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Case Reports and Series

Arthrodesis of the subtalar joint using a novel biphasic calcium phosphate bone graft

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ABSTRACT

Study design: Retrospective level IV study.
Background: Limited availability of autologous bone graft has led to a vast array of alternative bone graft options including allograft, demineralized bone matrices, cell-based matrices, and synthetic bone grafts. In this retrospective review, a control group of patients undergoing subtalar joint arthrodesis using a conventional bone graft was compared to a matched study group utilizing a novel synthetic biphasic calcium phosphate (BCP) bone graft with advanced surface topography.
Materials and methods: Seventeen consecutive patients underwent subtalar joint arthrodesis using a novel BCP with a unique submicron surface topography, either as a standalone graft or mixed with bone marrow aspirate. Fusion outcomes were assessed via radiographs at six-weeks and twelve-weeks. Clinical outcomes were assessed via weight bearing status at six-weeks and twelve-weeks. These results were compared to a matched study group of 15 patients undergoing subtalar joint arthrodesis using a conventional bone graft.
Results: Seventeen of seventeen (100%) of patients completed full follow up. Twelve of seventeen patients had complete fusion at 12 weeks (70%) and four of seventeen patients (23%) had partial fusion at 12 weeks. One of seventeen (5%) had revision arthrodesis. All patients were 100% weight bearing at 12 weeks. In the control group, fifteen of fifteen (100%) of patients completed full follow up. At 12 weeks, seven of fifteen (46%) had complete fusion, seven of fifteen (46%) had partial fusion, and one (6%) did not fuse and went on to revision surgery.
Conclusions: This novel submicron surface topography BCP offers a promising bone graft substitute for arthrodesis of the subtalar joint.

Introduction

Painful non-union is a challenging complication of arthrodesis procedures in the foot and ankle, with the subtalar joint specifically recognized throughout the literature as a difficult arthrodesis. Nevertheless, arthrodesis remains a common treatment for patients with posterior tibial tendon dysfunction, adult acquired flatfoot deformity, arthritic hindfoot conditions, or fracture. Due to the complex surface area of the subtalar joint, the intricate balance of motion in the hindfoot, and the lack of joint replacement options, surgical treatment of the subtalar joint remains technically challenging.[1,2]

One important factor in obtaining a solid fusion is the bone graft chosen for the procedure. Autograft bone in the form of Iliac Crest Bone Graft (ICBG) is the gold standard, but there is a limited supply and associated co-morbidities with harvesting, such as pain at the donor site.[3] Additionally, evidence suggests significant variability in autograft bone due to age, metabolic disease, or other co-morbidities.[4] As a result, multiple products have entered the market as a substitute or adjunct to bone graft.

Alternatives to autograft include allograft, demineralized bone matrices (DBMs), cell-based matrices (CBMs), and synthetic bone grafts. Each of these categories has risks and benefits, as well as published data on fusion rates. Synthetic bone grafts have quickly come to the forefront as an alternative to autograft bone, as they have a positive safety profile, and are cost-effective. Formulations include Calcium Sulfate, Hydroxyapatite (HA), β-Tri Calcium Phosphate (β-TCP), Biphasic Calcium Phosphate (BCP), Bioglass, and Silicated Calcium Phosphate (Si-CaP).[5] Because there is no standard research protocol for synthetic bone graft products, there is significant variability in the quality and quantity of research.

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Table 1
BCP<μm patient demographics, arthrodesis sites and procedures.

