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

Smith+Nephew

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	Study	Design	Joint	n=	Follow-up	Key findings
Interim results from an RCT (NCT03299959)	Conte P, et al. *Int Orthop.* 2024;48(12):3117–3126.[1] Available at: International Orthopaedics	RCT	Knee (with or without mild to moderate OA)	164 (CARTIHEAL AGILI-C Implant group) 83 (SSOC group; microfracture or debridement)	4 years	Compared to SSOC, patients that received the CARTIHEAL AGILI-C Implant demonstrated: ▪ 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 AGILI-C Implant ▪ Significantly higher IKDC scores in all lesion locations at 24 and 48 months (all p≤0.023) ▪ Significantly superior MRI imaging 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) 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) ▪ Significantly lowers risk of TKA or osteotomy by 87% – Significantly fewer patients required a TKA or osteotomy at 48 months (1.2% vs 9.5%; p=0.003)
	Sherman SL. Podium presentation at: American Academy of Orthopaedic Surgeons (AAOS) Annual Scientific Meeting; March 10–14, 2025; San Diego, CA.[2]	RCT sub-analysis of age and BMI	Knee (with or without mild to moderate OA)	164 (CARTIHEAL AGILI-C Implant group) 83 (SSOC; microfracture or debridement)	4 years	▪ A sub-analysis of the RCT at 4 years showed that BMI, age and pre-injury activity did not significantly impact clinical outcomes for patients in the CARTIHEAL AGILI-C Implant group ▪ Compared to patients treated with SSOC, patients receiving CARTIHEAL AGILI-C Implant had: – Significantly better KOOS Overall score for patients ≥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)

Interim results from an RCT (NCT03299959)

Study	Design	Joint	n=	Follow-up	Key findings
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 AGILI-C Implant group) 83 (SSOC; microfracture or debridement)	4 years	▪ A gender sub-analysis of the RCT at 4 years showed that both male and female patients receiving the CARTIHEAL AGILI-C Implant had similar clinical and radiographic outcomes, significantly outperforming those treated with SSOC – Significantly better KOOS Overall Score (both p<0.0001) – 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) – Significantly better radiographic outcomes at 12- and 24-months post-operatively (both p<0.0001) – Significantly better outcomes in KOOS Overall score, despite severity of OA (both p<0.0001) – Significantly fewer treatment failures (both p<0.0001) – Significantly less pain (both p<0.001)
Altschuler N, et al. *Am J Sports Med.* 2023;51(4):957–967.[4] Available at: The American Journal of Sports Medicine	RCT	Knee (with or without mild to moderate OA)	167 (CARTIHEAL AGILI-C Implant group) 84 (SSOC group; microfracture or arthroscopic debridement)	2 years	In patients affected by joint surface lesions, including patients with mild to moderate OA (KL grade 2–3), compared with SSOC, treatment with the CARTIHEAL AGILI-C Implant demonstrated: ▪ Increased KOOS Overall post-operatively – With the change being significantly greater than SSOC at each time point (p≤0.001) – A greater change in KOOS pain, QoL and ADL subscales ▪ Substantially higher post-operative improvements in IKDC than the MCID at each time point – Significant superiority was observed (p<0.001) ▪ At 2-year MRI assessment: – 88.5% had >75% defect fill (vs 30.9%; p<0.0001) – 1.3% had <50% defect fill (vs 50%; p<0.0001) ▪ At 2 years a responder rate (increase of ≥30 KOOS overall) of 77.8% (vs 33.6%; p<0.0001) ▪ Significantly lower treatment failure rate (defined as any secondary intervention in the treated joint, regardless if related or unrelated to the original treatment) 7.2% (vs 21.4%; p=0.002) ▪ A robust improvement regardless of age (<50 vs ≥50), lesion size (≤3cm^2 vs >3cm^2), or presence of OA (KL 1–2 vs 2–3)

Study	Design	Joint	n=	Follow-up	Key findings
Amin NH, et al. *Cureus*. 2025;16;17(6):e86127.[5] 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 AGILI-C Implant allowed surgeons to make intraoperative adjustments to the pre-operative plan to treat cartilage defects
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 AGILI-C 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
Kon E, et al. *Am J Sports Med*. 2021;49(3):588–598.[7] 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 AGILI-C 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 AGILI-C 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.[8] 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 AGILI-C Implant with no implant removals (0 vs 10.5%)

References

1. 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. **2.** 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 at: American Academy of Orthopaedic Surgeons (AAOS) Annual Scientific Meeting; March 10–14, 2025; San Diego, CA. **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;13;26(1):17. **4.** 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. **5.** 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;16;17(6):e86127. **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.** 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. **8.** 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.

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; MCID = minimal clinically important difference; 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.

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