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Overview of CARTIHEAL◊ AGILI-C◊ Cartilage Repair Implant clinical data publications

August 2026

Study	Design	Joint	n=	Follow-up	Key findings
NCT03299959 Altschuler N, et al. *Am J Sports Med.* 2026;54(6):1376–1385[1] Available at: American Journal of Sports Medicine	RCT primary analysis and sub-analysis by presence/absence of OA	Knee (with or without mild-to-moderate OA)	**Randomized and safety analysis set** 167 (CARTIHEAL Implant group) 84 (SSOC group; microfracture or debridement) **Full analysis set** 164 (CARTIHEAL Implant) 83 (SSOC)	5 years	The primary analysis of this RCT demonstrated that at 5 years, compared with SSOC, patients affected by joint surface lesions (including patients with mild-to-moderate OA) who received the CARTIHEAL Implant had: ▪ Significantly greater improvements in KOOS Overall score (primary endpoint)*, and six confirmatory secondary endpoints (responder rate and KOOS subscales), which demonstrated the superiority of the CARTIHEAL Implant† – KOOS Overall score means at 5 years: 81.0 (n=146) vs 59.1 (n=71); difference in change from baseline 22.6 (p<0.001) – KOOS Overall score change from baseline was also significantly higher at all intermediate time points (6, 12, 24, 36 and 48 months; all p<0.001) – Responder rates (≥30-point improvement in KOOS Overall score): 74.7% vs 29.6%, p<0.001 – KOOS subscales (pain, symptoms, activities of daily living, sports, quality of life): all p<0.001 ▪ Significantly greater improvements in IKDC score, Tegner score, and SF-12 PCS (all p<0.001) with similar SF-12 MCS scores between groups (p>0.025) ▪ Significantly lower incidence of treatment failure (surgery and/or injection): 15.0% vs 35.7%, p<0.001 ▪ Significantly lower risks of knee replacement or osteotomy (1.8% vs 9.5%; p=0.008) and intra-articular injection (6.6% vs 27.4%; p<0.001) with similar subsequent knee surgery (11.4% vs 14.3%; p>0.025) In prespecified sub-analyses by the presence or absence of mild-to-moderate OA: ▪ For patients with mild-to-moderate OA (KL grade 2–3) and patients without OA (KL grade 0–1), mean improvements in KOOS Overall and subscale scores were significantly better at all time points (12, 24, 36, 48 and 60 months) with the CARTIHEAL Implant than with SSOC (all p<0.05) ▪ At 60 months, for patients receiving the CARTIHEAL Implant, improvements in KOOS overall score and responder rates were comparable in those with mild-to-moderate OA (n=74) and those without OA (n=90), at 39.8 and 39.4, and 74.6% (50/67) and 74.7% (59/79), respectively *Note: interim sub-analyses by defect fill,[2] gender,[3] age, BMI[4] and defect location[5] are in subsequent rows; at the time of writing these had not been published for the final 5 year time point.*

*Patients with baseline KOOS Overall score <20 or >65 were excluded.
†The Bayesian posterior probability of superiority was >0.999 for all seven of these endpoints; this exceeded the prespecified value of 0.975.

