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Outcomes of Surgical Reconstruction Using Custom 3D Printed Porous Titanium Implants for Critical-Sized Bone Defects of the Foot and Ankle

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Abstract

Background: Treating critically sized defects (CSDs) remains a significant challenge in foot and ankle surgery. Custom 3D printed implants are being offered to a small but growing subset of patients as a salvage procedure in lieu of traditional alternates such structural allografts after the patient has failed prior procedures. The long-term outcomes of 3D printed implants are still unknown and understudied due to the limited number of cases and short follow-up durations. The purpose of this study was to evaluate the outcomes of patients who received custom 3D printed implants to treat CSDs of the foot and ankle in attempt to aid surgeons in selecting appropriate surgical candidates.

Methods: This was a retrospective study to assess surgical outcomes of patients who underwent implantation of a custom 3D printed implant made with medical grade titanium alloy powder (Ti-6Al-4V) to treat CSDs of the foot and ankle between 6/1/2014 and 9/30/2019. All patients had failed previous nonoperative or operative management prior to proceeding with treatment with a custom 3D printed implant. Univariate and multivariate odds ratios (OR) of a secondary surgery and implant removal were calculated for perioperative variables.

Results: There were 39 cases of patients who received a custom 3D printed implant with least one year follow-up. The mean follow-up time was 27.0 (12–74) months. 13/39 (33.3%) of cases required a secondary surgery and 10/39 (25.6%) required removal of the implant due to septic nonunion (6/10) or aseptic nonunion (4/10). The mean time to secondary surgery was 10 (1–22) months. Multivariate logistic regression revealed that patients with neuropathy were more likely to require a secondary surgery with an OR of 5.76 (p= 0.03).

Conclusion: This study demonstrated that 74% of patients who received a custom 3D printed implant for CSDs did not require as subsequent surgery (minimum of 1 year follow-up). Neuropathy was significantly associated with the need for a secondary surgery. This is the largest

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series to date demonstrating the efficacy of 3D printed custom titanium implants. As the number of cases using patient-specific 3D printed titanium implant increases, larger cohorts of patients should be studied to identify other high-risk groups and possible interventions to improve surgical outcomes.

Keywords

3D Printing; Additive Manufacturing; Critically Sized Defects; Foot and Ankle Surgery; Neuropathy; Nonunion; Osseous Integration; Outcome Studies; Patient Specific Implant; Patient Specific Implant

INTRODUCTION:

Critically sized defects (CSD) are bone voids that exceeds the bone's natural ability to heal. While the exact amount of bone loss needed to qualify as a CSD may vary between anatomic locations and has been debated in the literature, CSDs are commonly defined as defect greater than 1–2 cm in length or greater than 50% loss in bone circumference.[26] CSDs can be secondary to multiple etiologies including trauma, osteonecrosis, infection, tumor, after acute deformity correction, and after removal of failed total ankle replacement.[8,24,39]

Current treatment options for patients with CSDs in the foot and ankle include bone transport, bulk allografts, autografts, vascularized bone transfer, or the induced membrane technique. Often, these treatments are performed for limb salvage. However, these options are not without drawbacks. They are susceptible to donor site morbidity, nonunion, infection, can necessitate long-term external fixation, and can require several surgical episodes to complete.[5,6] Unfortunately, a substantial number of patients ultimately fail these treatments and are left with a chronically painful extremity or require an amputation because of unsuccessful treatment.[9,19,27,31] The risk of complication such as amputation is especially high in patients with diabetes.[37] For example, in a study of 32 patients undergoing a tibiotalocalcaneal (TTC) arthrodesis with bulk femoral head allograft, the fusion rate was 50% in the overall cohort and 0% in all nine patients with diabetes.[15] A similar study found complete fusion in 63% of the 23 patients also undergoing TTC with bulk femoral head allograft, but was not powered to determine the significance of diabetes.[30]

A promising potential solution from the field of additive manufacturing is the use of custom, 3D printed porous titanium implants.[34] These implants offer several advantages over current options, including the ability to provide the exact, patient-matched size and shape needed to fill the CSD, improved structural integrity over allograft bone, lack of invasive harvesting of a patient's own tissues, and a single operation.[21] Moreover, 3D printed implants continue to provide the ability to integrate the surgeon's preferred hardware and/or existing hardware in the patient, to carry and deliver biological agents to the surgical site, and to be used in conjunction with other surgical techniques and treatments.[4,20,38] Compared to allograft, custom implants 3D printed implants can be produced on-demand, do not share the same level of potential risk in terms of disease transmission or rejection from immune response.[16,22] In principle, 3D printed implants also do not require the intraoperative modifications needed for both allografts and autografts, offering a better fit and shorter anesthesia time.[25] The adoption of 3D printed implants is relatively new, and the field is still learning if printed implants offer superior bony fusion as some early studies have shown.[35]

