Zimmer® Trabecular Metal™ Total Ankle Post- Market Clinical Follow-Up Study Annual Report 2019

Zimmer TM Ankle PMCF 3 yr Summary of Results:

- 92.5% of subjects satisfied at 3 years follow-up.
- Statistically significant improvement in AOFAS score and statistically significant reduced pain at 3 years follow-up.
- 97.33% implant survivorship at 3 years follow-up.

Introduction

The Trabecular Metal Total Ankle System is a treatment option for subjects that need replacement of the articulating surfaces of the ankle that have been affected by disease or injury and where ankle fusion/arthrodesis is an undesirable solution. The Trabecular Metal Ankle System is intended to be used for primary or revision cases.

The objective of the on-going Prospective Post Market Clinical Follow-Up Study of the Trabecular Metal Total Ankle System is to assess the safety and performance of the device when used in primary or revision total ankle replacement on a cohort of 120 subjects. The study objective will be met through assessment of outcome and survival data. Performance is assessed by analyzing the implant survival, overall pain and functional performances, subject health status, and radiographic parameters (radiolucencies, osteolysis, hypertrophy, subsidence, etc.). Safety is assessed by monitoring the frequency and incidence of adverse events (AEs), serious adverse events (SAEs), adverse device effects (ADEs) and serious adverse device effects (SADEs).

Between May 2014 and March 22, 2017, 121[1] subjects were enrolled in this study. Eleven investigational sites have enrolled subjects. Table 1 summarizes the ankles available for analysis, per investigator at each follow-up interval for the current interim analysis.

Table 1: Follow-up Summary

Country	Inv. ID	Pre -Op	6 Wk	6 Mo	1 Yr	2 Yr	3 Yr
US	3810	6	6	6	6	6	4
Italy	6286	26	26	26	25	16	13
US	3559	14	14	14	14	14	11
US	3786	1	1	1	1	1	1
US	3800	5	5	5	4	3	3
Finland	6293	18	18	18	18	17	5
Canada	3827	26	26	25	25	22	12
US	3554	7	7	7	7	2	-
Switzerland	6287	10	10	10	9	4	-
Germany	6326	6	6	6	5	3	-
Switzerland	6324	2	2	2	2	1	-
Total		**121**	**121**	**120**	**116**	**89**	**49**

Materials/Methods

Consecutive subjects qualifying for primary or revision unilateral or bilateral total ankle arthroplasty based on physical exam and medical history were enrolled in the study. All subjects received the Trabecular Metal Ankle System device (Zimmer, Inc., Warsaw, IN). The system consists of three implant components: a talar component, a tibial base component, and a modular tibial articular surface. The implants are available in six different sizes to accommodate variations in subject anatomies. All enrolled study subjects have undergone preoperative clinical and radiographic evaluation and total ankle arthroplasty. Additionally, all subjects have or will undergo post-operative clinical, functional and radiographic evaluations at 6 weeks, 6 months, 1 year, 2 years, 3 years, 5 years, 7 years, and 10 years. These evaluations include the EuroQol five dimensions questionnaire (EQ-5D), General Ankle Exam, Ankle Osteoarthritis Scale (AOS), and the American Orthopedic Foot and Ankle Score (AOFAS). Follow-up surveys are gathered at 4 years, 6 years, 8 years and 9 years after surgery in order to reduce the potential for loss to follow-up and to collect Adverse Event (AE) data which may occur. Institutional Review Board (IRB)/Ethic Committee (EC) approval was obtained at each clinical site prior to starting enrollment of subjects in the study. The statistical analysis was performed using SAS 9.2. Statistical significance was tested by the Wilcoxon Signed Rank Test26 and set at $p \leq 0.05$.

