Treatment of hallux rigidus by a novel bi-phasic aragonite-based implant: results of a two year multi-centre clinical trial

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ORIGINAL PAPER

Treatment of hallux rigidus by a novel bi-phasic aragonite-based implant: results of a two year multi-centre clinical trial

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Abstract

Purpose The two year results of a multi-centre clinical trial were examined to evaluate surgical treatment of hallux rigidus using a novel, bi-phasic, biodegradable, and cell-free aragonite-based scaffold (Agili-C™, CartiHeal Ltd, Israel).

Methods Twenty patients with moderate-to-severe hallux rigidus were recruited. After thorough metatarsophalangeal joint (MTPJ-1) debridement, the scaffolds were implanted into the defect centre. Eight patients received concomitant osteotomy. Treatment outcome was followed clinically (Pain VAS, FAAM-ADL, FAAM-Sport, AOFAS-HMIS, maximum active range of extension ROM-EXT, and flexion ROM-FLEX), and by medical imaging, at six month intervals for two years. Adverse events were recorded throughout the study follow-up period.

Results Significant clinical improvement over time was observed in all evaluated parameters (screening to final evaluation averages: Pain VAS 59 to 26, FAAM-ADL 57 to 77, FAAM-Sport 39 to 66, AOFAS-HMIS 51 to 81, ROM-EXT 18° to 36°), except for ROM-FLEX. Radiographs showed stable MTPJ-1 width over the two years in 17/18 cases (94%). MRI demonstrated progressive implant biodegradation, coupled with articular cartilage and subchondral bone regeneration, with a repair tissue defect fill of 75–100% in 14/17 (82%) subjects at their final visit. Revision surgery with implant removal was performed in two patients.

Conclusion Bi-phasic, osteochondral, biodegradable, aragonite-based scaffold demonstrated positive clinical outcome and a good safety profile in the treatment of medium-to-advanced hallux rigidus. According to the medical imaging, this implant has the potential to restore the entire osteochondral unit of metatarsal head.

Keywords Agili-C · Osteochondral · Aragonite · Biodegradable · Bi-phasic · Cartilage · Great toe · Metatarsophalangeal · Osteoarthritis · Joint space · Osteophytes · Defect fill

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Introduction

Hallux rigidus is the most common arthritic condition in the foot, with cartilage degeneration, synovitis, and osteophyte formation of the first metatarsophalangeal joint (MTPJ-1), causing activity-related pain and stiffness associated with restricted dorsiflexion [1]. The estimated incidence of this condition is 2.5% in subjects over 50, with a 2:1 female predominance [2]. Despite known aetiology, such as long first ray, abnormally elevated or abducted first metatarsal (MT-1), previous trauma, and positive family history of increased incidence of hallux rigidus, most cases are idiopathic. According to clinical and radiographic criteria, Coughlin and Shurnas graded MTPJ-1 degeneration into five (0–4) stages [3]. Initial treatment is typically conservative [4], but due to the ongoing degenerative process, surgical treatment is warranted in about half of the cases [5]. The golden-standard for surgical interventions are MTPJ-1 cheilectomy without/with dorsiflexion osteotomy of proximal phalanx for symptomatic hallux rigidus grades 1 and 2 [6], or MTPJ-1 arthrodesis in later stages of the disease [7]. Alternatively, MTPJ-1 motion-preserving surgery may be performed, such as decompression MT-1 osteotomy [8], inter-positional arthroplasty with local soft-tissues [9, 10], synthetic absorbable biomaterials (polyurethane-urea [11]; poly-L/D-lactic acid [12]; polyvinyl alcohol hydrogel [13]), or partial/total metal joint arthroplasties [14]. However, the clinical outcome and durability of these procedures is less predictable [15, 16].

Due to an increasing awareness that subchondral bone restoration is essential for high-quality durable cartilage repair, a novel, aragonite-based, bi-phasic scaffold was developed (Agili-C™, CartiHeal) [17, 18]. The implant demonstrated excellent preclinical results and has shown to enhance hyaline cartilage and subchondral bone restoration in the knee and ankle [19–21]. Herein, we present the results of a prospective, interventional, non-randomized, open-label, single-group assignment, multicenter clinical trial, with a follow-up of 24 months in the MTPJ-1. We hypothesized that surgical treatment of hallux rigidus with this implant would be safe, significantly decrease pain, increase range of motion in MTPJ-1, improve patients' foot function, and demonstrate stable repair-tissue formation over the implant.