Additionally, additive manufacturing allows for the precise creation of sophisticated porous lattices for bone ingrowth and ongrowth, previously unattainable from traditional subtractive manufacturing methods used to make implants for arthroplasty and bone defect repairs.[29] The advantage of these porous implants is the hope for improved osseointegration enabling long term stability of the construct. Additionally, engineers can easily change the amount of void space in the 3D model to tune the porosity of the final print in theory to promote bone growth by decreasing the modulus of the implant reducing the effect of stress shielding by the implant.[1,32] Porosity in 3D printed titanium hardware is typically achieved with a truss based or sheet based lattice structures. The specific sheet based lattice used in 3D printed titanium implants is the triply period minimal surface, commonly referred to as the gyroid lattice.[2,7,11,40]

The adoption of 3D printed custom implants in high-risk patients is relatively new with few reports characterizing their efficacy.[36] The long-term outcomes are still unknown and understudied due to the limited number of cases and short follow-up. Previous publications are limited to case reports and small case series, thus demonstrating an unmet need to systematically study and evaluate surgical outcomes of patients who receive these 3D printed implants.[13] Moreover, there is no data on patient or implant characteristics that may portend implant removal. Such studies and reviews are imperative as a wide range of patients could potentially benefit from the adoption of these new techniques and devices. Thus, the purpose of this study is to evaluate and report the initial outcomes of consecutive patients who received custom 3D printed implants to treat CSDs of the foot and ankle.

MATERIALS AND METHODS:

Study Design:

This was a retrospective study that included all patients who had failed previous nonoperative or operative management prior to proceeding with treatment with a custom 3D printed implant. Patients consented to the procedure after an extensive discussion when alternative surgical options were considered. The clinical indications for procedure included traumatic defects/deformities, post reconstruction defects, failed arthrodesis, failed total ankle replacements (TAR), avascular necrosis (AVN) and Charcot deformities. The contradictions included an active infection, neurovascular compromise, poor quality of the sounding bone or soft tissue envelope, and foreign body sensitivity. (Figure 1) A consecutive series of patients were included in this study if their reconstructive surgery took place between 6/1/2014 and 9/30/2019 with a minimum of 1 year clinical and radiographic follow-up. All implants were performed by the senior author. Each implant was a custom case specifically designed for each surgery. For the purpose of this study, the type of implants were generalized to seven groups outlined in Figure 2 along with the procedure performed and the clinical indication. Following approval by the Institutional Review Board, pre-surgical risk factors, perioperative variables and surgical outcomes were compiled for each patient. Pre-surgical risk factors investigated in this study included age, gender, race, BMI, diabetes status, neuropathy, tobacco use, number of foot and ankle surgeries, prior limb infections, laterality of defect, and indication for surgery. Perioperative variables included manufacturer of the implant, internal geometric structure of the implant, duration of surgery, and perioperative antibiotics.

Custom Implant Design:

All of the implants in this series were fusion implants. There were no total talus replacements or joint arthroplasties. In each case, the 3D implant was created as previously described.[18] Briefly, a CT scan was obtained of the involved extremity and sent to the device manufacturer (either 4WEB Medical, Frisco, TX or Restor3D, Durham, NC). Next, a team of engineers worked with the surgeon to design the implant based on the size and shape of the CSD and any additional surgical instrumentation (cutting guides, sizers) needed. After surgeon approval, the implant was 3D printed, underwent post-processing, and sent to the hospital for sterilization.

Statistical Analysis:

The primary outcome of this study was the need for a secondary surgery for any reason. The secondary outcome was the need for removal of the implant for any reason. The term "implant failure" was not used as none of the implants were found to be broken. Therefore, reasons for implant removal included septic nonunion and aseptic nonunion. The odds ratios (OR) of having a secondary surgery or implant removal were calculated for each perioperative variable. A multivariable logistic regression model was created to adjust OR calculations for potentially confounding variables by including the most significant variables in the univariate analysis as baseline characteristics including age, gender, BMI, lattice type of implant and tobacco use. For the demographic table, categorical variables were compared with a Pearson's Chi-squared Test and continuous variables were compared with Welch Two Sample T-Test. The binary outcomes were fitted in both a univariate and multivariate logistic regression model to calculate OR for each perioperative variable. P values less than .05 were considered statistically significant. All statistical analysis was performed using RStudio (RStudio, PBC, Version 1.3.9590).