Subject Demographics

Sixty-one (50.4%) of the 121 subjects enrolled in the study were female, while 60 (49.6%) of the subjects were male. The top three indications for surgery were rheumatoid arthritis (15 cases, 12.4%), post-traumatic arthritis (68, 56.2%), and degenerative arthritis (38, 31.4%). Out of the 121 subjects, 83 had a prior operative procedure. Of the 83 cases, 65 cases (85.5%) had a prior procedure on the operative ankle with 18 cases having previously undergone a contralateral operation (23.7%). The average age at the date of consent was 60.0 (range 18 to 82 years).

Surgical Information

Complete surgical procedure details were available for all 121 cases. Of the 121 cases, an additional medial incision was used on 26 cases (21.5%), whereas 95 cases (78.5%) did not use an additional medial incision for the surgical approach. Sixty (49.6%) of the cases used cement tibial fixation, while 62 (51.2%) of the cases used press-fit talar fixation. Fifty-nine (48.8%) of the cases used cement talar fixation, while 61(50.4%) of the cases used press-fit tibial fixation. To note, press-fit fixation is not cleared for use in the United States and can only be used at sites outside the United States. All subjects enrolled in the United States received cemented fixation.

Eighty-five cases (70.2%) had normal tibial bone quality, 26 cases (21.5%) had sclerotic tibial bone quality, 7 cases

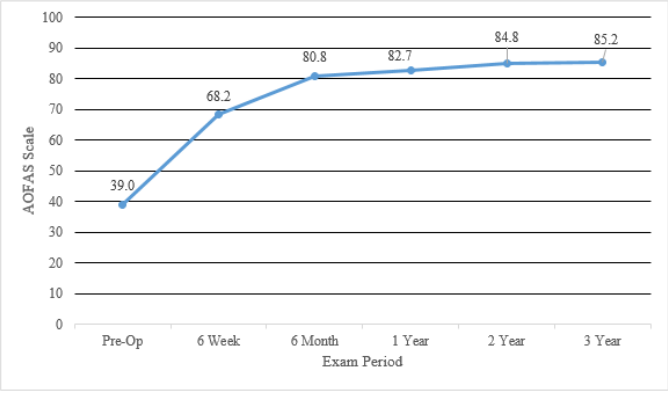
(5.8%) had osteoporotic tibial bone quality, 2 cases (1.7%) had necrotic tibial bone quality, and 1 case (0.8%) had focal avascular necrosis (AVN) tibial bone quality. Seventy-eight cases (64.5%) had normal talus bone quality, 31 cases (25.6%) had sclerotic talus bone quality, 9 cases (7.4%) had osteoporotic talus bone quality, 2 cases had necrotic tibial bone quality, and 1 case (0.8%) had focal AVN talus bone quality. The Trabecular Metal Total Ankle System is contraindicated for severe osteoporosis and severe vascular disease affecting the extremity, however, the operating surgeon has discretion to evaluate the severity and eligibility of each patient. Three cases reported intraoperative complications (2.5%): partial tear of peroneal tendon, partial cut on tibialis, and fracture next to screw with forefront realignment procedure. The average procedure lasted 161.1 minutes and the average hospital stay was 4.1 days.

Results

As of April 2019, 121 subjects have reached 6-week follow-up, 120 subjects have reached the 6-month follow-up interval, 116 have reached the 1-year follow-up interval, 89 have reached the 2-year interval, and 49 have reached the 3-year follow-up interval.