Materials and methods

Study design

The study was designed as a prospective, interventional, non-randomized, open-label, single-group assignment, multicenter clinical trial, with a follow-up of 24 months, conducted in four centres. The study was registered on the ClinicalTrials.gov website (under Clinical_trials Identifier NCT02831244) and approved individually by each participating institution. Adult subjects with symptomatic hallux rigidus were enrolled. The inclusion criteria were the following: age 18 years or older, osteoarthritis of MTPJ-1, presence of good bone stock, physically and mentally willing and able to comply with post-operative rehabilitation, and routinely scheduled clinical and radiographic visits. The main exclusion criteria were any past or present evidence of infection of the treated joint, any known malignant tumour of the foot, known inflammatory arthropathy or crystal-deposition arthropathy, and history of any significant systemic disease.

Subjects and surgical intervention

Twenty patients (11 female, 9 male) 56 (13) years, BMI 27.5 (3.4) kg/m^2 were enrolled and treated with the study device. Based on Coughlin and Shurnas criteria, the enrolled patients suffered from hallux rigidus grades 2 (7 pts), 3 (10 pts), and 4 (3 pts). Patients were operated on in an outpatient surgery setting using general, spinal, or peripheral anaesthesia. Routine intra-operative antibiotic prophylaxis was administered, and a tourniquet was used upon surgeon's preference. A dorsomedial approach to the MTPJ-1 was typically used. First, the synovitis and osteophytes were debrided, and the joint capsule was mobilized. The articular surface of the proximal phalanx was left intact. In the centre of the most prominent cartilage damage on MT-1 head a single, bi-phasic, biodegradable, osteochondral implant was positioned. The implant diameters ranged from 7.5 mm (8 pts), 10 mm (10 pts), to 12.5 mm (2 pts). A designated surgical toolset was used (CartiHeal, Israel) per the following surgical technique: (1) a guide wire positioning via a perpendicular aligner in the centre of MT-1 head, (2) a wire alignment along MT-1 shaft additionally controlled using intra-operative radiographs, (3) perpendicular drilling over the guide wire to the designated depth in order to assure implant positioning 2 mm below the articular surface, (4) a shaper that was used to adjust the lesion diameter, and (5) a gentle manual implant insertion with slight implant tapping to ensure press-fit fixation below the articular surface. Necessary concomitant osteotomy procedures were allowed, and they included seven extension osteotomies of the proximal phalanx and one proximal MT-1 osteotomy for the realignment of the first ray. A case presentation with pre-/intra-/post-operative details is presented in Fig. 1.

Rehabilitation

Post-operatively, the operated toe was immobilized with a soft-padded bandage for approximately two to three weeks. Cooling, foot elevation, and oral pain medications per request were employed. Ambulating in an unloading shoe was advised for a total of six weeks post-operatively. The rehabilitation protocol was as follows and was adjusted according to the