RESULTS:

There were 45 cases of patients receiving a custom 3D printed implant within the study time period. Data from six patients was lost from lack of follow-up, leaving 39 cases of 3D printed patient specific implants with a minimum of one-year follow-up (Figure 3). The mean follow-up time was 27.0 (12–74) month (Table 1). 11 (28%) of the patients had a relative contradiction with prior infection of the ipsilateral limb where the implant was placed (Table 1). The implants were used for the following indications: trauma with bone loss (15), nonunion following prior surgical fixation attempts (13), avascular necrosis (4), Charcot arthropathy (3), failed total ankle replacement (2), debridement following osteomyelitis (1) and correction of congenital deformity (1).

Of the 39 cases in the study cohort, 13 (33.3%) required an additional surgery. The mean time to secondary surgery was 10 months. Of the 13 subsequent surgeries, three were for non-3D printed implant hardware problems and 10 (26% of the entire cohort) required the removal of the 3D implant. Thus, 74% of the 3D printed implants remained in vivo. Figure 4 highlights representative examples where the 3D printed implant facilitated osseous integration across the CSD. Representative examples of cases that resulted in implant removal are shown in Figure 5. Of the three hardware complications (non-3D printed implants), one case was due to multiple broken screws and two cases were due to prominent, symptomatic screws. All 10 removal of 3D printed implants were for nonunion, six (60%) for septic non-union and four (40%) for aseptic nonunion. Implant removal occurred at a mean of 8.3 months and ranging from 1 to 22 months after implantation. Five (50%) of the 3D printed implant removal patients ultimately underwent a below-knee-amputation. Descriptions of all patients that required a secondary surgery are given in Table 2. Notably, seven of the 13 patients in this group had previously documented neuropathy. One patient is represented twice, as s/he underwent revision to a new 3D printed cage after electing to try a 3D printed again as s/he was not ready for amputation, which subsequently required another revision surgery.

The only significant difference in perioperative variables between the cohort that did and did not need a secondary surgery was the presence of neuropathy for any reason (Table 1). A Pearson's Chi-squared Test showed that a statically higher proportion of patients who had a secondary surgery had neuropathy. 69.2% of patients who required a secondary surgery had neuropathy compared to only 34.6% of patients who did require a secondary surgery ($p = 0.041$).

Logistic Regression Analysis

In the univariate logistic regression model, no variables were statistically significant. The multivariate logistic regression model revealed that a diagnosis of neuropathy was statistically significant with an OR 5.76 ($p = 0.03$) for subsequent surgery (Table 3). The remaining variables in the model, gyroid lattice (sheet-based lattice in contrast to a strut-based lattice), age, BMI, male gender and tobacco were not independently predative of surgical outcomes with an OR estimates near one.

DISCUSSION:

Advances in additive manufacturing now allow surgeons and engineers to collaborate potentially advance patient care by 3D printing high strength, anatomic and porous implants designed to meets the needs of each patient.[17,21,29] This study provides data on the largest known cohort of patients receiving custom 3D printed titanium implants for distal tibia, ankle, and hindfoot CSDs in a foot and ankle surgeon's practice. Previously, our group reported on a smaller, 15-patient cohort, demonstrating successful overall outcomes.[13] In another study, our group demonstrated improved fusion rates with the use of 3D printed implants for tibiotalocalcaneal (TTC) arthrodesis compared to the use of femoral head allografts.[36] The current, larger study adds to the literature by demonstrating the efficacy of these implants at the longest known follow-up, a mean of 27 months. It concurrently demonstrates that neuropathy is a significant predictor of subsequent surgery with the reason for implant removal due only to aseptic or septic nonunion as none of the implants were found to have structurally failed.

The overall infection rate in the final cohort was 15% (6/39). Of the 10 (26%) patients that ultimately required removal of their implant, the majority (60%) were due to infection that required removal of the 3D printed implant. Periprosthetic infections in orthopaedic surgery account for a significant degree of morbidity and mortality, especially in foot and ankle patients. Bacteria can colonize the metal surfaces and form a biofilm that is resistant to antibiotic therapies.[12] Biofilm on 3D printed implants is likely harder to eradicate secondary to the much larger surface area and crevices of the interstices of the implant. The introduction to bacteria can occur from infected tissue remaining at the time of implantation, the environment while the skin is open in the intraoperative period, or even from distant unrelated postoperative infections. In fact, one patient in this series suffered transient bacteremia from a UTI two months after the implantation surgery. The implant was removed, and the patient underwent a below-the-knee amputation, where the same bacteria from the UTI (E.coli) was isolated in the wound bed . The 15% infection rate found in this study highlights the need to designs implants and therapies to mitigate the burden of infection. However, treatment alternatives such as bulk allografts also come with substantial risk of infections.[43] A large study of 133 patients undergoing limb salvage surgery following an oncological resection of the proximal tibia showed significantly higher rates of infection in patients who received a bulk allograft compared to a metal endoprosthesis; 42 % of the osteoarticular allograft reconstructions failed and had an overall infection rate of 20 %.[3]

In three cases, failure of non 3D printed fixation hardware resulted in secondary surgery without the removal of 3D printed implants. Notably, each of these cases were caused by isolated issues with the traditional accessory hardware (e.g., screws) rather than the 3D printed cages themselves. This issue is not unique to the implant systems utilized in this study. Hardware malfunction is one of the most common reasons for implant removal in foot and ankle surgery, largely because the thin layer of overlying tissue is especially sensitive to hardware abnormalities.[10,14] Nevertheless, the seamless integration of accessory hardware with 3D cages remains an important design criterion for future implant development and design.