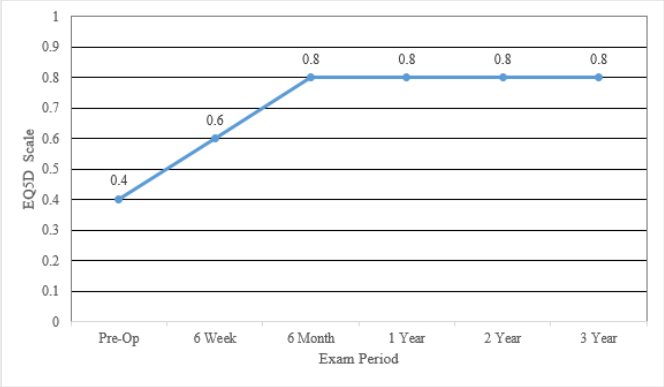
The American Orthopedic Foot and Ankle Score (AOFAS) is a clinician-based score that measures outcomes for four different anatomic regions of the foot: The ankle-hindfoot, midfoot, metatarsophalangeal (MTP)-interphalangeal (IP) for the hallux, and MTP-IP for the lesser toes. The questionnaire consists of nine items that are distributed over three categories: pain (40 points), function (50 points), and alignment (10 points) for a maximum score of 100 points and a minimum score of 0. The average total AOFAS score was 85.2 at 3 years, 84.8 at 2 years, 82.7 at 1 year, 80.8 at 6 months, and 68.2 at 6 weeks, with the baseline pre-operative average at 39.0.

Figure 1: Average Total AOFAS Score of Operative Ankle



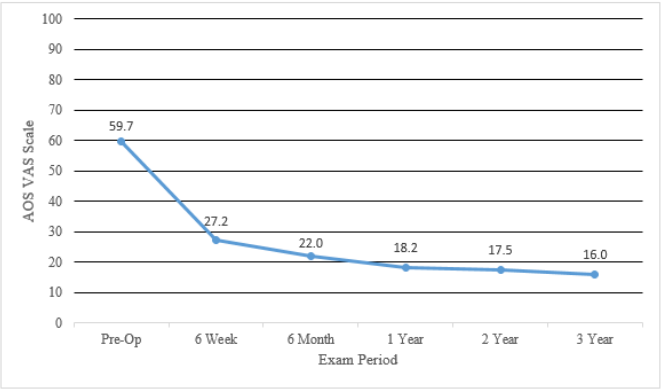
The EuroQol five dimensions questionnaire (EQ-5D) is a five dimensional self-assessment that is comprised of mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. These five dimensions can be used to index a subject's health utility on a scale of 0 to 1, where 0 is death and 1 is perfect health. The scoring rule for EQ-5D permits scores less than 0, implying that some health states may be worse than death. The average total EQ-5D scale was 0.8 at 3 year, 0.8 at 2 year, 0.8 at 1 year, 0.8 at 6 months, and 0.6 at 6 weeks, with the baseline pre-operative average at 0.4.

Figure 2: Average Total EQ5D Score of Operative Ankle



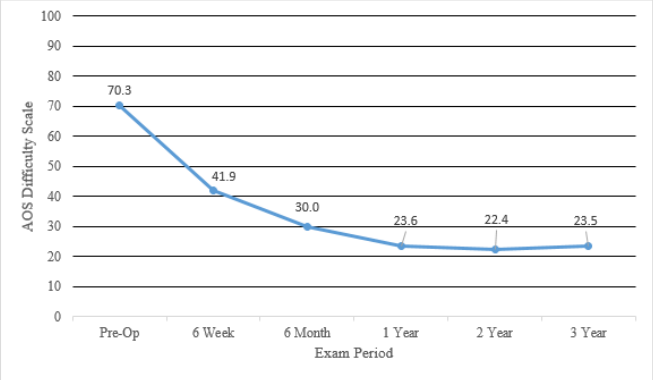
The maximum Ankle Osteoarthritis Scale (AOS) VAS pain score is 100 (most painful), while the minimum score is 0 (no pain). The average VAS pain score was 16.0 at 3 years, 17.5 at 2 years, 18.2 at 1 year, 22.0 at 6 months, and 27.2 at 6 weeks, from 59.7 pre-operatively.