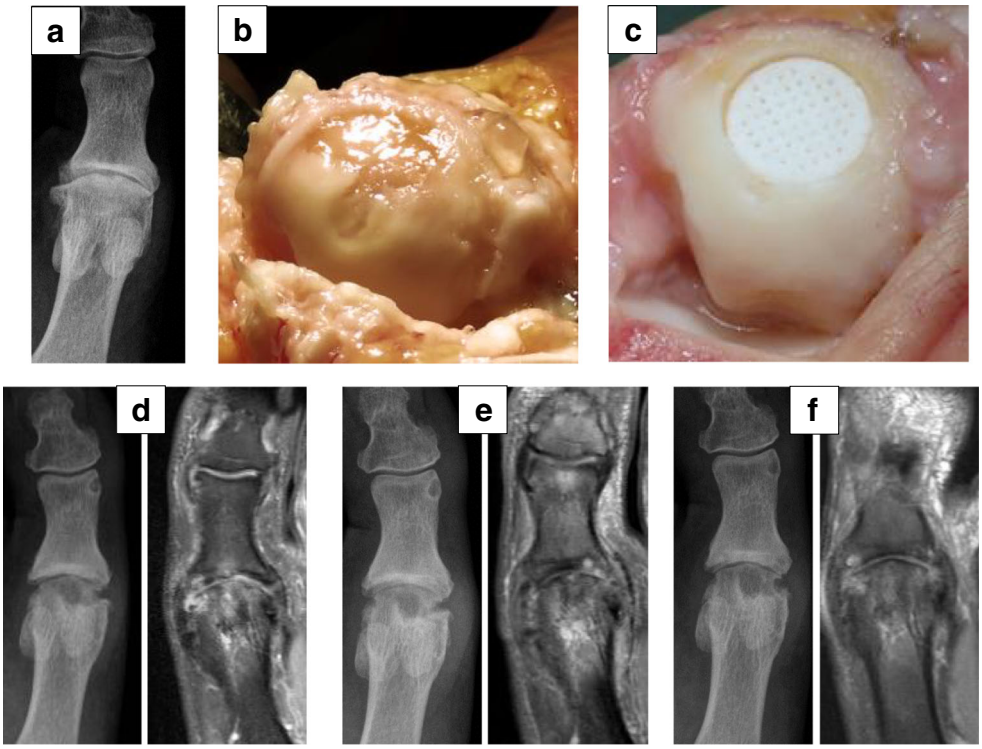

Fig. 1 Female, 56 years old, implanted with a single Agili-C™ implant. (**a**) Screening radiographs (Pain VAS 78); (**b**) intra-operative view of cartilage lesion; (**c**) implanted Agili-CTM; (**d**) 6-month radiographs and MRI; (**e**) 12-month radiographs and MRI (Pain VAS 37); and (**f**) 24-month radiographs and MRI (Pain VAS 0)

patient's progress. At three weeks, patients were instructed to perform easy active and passive ROM exercises in MTPJ-1. At 6 weeks, the patients progressed to a range of motion and proprioceptive exercises on the ground, as well as gait training. After three months, they were allowed strength training, including elliptical trainers, and Nordic walking on stable ground. Eight months after surgery (if the great toe functional status permitted), they were allowed activities on an uneven ground, including easy jogging. Return to full activity was allowed only one year after the procedure.

Clinical and imaging evaluation

The patients were followed clinically and with medical imaging prior to the procedure (screening), and then at two weeks, six weeks, three months, six months, 12 months, 18 months, and 24 months. Safety endpoints were followed up to 24 months by tracking all adverse events and serious adverse events (SAEs). Common patient-reported outcome measures were used such as visual analog scale for pain (Pain VAS), Foot and Ankle Ability Measures (FAAM) for daily activities (FAAM-ADL) and sport-recreation (FAAM-Sport), and American Orthopedic Foot and Ankle Society Hallux Metatarsophalangeal-Interphalangeal Scale (AOFAS-HMIS) [22, 23]. Maximum active MTPJ-1 range of motion in extension (ROM-EXT) and flexion (ROM-FLEX) was recorded. Standard foot radiographs (antero-posterior, lateral, and oblique views) were taken at screening, post-operatively, and then repeatedly at every six month evaluation point. Screening radiographs were used for the determination of Coughlin and Shurnas hallux rigidus grade [24]. Post-operative radiographs were scored (0–3) for joint space width (JSW) and osteophyte formation according to a validated atlas [25]. Radiographs were additionally analyzed for any unwanted changes related to the surgical intervention, such as implant fragmentation, bone breakage, ossifications, crystal release, and peri-implant osteolysis. Magnetic resonance imaging (MRI) of the foot in routine sequences was conducted every six months post-operatively until the final two year visit. Lesion defect fill over the implant, at the final time point, was calculated by comparing the amount of cartilage defect fill compared to the native articular cartilage line [17]. The following five defect fill grades were used: I (0–24%), II (24–49%), III (50–74%), IV (75–99%), and V (100%).