Patient Number	Age(yrs)	Sex	BMI	Tobacco	Revision	BMA	BCP<μm Volume (cc)	Diagnosis	Additional Fusion Sites	Additional Procedures
BCP<μm 1	43	F	24	Yes	No	Yes	5	OA. Talus Fracture		Ankle arthrotomy, HWR
BCP<μm 2	71	F	34	No	Yes	No	10	Non-Union TTC Arthrodesis	Ankle	HWR
BCP<μm 3	48	F	36	No	Yes	Yes	5	Non-Union Subtalar arthrodesis		HWR
BCP<μm 4	20	M	22	No	No	Yes	10	TC coalition		Peroneal tendon debridement and groove deepening
BCP<μm 5	31	M	33	Yes	No	Yes	5	Calcaneus fracture	CC	
BCP<μm 6	69	F	26	No	Yes	Yes	10	Non-Union Subtalar arthrodesis		HWR
BCP<μm 7	40	F	26	No	No	Yes	5	Talus Fracture		ORIF Talus
BCP<μm 8	68	M	38	No	No	Yes	10	OA	Ankle	
BCP<μm 9	49	F	39	No	No	No	10	OA	Ankle, TN	HWR
BCP<μm 10	53	M	25	No	No	No	10	Calcaneus fracture		ORIF Calcaneus
BCP<μm 11	47	F	39	No	No	Yes	10	OA		GR
BCP<μm 12	60	F	30	No	No	No	10	OA	TN	GR, Kidner
BCP<μm 13	60	F	35	No	No	Yes	10	PTTD, OA	TN	GR, PTT debridement
BCP<μm 14	53	F	34	Yes	No	Yes	10	PTTD, OA	TN	
BCP<μm 15	73	M	28	No	No	No	10	OA		HWR, Partial 5th Metatarsal Head Resection
BCP<μm 16	55	M	35	No	Yes	No	10	Non-union Subtalar Arthrodesis	Medial Column	HWR, GR
BCP<μm 17	20	M	39	No	No	No	10	PTTD	TN	GR

Abbreviation Key: Osteoarthritis = OA; Posterior Tibial Tendon Dysfunction = PTTD; TTC = Tibiotalocalcaneal; TC= Talocalcaneal; CC = Calcaneocuboid; TN = Talonavicular; HWR = Hardware Removal; ORIF = Open Reduction Internal Fixation; GR = Gastrocnemius Recession; PTT = Posterior Tibial Tendon.

Biphasic calcium phosphate

In recent years, research on biphasic calcium phosphates has led to increased utilization in arthrodesis surgery, owing to BCPs ability to support bone formation.[6,7] This class of bone graft material is cost-effective, has been proven to have an appropriate safety profile, and has a low incidence of reaction or material-related complications.[8] Additionally, BCP<μm bone graft has a resorption rate equal to that of anatomic bone, due to the ratio of HA and ß-TCP.[9]

Objective

The purpose of this retrospective cohort study is the evaluation of safety and performance of a novel biphasic calcium phosphate (BCP<μm) with a unique needle-shaped submicron surface topography (BCP<μm; MagnetOs™ Putty, Kuros Biosciences, B.V.) in 17 subtalar joint arthrodesis patients.

Materials and methods

Following investigational review board approval (WCG IRB # 20,202,829, August 2020), a systematic review was initiated to extract patients undergoing subtalar arthrodesis. All surgeries utilizing BCP<μm were performed by one surgeon at one institution between October 2019 and June 2021. Exclusion criteria included patients diagnosed with infection, a large bony defect requiring structural graft, Charcot neuropathy, and patients previously exposed to therapeutic levels of bone morphogenetic proteins (BMP). Thirty-seven patients were initially identified, and seventeen met inclusion criteria. Fifteen consecutive patients undergoing subtalar joint arthrodesis using a conventional bone graft performed by the same surgeon were identified from the time period of August 2018 – October 2019. Demographic data, surgical procedure, and postoperative data were retrieved for both cohorts.

In the BCP<μm group, concomitant diagnoses included post-traumatic osteoarthritis, talus fracture, ankle fracture, calcaneal fracture, non-union of subtalar arthrodesis, talocalcaneal coalition, and posterior tibial tendon dysfunction. There were 13 (76%) primary fusions and 4 (24%) revision fusions. In the control group, concomitant diagnoses included post-traumatic osteoarthritis, non-union of subtalar arthrodesis, talocalcaneal coalition, and posterior tibial tendon dysfunction. There were 13 (86%) primary fusions and 2 (13%) revision fusions. For patient demographics, arthrodesis sites and concomitant procedures of the BCP<μm group, see Table 1. For patient demographics, arthrodesis sites and concomitant procedures of the control group, see Table 2.