Figure 3: Average AOS VAS Pain Score of Operative Ankle



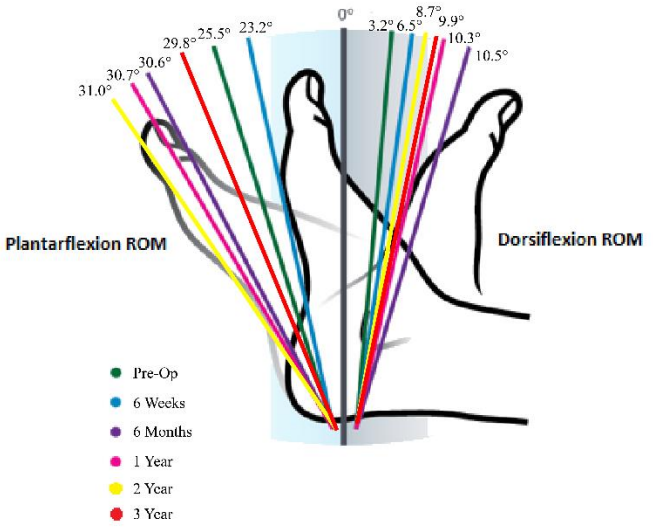
The maximum AOS Difficulty Scale score is 100 (very difficult), the minimum score is 0 (not difficult). The average difficulty score was 23.5 at 3 years, 22.4 at 2 years, 23.6 at 1 year, 30.0 at 6 months, and 41.9 at 6 weeks, compared to 70.3 pre- operatively.

Figure 4: Average AOS Difficulty Pain Score of Operative Ankle



The average plantar flexion range of motion of the operative ankle was measured at 29.8º at 3 years, 31.0º at 2 years, 30.7º at 1 year, 30.6º at 6 months and 23.2 º at 6 weeks, with an average plantar flexion range of motion of 25.5º pre-operatively. The average dorsiflexion range of motion of the operative ankle was measured at 9.9^0 at 3 years, 8.7º at 2 years, 10.3º at 1 year, 10.5º at 6 months, and 6.5º at 6 weeks, with and average dorsiflexion range of motion of 3.2º pre-operatively.

Figure 5: Average Range of Motion of Operative Ankle



Note: Diagram not to scale

Based on radiographic data, there has been 3 instances (2 at 1 year visit and 1 at the 2 year visit) of tibial component subsidence/migration and 2 cases of talar component subsidence/migration; one being at the 2 year mark and the other at 3 years. At the 3 year visit, 10 subjects showed abnormal radiographic readings (4 radiolucency's, 1 osteolysis, 3 heterotopic ossifications, 1 possible subtalar impingement, and 1 continued partial healing of fibula). At the 2 year visit, 14 subjects showed abnormal radiographic readings (2 osteolysis, 4 heterotopic ossification, 6 radiolucency's, 1 impingement between talus and medial malleolus, and 1 subsidence). At the 1 year visit, 10 subjects showed abnormal radiographic readings (3 heterotopic ossifications, 1 fibula non-union and 6 radiolucency's). At the 6 months visit, 8 subjects showed abnormal readings (delayed union of fibula, 2 heterotopic ossifications, broken syndesmotic screw, broken fibular screw, fractured screw, 3 radiolucency's and lateral subluxation of talus on tibia), and the 6 week visit showed 2 subjects with abnormal radiographic readings (fibula not healed and 1 radiolucency).

There have been 135 adverse events reported as of April 2019. Of the 135, 31 of the events reported were either related or potentially related to the device. These events are summarized in Table 2. Nine of the 135 events were recorded as an adverse device effect (ADE) or serious device effect (SADE).