Patient diagnosis of neuropathy was associated with a statistically significantly increased risk for secondary surgery but not necessarily implant removal, although six (60%) patients who underwent implant removal had neuropathy. Given that the implants in our study required revision for a variety of different reasons, the mechanism by which neuropathy could mediate this effect is likely multifactorial in nature. However, preoperative neuropathy has been well documented as a risk factor for poor bone healing, nonunion, reoperation and hardware failure following various foot and ankle surgeries.[23,28,33] Neuropathy may have also contributed by way of infection, especially considering that infection accounted for half of the revision cases. A number of studies have identified neuropathy as an independent predictor for postoperative infection following foot and ankle surgery.[41,42] While neuropathy is not an absolute contraindication for 3D printed implants, foot and ankle surgeons should be especially cautious and appropriately inform patients with this comorbidity.

Five of the patients who had their implant removed ultimately underwent below knee amputation. In general, amputation is only carried out after all treatment options have been extensively exhausted. However, in these five patients, amputation was discussed as a treatment option prior to proceeding with 3D printed implant surgery.

This study contains several limitations. Although the cohort in this study is substantially larger than its predecessor, it is still relatively small. The small cohort size and the heterogenous indications for the custom cases may make the study underpowered to detect further associations between other perioperative variables and the surgical outcomes. There may also be differences between the general groups of 3D printed implants that were not detected due to the small sample size but should be the analyzed in future studies. Furthermore, the surgeries included in this study were performed at one institution by a single surgeon. As such, we are unable to discern the degree to which surgeon experience, volume and institutional support may impact the outcomes of these implants. For several patients included in this study, follow-up data was available for five years or more. However, patients with a minimum follow-up of one year were included in this analysis because we found that most failures happened within the first year of implantation. If we had chosen a two-year implant cut-off, those patients would not have been reported upon in this manuscript, artificially increasing the success rate (retained 3D printed implant) and misleading the reader. Patient reported outcomes were not included in this study since they were inconsistently recorded in the electronic medical record and therefore unavailable in this retrospective study. Future prospective studies are needed to capture these important functional outcomes of the 3D printed implants.

Based on this study, we believe surgeons considering using a patient-specific 3D printed implant should screen for symptoms of neuropathy to identify high risk patients for implant failure. The presence of neuropathy should not be an absolute contraindication to custom 3D printed implant as many patients are facing amputation after exhausting other surgical options and there are many forms and reasons for neuropathy that a series such as ours could not delineate. Additionally, in this study multiple patients with a diagnosis of neuropathy benefited from the procedure. By identifying high-risk groups, interventions such as increased follow up, tighter blood sugar control, additional surgical fixation and more extensive antibiotic therapy may be considered to possibly improve clinical outcomes. A focus on this particular subgourp should be the subject of future clinical studies.

CONCLUSION:

This is the largest study of custom 3D printed titanium foot and ankle fusion implants to treat CSDs to date. Multivariate logistic regression revealed that patients with neuropathy had increased odds of requiring a secondary surgery. The indication of the high-risk groups will allow providers to modify their practice to better identity and treat neuropathic patients with CSD needing a 3D printed implant. As the number of cases using patient-specific 3D printed titanium implant increases, larger cohorts of patients should be studied to identify other high-risk groups and possible interventions to improve surgical outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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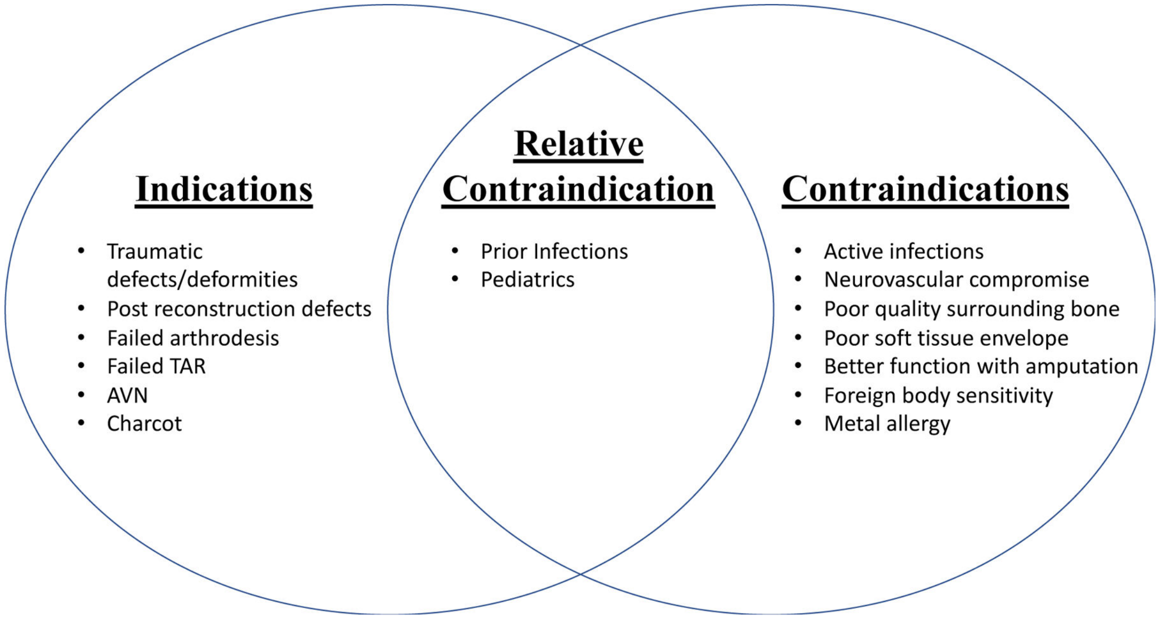


Figure 1:

Overview of the indication and the contraindication to receive a custom 3D printed foot and ankle implant

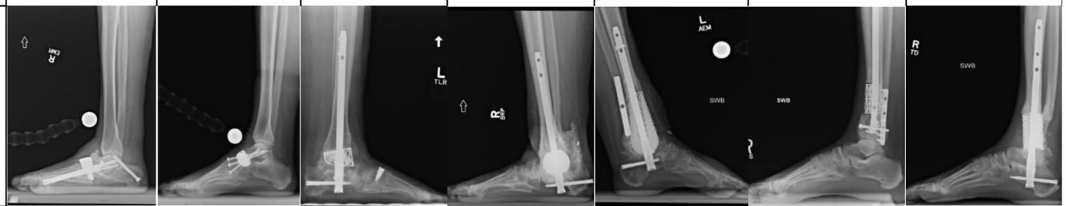
Type of Implant	Midfoot Wedge	Navicular Replacement Cage	Hindfoot Wedge	Talus Replacing Sphere	Tibial and Talar Replacement Tower	Intratibial Cage	Tibial Replacement Tower
Post Op Imaging							
Total	6	2	2	12	8	3	5
Procedure	Midfoot Arthrodesis (6)	Navicular Reconstruction (1) Medial Column Arthrodesis (1)	TTC (2)	TTC (12)	TTC (8)	Tibia Nonunion Repair (3)	TTC (5)
Indication	Charcot (2) Navicular Fracture (2) Midfoot Deformity (1) Nonunion of Midfoot Osteotomy (1)	AVN (1) Nonunion of Prior Arthrodesis (1)	Hind Valgus Malunion (2)	Nonunion from prior arthrodesis (5) Failed TAR (2) Charcot (2) Nonunion from Fracture (1) AVN (1) Hindfoot and Ankle Deformity (1)	Nonunion of Pilon Fracture (4) Nonunion of TTC Arthrodesis (1) Charcot (1) Bone Loss (1) Nonunion of Tibial Talar Joint (1)	Nonunion of Pilon Fracture (1) Nonunion of Tibial Shaft Fracture (1) Neurofibromatosis Tibial Pseudarthrosis (1)	Nonunion of Pilon Fracture (2) Nonunion of Prior Custom Implant (1) Tibial Bone Loss (1) Failed TAR (1)

Figure 2:

Outline of the different types of 3D printed implants analyzed in this study along with the procedure and indication for the surgery. Each implant was uniquely designed for a custom case, but was generalized into one of seven categories shown in the figure.