Statistical analysis

Numerical data is presented as averages with standard deviations (SD), while the number of cases is given for categorical variables. Primary study endpoints were Pain VAS, FAAM-ADL, and FAAM-Sport increase from screening to final evaluation. Secondary endpoints were Pain VAS, FAMM-ADL, FAAM-Sport, AOFAS-HMIS, ROM-EXT, ROM-FLEX, radiographic MTPJ-1 JSW, radiographic MTPJ-1 osteophyte grade, and MRI cartilage fill at every evaluation time point. Missing values were handled by the Last Observation Carried Forward (LOCF) protocol. The baseline scores of the two subjects that underwent implant removal were imputed for

all the follow-up visits from the time point of implant removal. Each study endpoint was first analyzed for possible statistical differences between all time points with one-way ANOVA, which was followed by a Tukey's HSD post test comparing the values at every time point toward the screening. Improvement amounts (differences between the final and screening values) were calculated for Pain VAS, FAAM-ADL, FAAM-Sport, and ROM-EXT. These improvement amounts were included in a multivariate general linear model to be tested against the influence of gender, age, BMI, Coughlin and Shurnas hallux rigidus grade, concomitant osteotomies, or implant diameter. Statistical analysis was performed using the statistical software IBM SPSS ® Statistics V23.0 (IBM Corp, Armonk, NY, USA). A post hoc analysis, calculated by G*Power Ver 3.1.9.4 (University of Kiel, Germany), for Pain VAS difference between screening and final values yielded a statistical power of 99.8% ($p < 0.05$, $N = 20$, effect size = 1.098).

Results

The patient cohort reported significant improvement in all primary and secondary endpoints, except for ROM-FLEX, from screening to final evaluation: Pain VAS from 59 (29) to 26 (31), FAAM-ADL from 57 (23) to 77 (24), FAAM-Sport from 39 (33) to 66 (33), AOFAS-HMIS from 51 (15) to 81 (14), ROM-EXT from 18 (9) to 36 (20), and ROM-FLEX from 32 (15) to 29 (18). Details on the results at each time point are detailed in Table 1.

The multivariate general linear model revealed the influence of BMI on improvement scores of FAAM-Sport (beta − 7.213, R squared 0.248, $p = 0.030$) and ROM-EXT (beta − 3.793, R squared 0.265, $p = 0.026$). The effect of other parameters (gender, age, Coughlin and Shurnas hallux rigidus grade, concomitant osteotomies, and implant diameter) was insignificant toward improvement scores of Pain VAS, FAAM-ADL, FAAM-Sport, or ROM-EXT.

Semi-quantitative analysis of radiographs identified predominately stable MTPJ-1 JSW over two post-operative years in 94% of patients. JSW decreased in only one patient (6%) between screening and 12 months, with no further deterioration at 24 months. Osteophytes were significantly reduced in size in 9 (47%) patients between screening and 12 months, but only in three (17%) patients between screening and 24 months. MRIs demonstrated progressive implant biodegradation coupled with restoration of the osteochondral unit, with a repair tissue defect fill 75–100% (grades IV and V) in 14 of 17 (82%) subjects at their final visit. Data on medical imaging is shown in Table 2.

Four SAEs occurred in three patients during the 24 months of follow-up. Two of the SAEs were not related to the implant (wound dehiscence at 1 month; haematemesis and melena due to multiple gastric ulcers at 17 months), while the other two events were considered implant- and/or procedure-related (swelling and mild pain over the operated MTPJ-1 in two patients at 5 and 7 months post procedure). These two patients required revision surgery with implant removal.

Discussion

This prospective, non-randomized, multi-centre clinical trial evaluating the use of the Agili-C™, bi-phasic, osteochondral, biodegradable, aragonite-based scaffold in the treatment of medium-to-advanced hallux rigidus suggests that the use of this implant offers substantial reduction of pain, improvement

Table 1 Patients' reported outcome and range of motion at 6-month intervals from screening to 2-year follow-up after Agili-C™ surgery for hallux rigidus. Data is presented as averages (SD). One-way ANOVA p values are given in the right column. Values that were significantly different (Tukey HSD posttest; $p < 0.05$) toward screening are marked with *

	Screening ($N = 20$)	6 months ($N = 20$)	12 months ($N = 20$)	18 months ($N = 20$)	24 months ($N = 20$)	p values
Pain VAS (0–100)	59 (29)	40 (27)	35 (27)	30 (28)*	26 (31)*	.004
FAAM-ADL (0–100)	57 (23)	71 (19)	73 (19)	77 (23)*	77 (24)*	.022
FAAM-Sport (0–100)	39 (33)	47 (23)*	69 (23)*	66 (30)*	66 (33)*	.002
AOFAS-HMIS (0–100)	51 (15)	76 (13)*	70 (20)*	78 (14)*	81 (14)*	< .001
Max active extension (degrees)	18° (9)	35° (23)	35° (25)	38° (24)*	36° (20)	.025
Max active flexion (degrees)	32° (15)	29° (15)	40° (24)	32° (17)	29° (18)	.324