Table 2: Device Related or Potentially Related Adverse Events

Case ID	Details of Event	Type of Event	Severity	Relation to Device	Outcome
355404	CONTINUED LATERAL PAIN CONSISTENT WITH NON-UNION OF FIBULA	AE	MODERATE	UNCERTAIN	PENDING
355905	MILD OSTEOLYSIS	AE	MILD	PROBABLY	PENDING
355907	MILD OSTEOLYSIS	AE	MILD	PROBABLY	PENDING
382703	DORSAL FOOT WOUND (TMT JOINT), DELAYED HEALING-ANKLE CLEAR	AE	MODERATE	UNCERTAIN	RESOLVED
382724	PAINFUL SCREW HEADS MEDIAL ANKLE	AE	MODERATE	UNCERTAIN	REOPERATION
628702	DEEP INFECTION LATERAL MALLEOLUS	SAE	MILD	UNCERTAIN	RESOLVED
629304	WOUND DEHISCENCE	SADE	SEVERE	DEFINITELY	REOPERATION
355901	TALONAVICULAR OA	AE	MODERATE	UNCERTAIN	RESOLVED
380003	HETEROTOPIC OSSIFICATION POSTERIOR ANKLE LIMITS ROM IMPINGEMENT SYMPTOMS	AE	MODERATE	PROBABLY	RESOLVED
380004	HETEROTOPIC OSSIFICATION ANTERIOR TO ANKLE	AE	MODERATE	PROBABLY	PENDING
380005	BROKEN SYNESMOTIC SCREW SEEN ON RADIOGRAPH. THERE IS NO DISPLACEMENT, WIDENING OR MA POSITIONING SEEN	AE	MILD	UNCERTAIN	TOLERATED
382701	HETEROTOPIC OSSIFICATION	AE	MILD	UNCERTAIN	TOLERATED
382710	PARTIAL TEAR OF PERONEAL TENDONS (INTRAOPERATIVE)	AE	MILD	PROBABLY	RESOLVED
382717	PARTIAL CUT ON TIBIALIS POSTERIOR TENDON DURING INDEX SURGERY	ADE	MILD	PROBABLY	RESOLVED
628603	LATERAL AND MEDIAL SURGICAL WOUND DEHISCENCE	ADE	MILD	UNCERTAIN	RESOLVED
629307	AT 4 WEEKS CONTROL WOUND OPEN, PLATE VISIBLE	SADE	MODERATE	DEFINITELY	REOPERATION
629315	INFECTION OF THE LATERAL PLATE	SADE	SEVERE	PROBABLY	TOLERATED
328704	DELAYED WOUND HEALING + NECROSIS T.P. OF LATERAL WOUND	AE	MODERATE	PROBABLY	RESOLVED
629308	AT 6 WEEKS CONTROL WHEN PLASTIC CAST REMOVED WOUND OPEN AND PLATE VISIBLE	SADE	MODERATE	DEFINITELY	REOPERATION
380004	2.0MM SUBSIDENSE OF TALAR COMPONENT	AE	MILD	DEFINITELY	RESOLVED
380004	OSTEOLYSIS OVER SUPERIOR LATERAL HALF OF TIBIAL COMPONENT	AE	MILD	DEFINITELY	RESOLVED
380005	5.0MM TALAR COMPONENT SUBSIDENSE	AE	MILD	UNCERTAIN	PENDING
380005	MECHANICAL SIGN OF CLICKING	AE	MILD	PROBABLY	PENDING
382702	MEDIAL IMPINGEMENT + PAIN POST TOTAL ANKLE	SAE	SEVERE	UNCERTAIN	RESOLVED
382706	MEDIAL ANKLE PAIN; IMPINGEMENT	SAE	SEVERE	UNCERTAIN	RESOLVED
382714	INCREASED NUMBNESS PLANTAR FOOT SECONDARY TO NERVE COMPRESSION	SAE	SEVERE	UNCERTAIN	RESOLVED
382722	RECURRENT + RAPID BONE FORMATION FRONT OF ANKLE	SAE	MODERATE	UNCERTAIN	REOPERATION
382722	ANKLE PAIN MEDIAL SIDE IMPINGEMENT	SAE	SEVERE	UNCERTAIN	RESOLVED
629308	VALGUS MALALIGNMENT, REVISION	SADE	MODERATE	DEFINITELY	DEVICE REMOVAL
629313	REARTHROPLASTY B/C OF VALGUS MALALIGNMENT	SADE	MODERATE	PROBABLY	REOPERATION
629315	INFECTION	SADE	SEVERE	PROBABLY	DEVICE REMOVAL