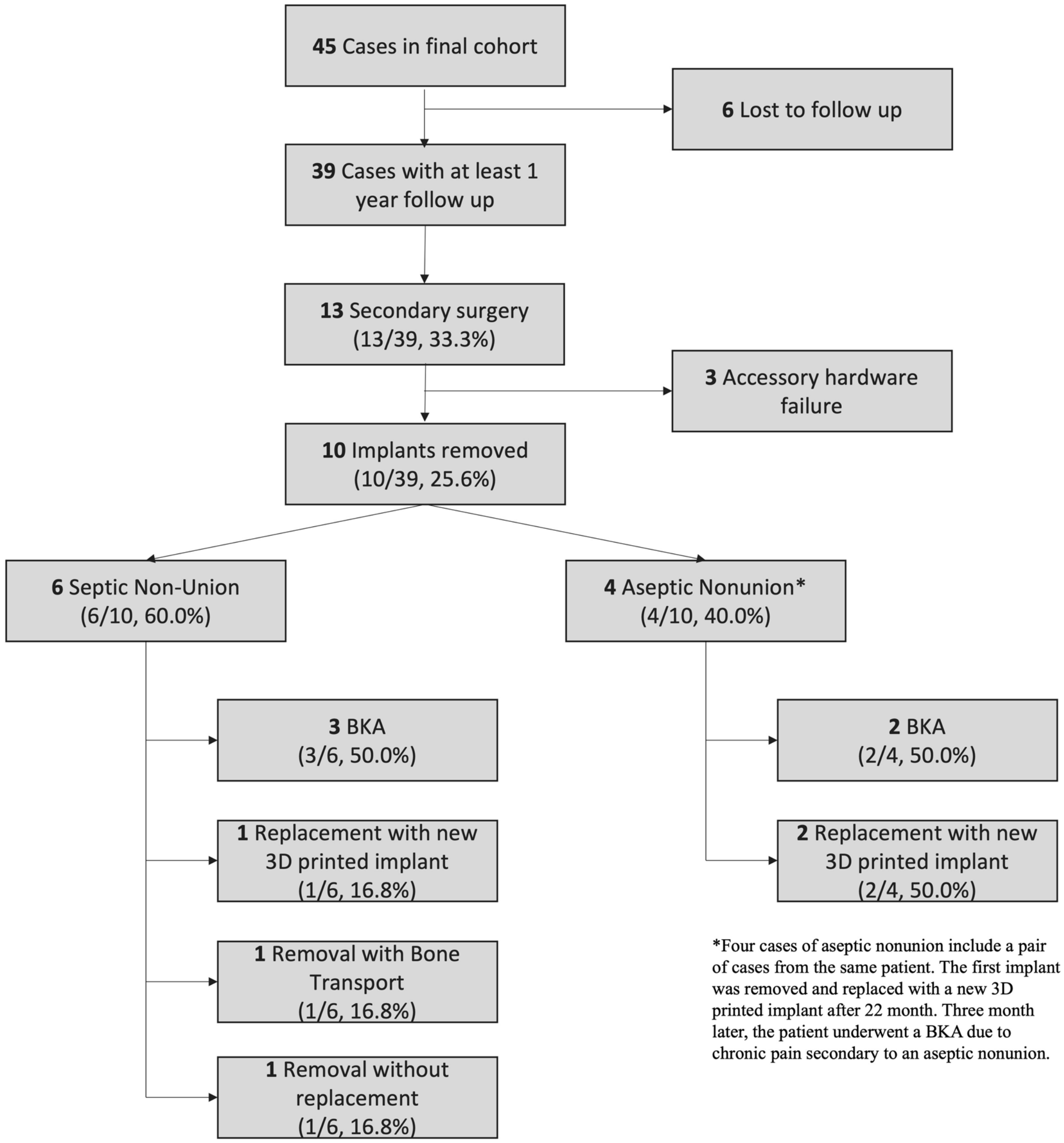


Figure 3:

Overview of the number of case and revision surgery in the study cohort.

Figure 4:

Examples of successful implants that did not require a revision surgery. (A-C) Patient with nonunion and varus collapse after unsuccessful open reduction and internal fixation of a pilon fracture. The hardware has collapsed into and destroyed the body of the talus. (A) Preoperative lateral radiograph showing the nonunion. A 3D printed custom implant was designed to fill the CSD gap after removal of the nonunion and talar body destruction. At 5 year follow-up, anteroposterior radiograph (B) and sagittal CT scan (C) images show anatomic alignment with evidence of osseous integration around (B) and in (C) an open truss 3D printed titanium cage. (D-F) An example of a non-operatively treated pilon fracture in a diabetic patient that went on to nonunion, collapse, and ankle arthritis. (D) Preoperative lateral radiograph demonstrating the nonunion and collapse of the distal tibia and anterior translation of the talus. A 3D printed custom implant was designed to fill the CSD gap after removal of the nonunion. At 2 years follow-up, lateral radiograph (E) and sagittal CT scan

(F) images show signs of osseous integration in a 3D printed gyroid lattice titanium cage. Both patients were asymptomatic.

