, for knee cartilage defect expansion or new high-grade defect formation between biopsy and Autologous Chondrocyte Implantation (ACI) or Matrix Autologous Chondrocyte Implantation (MACI).	Consecutive knee ACI and MACI cases by a single surgeon (128 knees in 111 patients) were reviewed. The relationship of time between biopsy and staged implantation and (1) progression in primary cartilage defect size and (2) development of a new high-grade (Outerbridge grade ≥3) cartilage defect were determined with adjustment for demographics, body mass index, smoking status, coronal alignment, initial cartilage status, and prior surgery.	After receiving institutional review board approval, a retrospective chart review of 128 knees in 111 consecutive ACI and MACI patient cases by a single surgeon over a 10-year period (2008-2018) was performed.

Patient demographics and cartilage defect characteristics

All characteristics of cartilage defects were recorded at time of biopsy and time of implantation.

Location of high-grade cartilage defects at time of biopsy (128 defects in 111 patients)



*MFC=medial femoral condyle, LFC=lateral femoral condyle

Patient Demographics and Knee Alignment

Variable	Mean (SD) or Number (%)
BMI	27.9 (4.5)
Age	31.3 (9.7)
ACI (n = knees) / MACI (n = knees)	77 / 51
Male / Female	56% / 44%
Tobacco use status	23.4%
Prior microfracture	7.2%
Coronal alignment (hip-knee-ankle angle)	0.56 degrees of varus (2.41)
% lateralization of mechanical axis at tibiofemoral joint line	48.44% (4.54)

Important Safety Information

Contraindications: MACI is contraindicated in patients with a known history of hypersensitivity to gentamicin, other aminoglycosides, products of porcine or bovine origin; in patients with severe osteoarthritis of the knee, inflammatory arthritis, inflammatory joint disease, or uncorrected congenital blood coagulation disorders; in patients who have undergone prior knee surgery in the past 6 months, excluding surgery to procure a biopsy or a concomitant procedure to prepare the knee for a MACI implant; or in patients unable to cooperate with a physician-prescribed post-surgical rehabilitation program.

Please see Important Safety Information and Full Prescribing Information.

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Delays in treatment—Knee cartilage defect expansion and high-grade lesion formation

Cartilage defect expansion

0.6 cm^2 mean change in defect size between biopsy & implantation

0.11 cm^2 increase in defect expansion per month delay to implantation

New high-grade cartilage defects

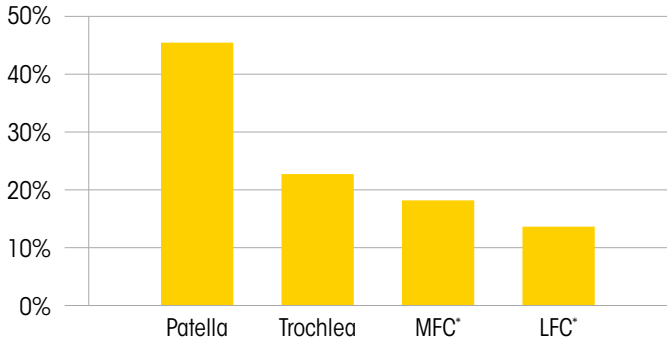
16.2% of patients (18/111) developed a new high-grade cartilage defect

155 days mean time between cartilage biopsy & implantation

Time between biopsy & implantation and defect characteristics at time of implantation

Variable	Mean (SD)
Initial defect size	4.3 cm^2 (2.1)
Time between biopsy & implantation	155 days (131)
Final Defect Size	4.9 cm^2 (2.3)
Mean change in size between biopsy and implantation	0.6 cm^2 (1.9)
Mean change in defect size per 1 month (30 day) delay	0.11 cm^2 (0.03)

Distribution of lesions in new high-grade cartilage defects (22 defects in 18 patients)



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Conclusions and Impact

In patients undergoing cell-based knee cartilage restoration, lesions can progress and new lesions can form as time between cartilage biopsy and implantation increases.

Patients who were male, had smaller initial defect size, and longer time between surgeries were at greater risk for defect expansion.

Surgeons, patients, insurance, and industry should coordinate efforts to expedite the interval between biopsy and implantation to prevent further deterioration of the knee joint and obtain better patient outcomes.

Important Safety Information

Warnings and Precautions:

- Malignancy: The risk of MACI in patients with malignancy in the area of cartilage biopsy or implant is unknown. Expansion of malignant or dysplastic cells present in biopsy tissue during manufacture and subsequent implantation may be possible.

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Indication

MACI® (autologous cultured chondrocytes on porcine collagen membrane) is an autologous cellularized scaffold product indicated for the repair of single or multiple symptomatic, full-thickness cartilage defects of the knee with or without bone involvement in adults.

Limitations of Use

Effectiveness of MACI in joints other than the knee has not been established.

Safety and effectiveness of MACI in patients over the age of 55 years have not been established.

Important Safety Information

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Warnings and Precautions:

- Malignancy: The risk of MACI in patients with malignancy in the area of cartilage biopsy or implant is unknown. Expansion of malignant or dysplastic cells present in biopsy tissue during manufacture and subsequent implantation may be possible.
- Transmissible infectious diseases: Because patients undergoing procedures associated with MACI are not routinely tested for transmissible infectious diseases, cartilage biopsy and MACI implant may carry risk of transmitting infectious diseases.
- Presurgical Comorbidities: Local inflammation or active infection in the bone, joint, and surrounding soft tissue, meniscal pathology, cruciate ligament instability, and misalignment should be assessed and treated prior to or concurrent with MACI implantation.
- Product Sterility: Final sterility test results are not available at the time of shipping.

Adverse Reactions: The most frequently occurring adverse reactions reported for MACI (≥5%) were arthralgia, tendonitis, back pain, joint swelling, and joint effusion. Serious adverse reactions reported for MACI were arthralgia, cartilage injury, meniscus injury, treatment failure, and osteoarthritis.

Specific Populations:

- Use of MACI in pediatric patients (younger than 18 years of age) or in patients over 65 years of age has not been established.
- The MACI implant is not recommended during pregnancy. For implantations post-pregnancy, the safety of breastfeeding to an infant has not been determined.

To report negative side effects, contact Vericel Corporation at 1-800-453-6948 or FDA at 1-800-FDA-1088 (1-800-332-1088) or www.fda.gov/medwatch.

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