All fusion procedures were carried out following standard surgical protocols. The joint surfaces were decorticated, and the bone graft was packed into the joint space. The arthrodesis was then held in place with instrumentation.

Post-operatively, patients followed up for radiographic evaluation at three weeks, six weeks, and 12 weeks. Fusion success was defined as evidence of bridging trabecular bone. Standard postoperative ankle and foot radiographs, including anterior-posterior, oblique, and lateral radiographs were reviewed for fusion assessment. Radiographic fusion criteria were defined as described by Moran et al.,[10] and modified on a scale of 0–3 in terms of evidence of continuous bridging bone. The scale is: 0 = no evidence of osteogenesis; 1 = slight, discontinuous bridging; 2 = partial, discontinuous bridging; and 3 = complete, continuous bridging. Multi-joint fusions were scored on the least fused joint. All clinical and fusion assessments were completed and recorded by the treating surgeon. Clinical outcome was determined by weight bearing status at six and twelve-weeks. See Table 3.

Table 2
Control patient demographics, arthrodesis sites and procedures.

Patient Number	Age(yrs)	Sex	BMI	Tobacco	Revision	Bone Graft Used	Diagnosis	Additional Fusion Sites	Additional Procedures
Control 1	60	M	26	Yes	No	BMA	PTTD	TN	
Control 2	58	M	39	No	No	CBM	OA		
Control 3	59	M	39	No	Yes	DBM	Non-union Subtalar Arthrodesis		HWR
Control 4	61	F	33	No	No	DBM	OA, PTTD	TN	
Control 5	63	M	33	No	No	DBM	PTTD	Medial Column	
Control 6	55	M	31	No	No	DBM	OA		
Control 7	55	M	31	No	Yes	DBM	Non-union Subtalar Arthrodesis		HWR
Control 8	77	F	27	No	No	DBM	PTTD	Medial Column	
Control 9	68	F	26	No	No	DBM	OA		
Control 10	78	M	24	No	No	DBM, PDGF	OA, PTTD	Ankle	
Control 11	60	F	31	No	No	DBM	PTTD	TN	GR, Kidner
Control 12	68	M	32	No	No	DBM	OA		
Control 13	19	F	46	No	No	DBM	TC coalition		
Control 14	63	F	35	No	No	DBM	PTTD	TN	GR, Kidner
Control 15	33	F	26	No	No	DBM	TC coalition		Calcaneal Slide Osteotomy,GR

Abbreviation Key: Osteoarthritis = OA; Posterior Tibial Tendon Dysfunction = PTTD; TTC = Tibiotalocalcaneal; TC= Talocalcaneal; CC = Calcaneocuboid; TN = Talonavicular; HWR = Hardware Removal; ORIF = Open Reduction Internal Fixation; BMA = Bone Marrow Aspirate; GR = Gastrocnemius Recession; PTT = Posterior Tibial Tendon; PDGF = Platelet Derived Growth Factor.

Results

BCP<μm group

There were 17 patients in the BCP<μm group, of which 10 were female (59%) and 7 male (41%). The mean age was 50.5 years of age (20 to 73 years). The mean BMI was 32.1 kg/m^2 (22 –39) with 11 (65%) obese subjects reporting a BMI > 30 kg/m^2. Co-morbidities included Hypertension (7), Diabetes Mellitus (3), Depression (3), Peripheral Arterial Disease (2), Neuropathy (2), Gout (2), Coronary Artery Disease (2), Rheumatoid Arthritis (2), Obstructive Sleep Apnea (2), Chronic Obstructive Pulmonary Disease (1), Chronic Kidney Disease (1), Asthma (1), Polymyalgia Rheumatica (1), Crohn's Disease (1), and Dystonia (1).

Table 3
Radiographic fusion criteria.