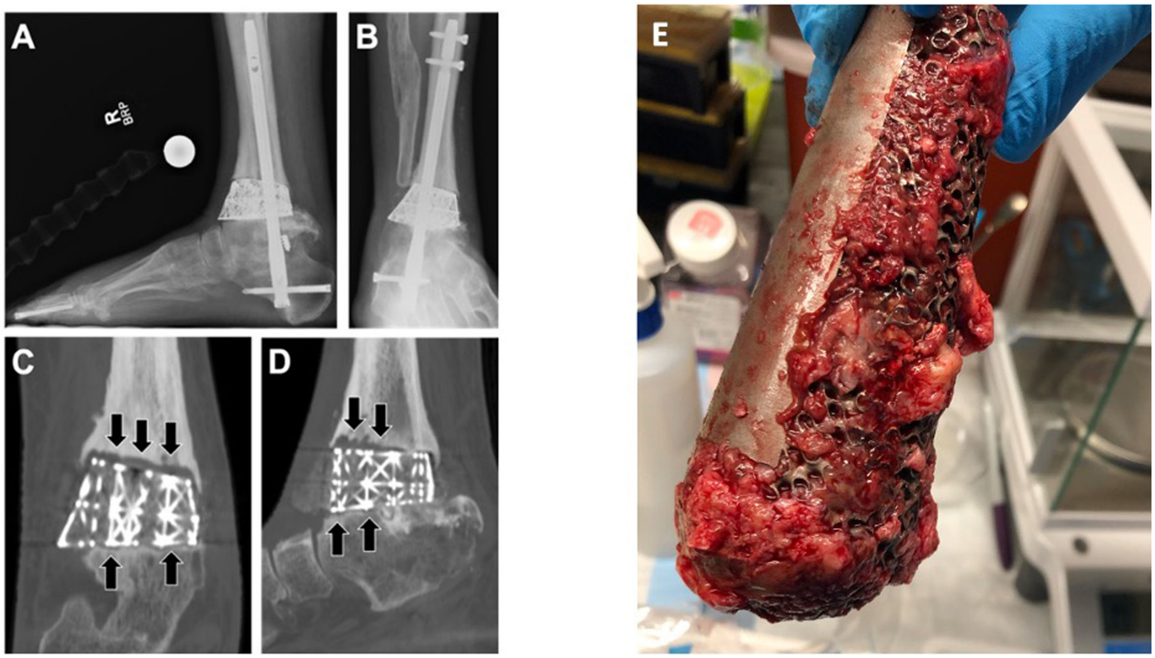


Figure 5.

Examples of implants requiring a revisions surgery. (A-D) 56-year-old male had custom implant removed because of failure of bone integration and continued pain, and underwent a below-the-knee amputation. Lateral (A) and anteroposterior (B) radiographs demonstrating the use of a 3D printed Titanium open truss cage to fill a critical sized bone defect between the tibia and talus. Coronal (C) and sagittal (D) CT scan images demonstrating no osseous integration of the surrounding bone into the implant (arrows), contrary to figures 5C and 5F. (E) An example of gyroid lattice cage that was removed from a 60-year-old male due to a septic nonunion, extensive osseointegration was evident in this implant removed due to infection.

Table 1:

Demographic table examining the difference between patients who did not require a secondary surgery compared to patients who did require a secondary surgery.

	No Secondary Surgery (N=26)	Secondary Surgery (N=13)	Overall (N=39)	P Value
Follow-up Time (Month)				0.6187
Mean (SD)	28.4 (18.4)	25.8 (14.3)	27.5 (17.0)	
Sex				0.3649
F	14 (53.8%)	5 (38.5%)	19 (48.7%)	
M	12 (46.2%)	8 (61.5%)	20 (51.3%)	
Age (Years)				0.5123
Mean (SD)	57.4 (16.5)	54.0 (14.0)	56.3 (15.6)	
Race				0.6376
Black or African American	4 (15.4%)	1 (7.7%)	5 (12.8%)	
Caucasian/White	20 (76.9%)	10 (76.9%)	30 (76.9%)	
Other	2 (7.7%)	2 (15.4%)	4 (10.3%)	
BMI				0.6142
Mean (SD)	35.1 (8.69)	33.7 (7.21)	34.6 (8.16)	
Diabetes				0.8013
N	19 (73.1%)	9 (69.2%)	28 (71.8%)	
Y	7 (26.9%)	4 (30.8%)	11 (28.2%)	
Neuropathy				**0.04094**
N	17 (65.4%)	4 (30.8%)	21 (53.8%)	
Y	9 (34.6%)	9 (69.2%)	18 (46.2%)	
Tobacco Use				0.8208
N	13 (50.0%)	6 (46.2%)	19 (48.7%)	
Y	13 (50.0%)	7 (53.8%)	20 (51.3%)	
Prior Limb Infection				0.3142
N	20 (76.9%)	8 (61.5%)	28 (71.8%)	
Y	6 (23.1%)	5 (38.5%)	11 (28.2%)	
Number of Prior Ankle Surgeries				0.5575
Mean (SD)	2.73 (2.63)	3.31 (2.95)	2.92 (2.72)	
Laterality				0.173
L	16 (61.5%)	5 (38.5%)	21 (53.8%)	
R	10 (38.5%)	8 (61.5%)	18 (46.2%)	
Width of Cage (mm)				0.5733
Mean [Min, Max]	42.2 [21.8, 85.0]	46.2 [27.5, 118]	43.5 [21.8, 118]	
Length of Cage (mm)				0.375
Mean [Min, Max]	56.8 [17.3, 181]	68.4 [28.5, 134]	60.7 [17.3, 181]	
Lattice Type				0.8134
Truss	17 (65.4%)	8 (61.5%)	25 (64.1%)	
Gyroid	9 (34.6%)	5 (38.5%)	14 (35.9%)	