Study	Design	Joint	n=	Follow-up	Key findings
NCT03299959 Altschuler N, et al. *Am J Sports Med.* 2023;51(4):957–967.5[2] Available at: The American Journal of Sports Medicine	RCT sub-analysis of defect fill	Knee (with or without mild to moderate OA)	164 (CARTIHEAL◊ Implant group) 83 (SSOC group; microfracture or debridement)	2 years (MRI outcomes)	MRI outcomes were assessed at 2 years in this RCT. Compared with SSOC, patients that received the CARTIHEAL Implant has significantly better defect fill ▪ ≥75% defect fill: 88.5% vs 30.9% (p<0.0001) ▪ <50% defect fill: 1.3% vs 50% (p<0.0001)
NCT03299959 Kon E, et al. *J Orthop Traumatol.* 2025;26(1):17[3] Available at: Journal of Orthopaedics and Traumatology	RCT sub-analysis of gender	Knee (with or without mild -to-moderate OA)	164 (CARTIHEAL Implant group) 83 (SSOC group; microfracture or debridement)	4 years (interim)	Interim gender sub-analyses of this RCT at 4 years showed that both male and female patients receiving the CARTIHEAL Implant had similar clinical and MRI outcomes, which were significantly better than in those treated with SSOC‡ ▪ Significantly better KOOS Overall Score (both p<0.0001) – Significantly better KOOS Overall score, despite severity of OA (both p<0.0001) ▪ Significantly better MRI outcomes at 12- and 24-months post-operatively (both p<0.0001) ▪ Significantly fewer treatment failures (both p<0.0001) ▪ Significantly less pain (both p<0.001) Female patients showed greater mean improvements in KOOS Sports and QOL subscales compared to males at 48-months post-operatively (p=0.013 and p=0.025, respectively)
NCT03299959 Sherman SL. Podium presentation at: American Academy of Orthopaedic Surgeons (AAOS) Annual Scientific Meeting; March 10–14, 2025; San Diego, CA, USA.[4]	RCT sub-analyses of age and BMI	Knee (with or without mild -to-moderate OA)	164 (CARTIHEAL Implant group) 83 (SSOC group; microfracture or debridement)	4 years (interim)	Interim sub-analyses of this RCT at 4 years showed that BMI, age and pre-injury activity did not significantly impact clinical outcomes for patients in the CARTIHEAL Implant group ▪ Compared with patients treated with SSOC, patients receiving CARTIHEAL Implant had: – Significantly better KOOS Overall score for patients with BMIs ≥30kg/m^2 or <30kg/m^2 (p=0.0009 and p<0.0001, respectively) – Significantly better KOOS Overall score for patients aged 21 to <45 years or aged 45 to <65 years (p<0.0001 and p=0.035, respectively)

‡Patients with pre-operative KOOS pain subscale score <30 or >65 were excluded.

Study	Design	Joint	n=	Follow-up	Key findings
NCT03299959 Conte P, et al. *Int Orthop.* 2024;48(12):3117–3126.[5] Available at: International Orthopaedics	RCT subgroup analysis by defect location	Knee (with or without mild-to-moderate OA)	164 (CARTIHEAL◊ Implant group) 83 (SSOC group; microfracture or debridement) **MRI outcomes** 156 (CARTIHEAL Implant group) 68 (SSOC group; microfracture or debridement)	4 years (interim) 2 years (MRI outcomes)	Interim sub-analyses by defect location in this RCT showed that, compared with SSOC, patients who received the CARTIHEAL Implant had: ▪ Significantly higher KOOS Overall score in condylar defects, trochlear defects and mixed lesions at 48 months (all p≤0.0198) – The absence or presence of OA did not affect the greater performance of CARTIHEAL Implant ▪ Significantly higher IKDC scores in all lesion locations at 24 and 48 months (all p≤0.023) ▪ Significantly superior MRI outcomes at 24 months showing ≥75% defect fill: – 93.9% in condylar defects (vs 39.0%; p<0.0001) – 62.5% in trochlear defects (vs 18.2%; p=0.012) – 97.6% in mixed lesions (vs 18.8%; p<0.0001) ▪ Significantly higher responder rate (≥30-point improvement in KOOS Overall score) in all lesion locations at 24, 36 and 48 months (all p≤0.004) ▪ Significantly lower treatment failure rate in condylar defects and mixed lesions at 48 months (p=0.001 and p≤0.017, respectively) – Lower treatment failure rate in trochlear defects, but not statistically significant (p=0.099)
de Caro F, et al. *Cartilage.* 2024;15(4):399–406.[6] Available at: CARTILAGE	Prospective case series	Knee (isolated chondral or osteochondral lesions)	12	6.5 years average follow-up (range: 5–8 years)	In patients affected by isolated chondral or osteochondral lesions (ICRS grade 3–4) of the femoral condyle or trochlea, treatment with the CARTIHEAL Implant at latest follow-up demonstrated: ▪ Significant increase in KOOS by 41 points compared with pre-operative scores (86 vs 45; p≤0.05) ▪ Significant increase in KOOS subscales (all p≤0.05) – Pain increased by 44 points (92 vs 48 points) – Symptoms increased by 25 points (91 vs 66 points) – ADL increased by 30 points (90 vs 60 points) – Sport increased by 52 points (75 vs 23 points) – QoL increased by 50 points (77 vs 27 points) ▪ Mean MOCART score was 64, indicating a moderate level of cartilage repair ▪ A defect filling ranging from 75–100% in all patients ▪ Complete integration of the implant, with cartilage formation and bone remodeling observed, without any significant bony abnormalities (n=8) – Remaining patients had a split-like defect <2mm present (n=4) ▪ One patient failed and was revised with a custom-made metal implant Further analysis of these results showed: ▪ Patients without previous cartilage surgery experienced significantly improved KOOS, compared to patients with previous cartilage surgery (p=0.044)