Scale	Description
0	No evidence of Osteogenesis
1	Slight, discontinuous bridging
2	Partial, discontinuous bridging
3	Complete, continuous bridging

At six weeks, 2 of 17 patients (12%) had complete fusion, 11 of 17 (65%) had partial fusion, and 4 of 17 (24%) had slight bridging. At 12 weeks, 12 of 17 (70%) patients had complete fusion, 4 of 17 (24%) had partial fusion, and 1 of 17 had slight bridging.

The mean volume of BCP<μm implanted was 8.8 cc. Thirteen patients were implanted with 10 cc, and 4 patients were implanted with 5 cc. Ten of seventeen patients (59%) were augmented with BMA in addition to BCP<μm. In all cases where bone marrow aspirate was harvested, it was taken from the tibial tubercle and mixed with the bone graft. It was not concentrated.

Eight of the 17 (47%) were single arthrodesis procedures, and 9 of 17 (53%) were multiple joint arthrodesis. The multiple joint fusions were: Talonavicular (4), Ankle (2), Ankle + Talonavicular (1), Calcaneocuboid (1), and Medial Column (1). Four of 17 (24%) were revisions.

Several concomitant procedures were performed with the arthrodesis. These included hardware removal (7); gastrocnemius recession (5); open reduction internal fixation of fractures (2); Kidner procedure (1); ankle arthrotomy (1); peroneal tendon debridement and groove deepening (1), peroneal tendon debridement (1) and partial resection 5th metatarsal head (1).

Instrumentation was utilized in all arthrodesis cases and included a combination of screws, plates, staples, two IM arthrodesis nails, and one medial column beam.

Twelve of the seventeen patients (70%) returned to full weight bearing at six weeks post-operatively. Seventeen of seventeen patients (100%) returned to full weight-bearing by twelve weeks following surgery.

Postoperative complications were reported in 5 patients. This included delayed incision healing (2), plantar wound 1st metatarsal head (1), Post-operative hardware failure and removal (1), and non-union (1). This resulted in an overall complication rate of 30%. Of note, the non-union was in an obese tobacco user who reported a post-operative fall. This ultimately resulted in a revision arthrodesis. There were no graft material-related complications. See Table 4 for outcome data comparing the BCP<μm subgroup and the control subgroup. See Fig. 1 for Pre-operative and Post-Operative Radiographs.

Table 4
Demographic and Outcome data of BCP<μm subgroup vs control subgroup.

	BCP<μm	Control
Demographics		
Mean Age (years)	51	58
Female (%)	10 (59%)	7 (46%)
Male (%)	7 (41%)	8 (53%)
Mean BMI (kg/m^2)	32	32
Fusion%		
Partial at 6 weeks	65% (11/17)	53% (8/15)
Complete at 6 weeks	12% (2/17)	0% (0/15)
Partial at 12 weeks	24% (4/17)	46% (7/15)
Complete at 12 weeks	70% (12/17)	46% (7/15)
Full Weight Bearing%		
6 weeks	70% (12/17)	53% (8/15)
12 weeks	100% (17/17)	100% (15/15)