Pain VAS visual analog scale for pain, *FAAM* Foot and Ankle Ability Measures, *ADL* activities of daily living, *AOFAS-HMIS* American Orthopedic Foot and Ankle Society Hallux Metatarsophalangeal-Interphalangeal Scale

Table 2 Medical imaging evaluation after Agili-C™ surgery for hallux rigidus. Data is presented as number of cases (%)

A) Grading of joint space width (JSW) and osteophytes on native radiographs

Grade	Screening (N=20)		12-month visit (N=19)		24-month visit (N=18)	
	JSW	Osteophytes	JSW	Osteophytes	JSW	Osteophytes
0	0	0	0	0	0	1
1	8	12	8	2	8	12
2	9	7	7	16	7	5
3	3	1	4	1	3	0

B) Changes toward baseline for joint space width and osteophytes on native radiographs

		Screening to 12-month	Screening to 24-month
Joint space width	worsened	1 (5%)	1 (6%)
	equal	18 (95%)	17 (94%)
	improved	0	0
Osteophytes	worsened	0	0
	equal	10 (53%)	15 (83%)
	improved	9 (47%)	3 (17%)

C) Implant deviations on native radiographs

1 patient osteolysis around implant at 12 months – later implant removal due to SAE

D) MRI defect fill at final evaluation *(N=17)*

Defect fill grade	I (0-24%)	II (25-49%)	III (50-74%)	IV (75-99%)	V (100%)
No of cases (%)	/	/	3 (18%)	6 (35%)	8 (47%)

in patients' perceived foot function, and improved range of the great toe extension.

Surgery for hallux rigidus is largely divided into joint-sparing (cheilectomy, decompression osteotomies, cartilage repair) and joint-destructive procedures (arthrodesis, partial/total replacement, or inter-positional arthroplasty) or MTPJ-1-sparing procedures are typically employed in the early stages of this disease [16]. The underlying biomechanical causative factors, such as an elevated or elongated first ray, hallux valgus, pes planus, or ankle equinus, should be corrected before or at the time of MTPJ-1 reconstruction [15].

Cheilectomy with an excision of extra-articular spurring is favoured in the initial phases of MTPJ-1 degeneration, especially when the cartilage wear pattern on the metatarsal head is located in the upper quarter of the joint surface [26]. Under such circumstances various technique modifications reported excellent early results in up to 97% of patients and pain relief and function in 92% of patients [27–29]. This procedure keeps most future surgical options open should the joint continue to worsen toward the end stages of the disease. Nevertheless, there seems to be slow deterioration of clinical results later on. Sidon et al. demonstrated that 70% of treated patients were pain free at an average of 6.6 years post-operatively [6]. The rate of revision procedures was significantly greater in the cheilectomy group (8.21%) than in the decompression osteotomy group (1.22%) as reported by Cullen et al. [8]. As the degenerative changes progress to include pain at the midway range of motion or with continued collapse of MTPJ-1, the success rates of a cheilectomy diminishes significantly [30].

MTPJ-1 arthrodesis has consistently demonstrated good results and is the current "gold standard" of treatment for patients with advanced hallux rigidus. Arthrodesis is also the procedure of choice in patients with concomitant advanced hallux valgus, hallux varus, rheumatoid arthritis, or neuromuscular disorders. Many articles describing the use of different fixation techniques reported over 90% patient satisfaction rate, union rates from 92 to 99%, and revision rates between 1 and 4% [31–33]. Brodsky et al. examined sports participation at the mid-term after MTPJ-1 arthrodesis and found out that patients were able to return to hiking 92% of the time, golf 80% of the time, tennis 75% of the time, and jogging 75% of the time [34]. DeFrino et al. showed—after MTPJ-1 arthrodesis—restoration of the weight-bearing function of the first ray, with greater maximum force carried by the distal hallux at toe-off. Gait analysis was compared to the unaffected contralateral limb and to age- and sex-matched healthy subjects, although step length and ankle plantar flexion at toe-off was decreased compared to the non-operative limb [35]. Brodsky et al. further showed increased maximum ankle push-off power and single-limb support time in gait analysis of 23 patients [36]. However, regardless of the surgical technique MTPJ-1 arthrodesis results in marked shortening, 5 to 7 mm, of the great toe [37]. Great toe shortening and immobility, as shown by Stevens et al., resulted in a gait in which the hallux was less loaded, while the lesser metatarsals endured higher peak pressures. Additionally, the hindfoot and forefoot had to compensate in order to restore a more normal gait pattern [38].