Study	Design	Joint	n=	Follow-up	Key findings
Van Genechten W, et al. Cartilage. 2021;13 (Suppl 1):S1217–S1227[7] Available at: Cartilage	Prospective case series	Knee (with or without mild-to-moderate OA)	Clinical and safety outcomes 13 patients with 15 CARTIHEAL◊ Implants MRI outcomes 14 CARTIHEAL Implants	3 years	At 36-month follow-up in this single-centre case series, patients (including some with mild-to-moderate OA) with up to 3 condylar or trochlear lesions (ICRS grade 3–4) who received CARTIHEAL Implant(s) had: ▪ Significant improvements in KOOS pain subscale (primary endpoint; mean change 41.2, p<0.002), all other KOOS subscales, IKDC and Lysholm score (all p<0.05), but not Tegner score (p>0.05) – Significant improvements were also seen at 6, 12, 18 and 24 months for all these measures (p<0.05) except for Tegner score at 6 and 12 months (p>0.05) ▪ Defect fill (scaffold ingrowth) of ≥66% in 78.7% of implants, with mean MOCART 2.0 score 72.9 ▪ No serious AEs or cases of implant loosening, failure or infection ▪ A total of 5 AEs that were classified as 'possibly related' to the study device: 4 instances of joint arthralgia and 1 of hydrops (joint effusion) which was resolved by joint aspiration
Kon E, et al. *Am J Sports Med*. 2021;49(3):588–598.[8] Available at: The American Journal of Sports Medicine	Prospective case series	Knee (with mild to moderate OA)	86	2 years	In patients with knee joint surface lesions with mild to moderate OA (KL grade 2–3) treatment with the CARTIHEAL Implant demonstrated: ▪ Significant improvement on KOOS Overall and all subscales (pain, ADL, sport, QoL, symptoms; p<0.001) and IKDC subjective score (p<0.001) at 2-year follow-up, compared with baseline ▪ Significant increase observed in the area of the defect covered by cartilage – At 2 years MRI assessment showed a significant increase in defect filling (up to 78.7% ± 25.3%; p<0.001 vs 6 months) ▪ Treatment failure (defined as removal of the CARTIHEAL Implant for any reason during the follow-up period) occurred in eight patients (9.3%) ▪ Histology of an explant specimen from one patient showed newly formed hyaline-like cartilage, rich in collagen type II and proteoglycans integrated within the adjacent native cartilage and bone
Kon E, et al. *Injury*. 2016; 47 Suppl 6:S27–S32.[9] Available at: Injury	Case control	Knee	21 (tapered shaped implant) 76 (cylindrical shaped implant)	1 year	In a study comparing the treatment of chondral and osteochondral lesions, with either tapered shaped implants or cylindrical shaped implants, results showed: ▪ A significant improvement in all clinical scores (IKDC subjective score, Lysholm score and KOOS subscales: pain, symptoms, ADL, QoL and sport) was documented in both groups compared to pre-operative scores (p<0.005) ▪ MRI findings revealed graft integration with good bone and cartilage formation in both groups ▪ A lower revision rate in patients who received the tapered CARTIHEAL Implant with no implant removals (0 vs 10.5%)