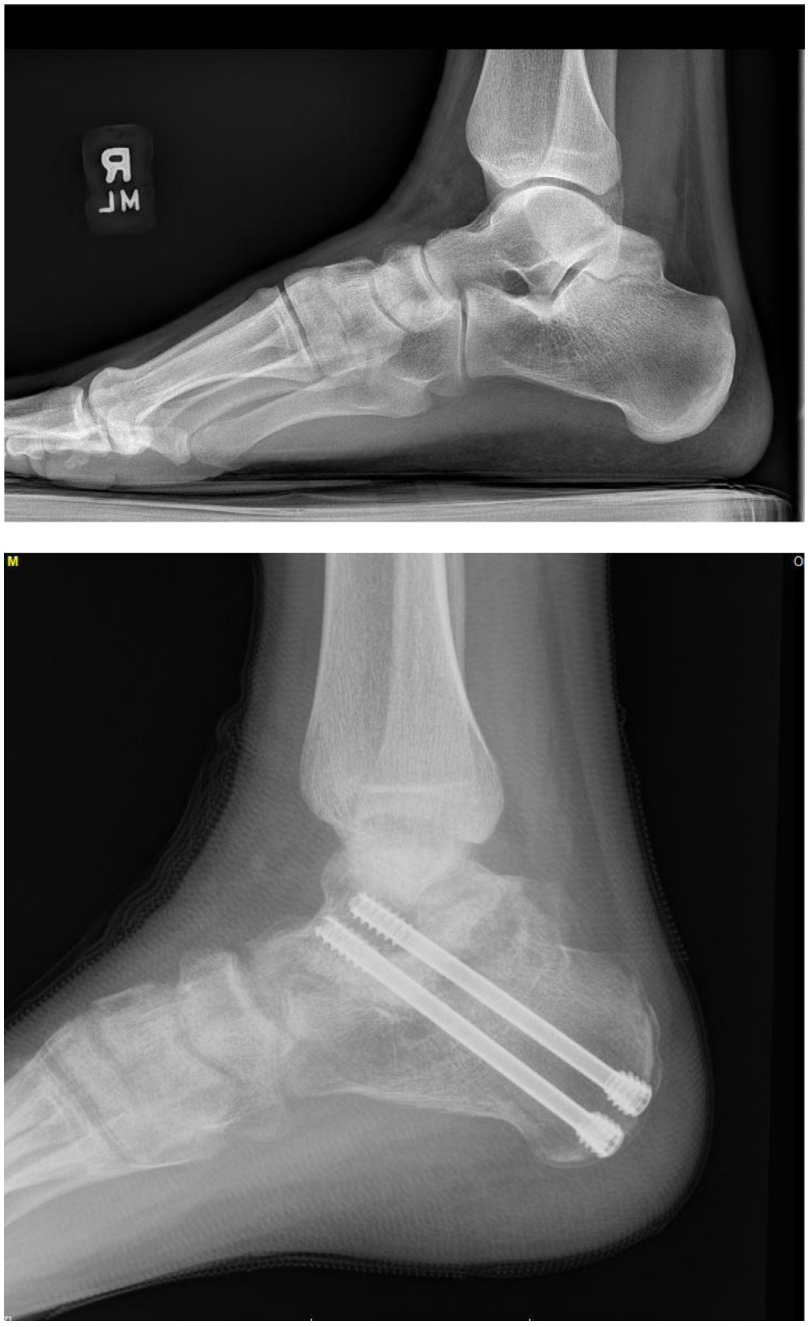

Fig. 1. Pre-Operative XR and 12 weeks Post-Operative XR.

Control group

There were 15 patients in the control group, of which 7 were female (46%) and 8 male (53%). The mean age was 58 years of age (19 to 77 years). The mean BMI was 32 kg/m^2 (24–46) with 10 (66%) obese subjects reporting a BMI > 30 kg/m^2. Co-morbidities included Hypertension (9), Diabetes Mellitus (3), Obstructive Sleep Apnea (3), Rheumatoid Arthritis (2), Asthma (2), Chronic Obstructive Pulmonary Disease (2), History of Myocardial Infarction (1), Anemia (1), Depression (1), History of Stroke (1), and Chronic Kidney Disease (1)

At six weeks, 0 of 15 patients (0%) had complete fusion, 8 of 15 (53%) had partial fusion, 6 of 15 (40%) had slight bridging, and 1 of 15 (6%) had no evidence of healing. At 12 weeks, 7 of 15 (46%) patients had complete fusion, 7 of 15 (46%) had partial fusion, 1 of 15 (6%) had slight bridging, and no patients had no evidence of healing.

The bone graft used varied among patients. DBM alone was used for 12 of 15 patients (80%). For the remaining three patients, one patient (6%) had CBM alone, one patient (6%) had BMA alone, and one patient (6%) had DBM and PDGF.

Eight of the 15 (53%) were single arthrodesis procedures, and 7 of 15 (46%) were multiple joint arthrodesis. The multiple joint fusions were: Talonavicular (4), Medial Column (2), Ankle (1). Two of 15 (13%) were revisions.