Table 2:

Relevant clinical information of the 13 patients that underwent a subsequent surgery. Abbreviations used: CIDP, Chronic inflammatory demyelinating polyneuropathy; CKD, Chronic Kidney Disease; CMT, Charcot-Marie-Tooth disease; CVD, Cardiovascular Disease; DM, Diabetes Mellitus; HIV, Human Immunodeficiency Virus; TTC, Tibiotalocalcaneal arthrodesis.

Etiology	Relevant Comorbidities	Procedure	Indication for Revision	Outcome	Microbiology if Infected (If cultures available)	Number of Prior Surgeries	Duration in vivo (months)
Charcot arthropathy	Neuropathy, DM, oral steroids, CVD, CKD, gout	Subtalar Arthrodesis	Septic non-union	Cage and hardware removal	MRSA, Enterobacter asburiae/cloacae, Proteus mirabilis	0	1
Closed Pilon Fracture	CVD	TTC	Septic non-union	Below knee amputation		3	3
Fracture	None	Arthroplasty with distal tibia reconstruction	Septic non-union	Below knee amputation	Streptococcus agalactiae, group B	10	3
Pilon fracture with fractured implants	CVD	TTC	Aseptic non-union. (After 2nd cage)	Below knee amputation		3	3
Charcot arthropathy with malunion	Neuropathy, DM, CVD	TTC	Septic non-union	Below knee amputation	E. coli	Multiple (at outside facility)	5
Abduction deformity	Neuropathy, CIDP, CVD, CKD	Navicular replacement	Septic non-union	New 3D-printed cage implanted	Staphylococcus schleiferi	3	5
Navicular fracture with nonunion	Neuropathy, CKD	Navicular replacement	Aseptic non-union	New 3D-printed cage implanted		0	9
Nonunion of subtalar arthrodesis	Neuropathy, CMT, CVD	Subtalar Arthrodesis	Septic non-union	Cage removal and subsequent bone transport	Cutibacterium acnes	7	13
Ankle arthritis 2/2 open fracture-dislocation	Asthma (without steroid use)	Subtalar Arthrodesis	Aseptic non-union	Below knee amputation		2	22
Pilon fracture with fractured implants	CVD	TTC	Aseptic non-union	New 3D-printed cage implanted		2	22
OA, Open pilon fracture	HIV	Ankle fusion	Accessory hardware failure	Additional fixation placed		6	NA
TTC nonunion	Neuropathy	TTC	Accessory hardware failure	Accessory hardware exchange		1	NA
Talus AVN and collapse	Neuropathy, CVD	TTC	Accessory hardware failure	Accessory hardware exchange		1	NA

Table 3:

ORs of subsequent surgery and implant removal for perioperative variables calculated using a univariate or multivariate logistic regression model

Univariate Logistic Regression				
	Subsequent Surgery		**Implant Removal**	
Variable	**OR**	**p**	**OR**	**p**
Prior Limb Infection	**2.08**	**0.32**	**2.10**	**0.34**
Neuropathy	**4.25**	**0.05**	**2.13**	**0.31**
Gyroid Infill	**0.94**	**0.81**	**1.27**	**0.75**
Age	**0.99**	**0.52**	**0.99**	**0.53**
BMI	**0.98**	**0.63**	**1.01**	**0.88**
Male Gender	**1.87**	**0.37**	**2.87**	**0.18**
Tobacco Use	**1.17**	**0.82**	**0.93**	**0.93**
Multivariate Logistic Regression				
	Subsequent Surgery		**Implant Removal**	
Variable	**OR**	**p**	**OR**	**p**
Prior Infection	**2.56**	**0.26**	**2.08**	**0.38**
Neuropathy	**5.76**	**0.03**	**2.31**	**0.31**
Gyroid Infill	**1.20**	**0.83**	**1.48**	**0.67**
Age	**0.97**	**0.30**	**0.97**	**0.34**
BMI	**0.96**	**0.36**	**1.00**	**1.00**
Male Gender	**1.75**	**0.47**	**2.94**	**0.19**
Tobacco Use	**1.08**	**0.93**	**0.68**	**0.65**