MTPJ-1 joint replacements for hallux rigidus have been introduced in the 1950s, but due to severe complications, the implant philosophy and technology underwent several upgrades [7, 14]. Currently, the fourth-generation implants, comprising cementless metal metatarsal and phalangeal components with a fixed-bearing polyethylene insert, are used [39]. The main advantage of replacement over arthrodesis is the preservation of great toe motion. The average post-operative range of motion improvement was about 30° in short-term studies [14], albeit this seems to be progressively lost at later periods [40]. In spite of partially preserved MTPJ-1 mobility, the patient-reported outcomes between arthrodesis and arthroplasty were similar, but lower postoperative pain levels and less surgical revisions gave advantage to arthrodesis [7, 41]. There has been a growing interest in MTPJ-1 hemiarthroplasties over the last decade. Such cementless partial metal implants cover either the proximal phalanx or metatarsal head, which are articulating against the degenerated native cartilage surface. Metatarsal head resurfacing seems to be the prevailing concept over the last years [42], as subsidence and lucency around proximal phalanx implants have been established [43]. A recent systematic review comparing total versus hemiarthroplasties for hallux rigidus established that their functional outcomes were similar, but range of motion gain and less post-operative complications favor the usage of metatarsal head resurfacing [14].

Biologic motion-sparing procedures may be offered to patients with symptomatic hallux rigidus [16]. Various interposition arthroplasties represent a joint-destructive biologic variety, where the worn out cartilage is replaced by a soft-tissue spacer to preserve the great toe length and part of its motion ability [10]. Local tissues, such as capsule or tendons, were initially used for the interposition [9], while absorbable biomaterials have been introduced in the last millennia [11, 12]. Although some biomaterials have remained on the market for over a decade, such as poly-L/D-lactic acid (RegJoint by Scaffdex), the published evidence on the long-term outcome is rather limited [44]. The main goal of all interposition arthroplasties is to replace MTPJ-1 by a functional pseudoarthrosis. During the duration of the biomaterial absorption, a prolonged swelling or osteolysis may occur [45]. If these implants fail, a complex arthrodesis with bone grafting is the only viable option for revision surgery [46]. Contrarily, joint-sparing biologic procedures tend to restore native MTPJ-1 articular surfaces, before they enter into the mid-stage OA. Limited reports on MTPJ-1 microfracturing or osteochondral autograft transfers may be found in the literature [47, 48].

When early cartilage defects are restored and underlying biomechanical misalignment is corrected, MTPJ-1 function can even be preserved for a lengthy period.

A recent biomaterial that has been introduced into clinical trials and later used also in limited clinical applications is polyvinyl alcohol hydrogel (Cartiva Wright). A plug, with a water content and tensile strength comparable to human articular cartilage, is implanted into the centre of MT-1 in 1.0–1.5 mm prone manner to provide slight expansion of MTPJ-1 space [49]. Glazebrook et al., reporting on early and mid-term results, showed that 9.2% patients had undergone implant removal and arthrodesis up until two years post procedure and another 7.6% of patients by 5.8 years. Pain VAS, FAAM-ADL, and FAAM Sports scores improved by 57.9 ± 18.6 points, 33.0 ± 17.6 points, and 47.9 ± 27.1 points, from the baseline. The authors of the article concluded that patient-reported outcomes and peak MTPJ-1 peak dorsiflexion from 24 months were maintained at 5.8 years in patients who were not revised [13, 50]. Active MTP joint peak dorsiflexion was maintained. The Cartiva hydrogel implant has also been assessed in a clinical trial against MTPJ-1 arthrodesis. The authors reported similar subjective outcomes and sporting ability between the two procedures, but surgical time and early recovery were faster with the implant. Range of motion improvement using the implant was minimal, averaging only 6 degrees [50–52]. Another study compared Cartiva hydrogel to a cheilectomy with Moberg osteotomy and demonstrated inferior subjective results of this implant, and a higher revision rate [53]. Some reports also indicate that failure rates of the Cartiva implant may be as high as 50% in routine clinical practice [54].