Study	Design	Joint	n=	Follow-up	Key findings
Amin NH, et al. *Cureus*. 2025;16;17(6):e86127.[10] Available at: Cureus	Retrospective case series	Knee (with or without concurrent mild to moderate OA)	33 patients, with 1 patient undergoing bilateral implantation	45 days	▪ Surgical success rate, defined as no identified postoperative complications, was 96.97% (n=33) based on clinical exam and 100% (n=25) based on post-operative radiography ▪ In 25 (73.5%) cases, the pre-surgical plan based on MRI was modified after arthroscopy due to discrepancies in lesion details (number, type, location, size) ▪ The CARTIHEAL◊ Implant allowed surgeons to make intraoperative adjustments to the pre-operative plan to treat cartilage defects
Drobnič M, et al. *J ISAKOS*. 2026;16:101040[11] Available at: Journal of ISAKOS	Case report	Knee (KL grade 1)	1 patient (2 implants in the same knee)	12 years	At 12-year follow-up of the first patient to receive CARTIHEAL Implants, a 47-year-old male recreational athlete with a full-thickness condylar lesion who underwent concomitant medial meniscectomy 5 years after initial trauma: ▪ KOOS Overall, IKDC, Lysholm, Tegner and VAS pain scores remained stable ▪ The defect was filled completely with slight hypertrophy, and OA had remained at KL grade 1 ▪ The patient reported high satisfaction and full return to pre-injury activities

References

1. Altschuler N, Zaslav KR, Di Matteo B, et al. Five-year follow-up of a multicenter randomized controlled trial comparing an aragonite-based scaffold with microfracture and debridement for chondral and osteochondral knee lesions. *Am J Sports Med*. 2026;54(6):1376–1385. **2.** Altschuler N, Zaslav KR, Di Matteo B, et al. Aragonite-based scaffold versus microfracture and debridement for the treatment of knee chondral and osteochondral lesions: Results of a multicenter randomized controlled trial. *Am J Sports Med*. 2023;51(4):957–967. **3.** Kon E, De Caro F, Dasa V, et al. Female patients report comparable results to males after the implantation of an aragonite-based scaffold for the treatment of knee chondral and osteochondral defects: a gender-based analysis of a RCT at 4 years' follow-up. *J Orthop Traumatol*. 2025;26(1):17. **4.** Sherman SL. Impact of activity level, age, and BMI on outcomes after the implantation of an aragonite-based scaffold for the treatment of knee chondral and osteochondral defects: analysis of a RCT at 4-year follow-up. Podium presentation presented at: American Academy of Orthopaedic Surgeons (AAOS) Annual Scientific Meeting; March 10–14, 2025; San Diego, CA, USA. **5**. Conte P, Anzillotti G, Crawford DC, et al. Differential analysis of the impact of lesions' location on clinical and radiological outcomes after the implantation of a novel aragonite-based scaffold to treat knee cartilage defects. *Int Orthop*. 2024;48(12):3117–3126. **6.** de Caro F, Vuylsteke K, Van Genechten W, Verdonk P. Acellular aragonite-based scaffold for the treatment of joint surface lesions of the knee: A minimum 5-year follow-up study. *Cartilage*. 2024;15(4):399–406. **7.** Van Genechten W, Vuylsteke K, Struijk C, Swinnen L, Verdonk P. Joint surface lesions in the knee treated with an acellular aragonite-based scaffold: A 3-year follow-up case series. *Cartilage*. 2021;13(Suppl 1):S1217–S1227. **8.** Kon E, Di Matteo B, Verdonk P, et al. Aragonite-based scaffold for the treatment of joint surface lesions in mild to moderate osteoarthritic knees: Results of a 2-year multicenter prospective study. *Am J Sports Med*. 2021;49(3):588–598. **9.** Kon E, Robinson D, Verdonk P, et al. A novel aragonite-based scaffold for osteochondral regeneration: early experience on human implants and technical developments. *Injury*. 2016;47 Suppl 6:S27–S32. **10.** Amin NH, Faucett SC, Qin C, et al. Clinical experience with an aragonite-based scaffold implant for knee cartilage repair: A multicenter case series. *Cureus*. 2025;17(6):e86127. **11.** Drobnič M, Kon E, Robinson D, Kolar M, Altschuler N. Osteochondral knee joint lesion treated with an aragonite-based scaffold. 12-year follow-up of the world's first implantation: Case report. *J ISAKOS*. 2026;16:101040.