Several concomitant procedures were performed with the arthrodesis. These included gastrocnemius recession (3); hardware removal (2); Kidner procedure (2); calcaneal slide osteotomy (1).

Instrumentation was utilized in all arthrodesis cases and included a combination of screws, plates, staples, and one TTC nail.

Eight of the fifteen patients (53%) returned to full weight bearing at six weeks post-operatively. Fifteen of fifteen patients (100%) returned to full weight-bearing by twelve weeks following surgery.

Postoperative complications were reported in 4 patients. This included wound dehiscence (1) and non-union requiring revision (3). This resulted in an overall complication rate of 26%. See Table 4 for outcome data comparing the BCP<μm subgroup and the control subgroup.

Discussion

Foot and ankle arthrodesis procedures have continued to increase.[11] With these growing numbers, pseudarthrosis rates of subtalar fusion procedures are well documented in the literature, with non-union rates ranging from 14 to 35%.[1,12,13] Utilizing an effective bone graft is a valuable tool in achieving successful arthrodesis, and several categories of bone graft are available to surgeons. ICBG is the gold standard, however limited quantity of autograft bone and relevant co-morbidities with harvesting impact the quantity that a surgeon can obtain.(3) Allografts and DBMs have a long track record and a relatively benign safely profile, but fusion rates are mixed, and there is risk of disease transmission.[14–16] In the 2000s, CBMs entered the market, with promising early fusion rates from level III and IV studies. In recent years however, unbiased published fusion rates of CBMs are lower, and the safety of these products has been questioned, as one well-known CBM contaminated with tuberculosis was implanted into patients, prompting an FDA recall.[17–19]

Because of these concerns with autograft, allograft, and CBMs, synthetic bone grafts have grown in popularity. In recent years, research on both hardware and bone grafts has focused on the ability of surface topography to modulate bony healing. Recent studies have shown that a surface area which is submicron in size and has needle-shaped topography, such as this novel BCP<μm, can manipulate macrophages in the immune system to a pro-healing phenotype.[20] Additionally, pre-clinical research demonstrated that when placed in a muscular pouch in canines, BCP<μm grew bone without the addition of cells or growth factors.[20]

In this retrospective cohort of seventeen patients with a matched cohort control group, we achieved a 70% complete fusion rate at 12 weeks, and a 24% partial fusion rate at 12 weeks, even with a 25% revision rate. This is in contrast to the control group, which used a variety of alternate bone grafts, and resulted in a 46% complete fusion rate at 12 weeks and a 46% partial fusion at 12 weeks. This was with a lesser revision rate in the control group of 13% (2/15 patients). Notably, there were two complete fusions at 6 weeks in the BCP<μm, versus no complete fusions at 6 weeks in the control group. It is also worth noting that in this BCP<μm cohort, BCP<μm was used both as an autograft extender and as a stand-alone bone graft, indicating that it is safe and effective in both scenarios.

One advantage of this study is that the cohort is indicative of a general patient population; there is continuity of the single surgeon technique; there are patients with co-morbidities known to affect fusion status such as tobacco use, BMI, and advanced age; and it represents outcomes in a real-world clinical application in a private practice setting. Disadvantages include the retrospective nature, the limited study population size, funding bias from the authors, and the absence of an independent radiologic reviewer.

The limitations of traditional bone grafts have led surgeons to investigate the advancing field of surface topography to modulate bone growth. The data from this retrospective foot and ankle arthrodesis cohort demonstrates that this novel BCP with needle-shaped submicron surface topography is safe to use without identified graft-related side effects. Future studies with longer-term follow-up and patient-reported outcomes are indicated. At this time, level-one prospective randomized studies,[21] as well as multiple prospective and retrospective reviews are currently being conducted on this novel BCP<μm.[22–2422]

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Informed patient consent

The authors declare that informed patient consent was taken from all the patients.

Declaration of Competing Interest

TF and KS have a financial relationship with Kuros Biosciences BV.

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