The current study uses a novel, aragonite-based, bi-phasic scaffold. The implant consists of natural crystalline aragonite derived from coralline exoskeleton. It is capable of recruiting bone marrow mesenchymal stem cells which differentiate into the desired chondrogenic and osteogenic phenotypes [55]. Gradual resorption of the implant occurs proportional to the rate of cartilage and bone regeneration. Preclinical studies showed its safety and good regenerative potential in promoting both bone and hyaline cartilage regeneration (without cell addition), which was further confirmed in clinical studies which evaluated treatment of the scaffold in knee osteochondral lesions [19, 20], as well as a small talus osteochondral lesion study [21]. Based on the experience in knee surgery, the Agili-C device has to be implanted slightly recessed to the native articular line, since it promotes cartilage restoration above and around its perimeter [17, 18]. As the cartilage layer is thin over the MT-1 head, the implant was actually positioned into the subchondral bone in hallux rigidus patients, which is compatible with tide-mark-level positioning in the knee. Nevertheless, post-operative MR evaluation demonstrated a nearly complete defect fill in the majority of operated patients; hyaline-like cartilage overgrown was confirmed also in MTPJ-1. The joint space remained the same over the post-operative two year follow-up period, indicating a potential slowdown of the joint degradation process. MTPJ-1 osteophytes were evidently reduced post-operatively due to the simultaneous MTPJ-1 debridement at the time of Agili-C^{TM} implantation. However, lesser osteophyte re-occurrence has already been noted in the final two year post-operative radiographs, but this did not correlate with symptom improvement. The observations above suggest that the best long-term performance of this implant is expected in mild to moderate OA, before MTPJ-1 space collapse occurs. Interestingly, the current clinical data did not show correlation with clinical outcome and pre-operative hallux rigidus staging. This study additionally proved that combined MTPJ-1 cartilage restoration with Agili-C and misalignment correction with osteotomies is feasible. To note, only proximal hallux valgus procedures or proximal phalanx osteotomies were allowed, as a minimum 3-cm safety margin from MTPJ-1 is required for safe implant lodging and later remodeling.

Study limitations to be acknowledged are non-randomized design, sample size, concomitant procedures could improve great toe status per se, and hallux rigidus grades from 2 to 4 were included. As this was the first study on the novel bi-phasic aragonite device, the main study intention was to show safety and feasibility, which was confirmed. Power analysis indicates that the statistical power was sufficient, despite cohort size. Additionally, multivariate analysis also excluded significant effect of hallux rigidus grades or concomitant osteotomies on the final study results.

Conclusions

The study provides important preliminary data for the treatment of hallux rigidus by using the Agili-C^{TM} implant. All the evaluated parameters significantly improved, excluding active plantar flexion, at all the time points compared to baseline. It was additionally confirmed that the Agili-C^{TM} implant has the potential to restore the osteochondral unit of metatarsal head.

Funding This multicenter clinical trial was sponsored by the CartiHeal Ltd., Israel.

Data availability Raw data (clinical, radiography, MRI) were generated in each participating center individually, and blindly archived and evaluated by the study sponsor CartiHeal Ltd., Israel. Derived anonymized data supporting findings of this study are available from the participating co-authors upon request.

Compliance with ethical standards

Conflict of interest The authors declare conflict of interest in relation to the presented work, either in the form of study funding, personal grants/fees, or employment by CartiHeal Ltd., Israel.

Ethics approval The multicenter clinical trial was conducted in four orthopedic centers. The study was registered on the ClinicalTrials.gov website (under Clinical_trials Identifier NCT02831244), and ethically approved individually by each participating institution.

Consent to participate Written informed consent was obtained from patients for their participation in the study.

Consent for publication Written informed consent was obtained from patients for their anonymized data to be published in this article.

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