Abbreviations

ADL = activities of daily living; BMI = body mass index; ICRS = International Cartilage Restoration and Joint Preservation Society; IKDC = International Knee Documentation Committee; KL = Kellgren-Lawrence; KOOS = Knee Injury and Osteoarthritis Outcome Score; MOCART = Magnetic Resonance Observation of Cartilage Repair Tissue; MRI = magnetic resonance imaging; OA = osteoarthritis; QoL = quality of life; RCT = randomized controlled trial; SSOC = surgical standard of care; TKA = total knee arthroplasty; VAS = visual analog scale.

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CARTIHEAL Implant Important Safety and Risk Information

Rx only. **INTENDED USE:** Treat articular cartilage and/or osteochondral defects. **INDICATIONS FOR USE:** The Agili-C◊ scaffold is indicated for the treatment of an International Cartilage Repair Society grade III or above knee-joint surface lesion(s), with a total treatable area of 1-7cm², without severe osteoarthritis (Kellgren-Lawrence grade 0-3). **CONTRAINDICATIONS:** Agili-C◊ should not be implanted in subjects with the following conditions: Active or latent, bone or joint infection at the surgical site; Active infection elsewhere in the body; Neuropathic joint; Hypersensitive, allergic, or intolerance of materials containing calcium carbonate or coral derivatives; Critical limb ischemia; Any known tumor of the knee area; Severe Osteoarthritis of the index knee, defined as grade 4 according to the Kellgren-Lawrence Grading; Uncontained lesion - lack of vital bone wall, at least 2mm thick, surrounding the implantation site; Subchondral bone defect or bone cyst depth deeper than 8mm; Inability to position the implant 2mm recessed relative to the articular surface; Osteochondral or cystic lesions larger than what the implant can cover; Implantation inside avascular necrosis. **WARNINGS:** The safety and effectiveness of the Agili-C◊ Implant has not been established in patients with the following conditions: Morbid obesity (BMI >35); Known insulin dependent diabetes mellitus; Immunocompromised patients; including patients receiving a previous intra-articular steroid injection within the last 1 month; Systemic conditions affecting wound healing; Systemic bone disorder, such as but not limited to, osteoporosis and osteogenesis imperfecta; Chemotherapy during the past 12 months; Ligamentous instability; Significant malalignment; Total or subtotal meniscectomy or lack of functional meniscus; Inflammatory arthropathy or crystal-deposition arthropathy; Skeletally immature; Inability to refrain from contact sports/high-impact activities during recovery period; Noncompliance due to major psychiatric disorder, alcohol or drug abuse; Skin conditions within the field of surgery. The implant is not indicated for treatment in Patellar cartilage and osteochondral defects or for use in other joints. **RISKS AND SIDE EFFECTS:** As with any surgical procedure, there are risks you should be aware of to help make your decision. The most common risks that occur with the Agili-C◊ implant include increased transient or chronic pain of the operated joint, increased swelling and/or effusion of the operated joint, decreased range of motion, hemarthrosis and contusion. In addition to the risks above, there are other risks that may occur. For full product information, including indications for use, contraindications, precautions, warnings and adverse events, please consult the product's applicable Instructions for Use (IFU) prior to use.

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