At 3 years following surgery, 92.5% of subjects were satisfied with their surgery, 2 years following surgery, 88.9% of subjects were satisfied with their surgery, 1 year following surgery, 90.6% of subjects were satisfied with their surgery, 90.0% were satisfied at 6 months, and 95.9% were satisfied at 6 weeks. Two subjects at the 3 year visit, three subjects at the 2 year visit, 5 subjects at the 1 year visit, 4 subjects at the 6 months visit, and 3 subjects at the 6 weeks visit stated that they felt the status of their ankle was worse compared to their previous visit.

Analysis

Using the average AOFAS Scale Score, average EQ5D score, average AOS VAS pain score, and average VAS difficulty score,

all showed statistically significant improvement at 6 week, 6 months, 1 year ,2 year, and 3 year follow-up intervals over the pre-operative baseline ($p<0.05$).

Table 3: Scoring Assessment Summary

	Preoperative	6 Weeks		6 Months		1 year		2 year		3 year	
Variable	Mean + SD [N] (Min, Med, Max)	Mean + SD [N] (Min, Med, Max)	P Value Compared to Preop	Mean + SD [N] (Min, Med, Max)	P Value Compared to Preop	Mean + SD [N] (Min, Med, Max)	P Value Compared to Preop	Mean + SD [N] (Min, Med, Max)	P Value Compared to Preop	Mean + SD [N] (Min, Med, Max)	P Value Compared to Preop
AOFAS Score	39.0 +/- 16.2 [121]	68.2 +/- 15.4 [119]		80.8 +/- 13.7 [119]		82.7 +/- 12.9 [113]		84.8 +/- 12.8 [91]		85.2 +/- 15.2 [53]	
	(0.0, 39.0, 75.0)	(36.0, 66.0, 100.0)	≤.0001	(44.0, 82.0, 100.0)	≤.0001	(47.0, 85.0, 100.0)	≤.0001	(47.0, 87.0, 100.0)	≤.0001	(32.0, 90.0, 100.0)	≤.0001
EQ5D Score	0.4 +/- 0.3 [121]	0.6 ± 0.3 [121]		0.8 +/- 0.2 [120]		0.8 +/- 0.2 [117]		0.8 +/- 0.2 [90]		0.8 +/- 0.3 [53]	
	(-0.3, 0.3, 0.9)	(-0.5, 0.7, 1.0)	≤.0001	(0.1, 0.7, 1.0)	≤.0001	(0.1, 0.8, 1.0)	≤.0001	(-0.2, 0.8, 1.0)	≤.0001	(-0.4, 0.8, 1.0)	≤.0001
AOS VAS Score	59.7 +/- 20.6 [119]	27.2 +/- 21.1 [60]		22.0 +/- 18.1 [120]		18.2 +/- 19.0 [117]		17.5 +/- 20.9 [90]		16.0 +/- 21.0 [51]	
	(1.0, 61.0, 99.0)	(0.0, 23.5, 100.0)	≤.0001	(0.0, 19.0, 80.0)	≤.0001	(0.0, 11.0, 79.0)	≤.0001	(0.0, 10.5, 93.0)	≤.0001	(0.0, 6.0, 87.0)	0.0001
AOS Difficulty Score	70.3 +/- 18.8 [119]	41.9 +/- 27.8 [75]		30.0 +/- 21.6 [120]		23.6 +/- 21.4 [117]		22.4 +/- 21.9 [90]		23.5 +/- 25.8 [51]	
	(15.0, 74.0, 100.0)	(3.0, 34.0, 97.0)	≤.0001	(0.0, 26.0, 84.0)	≤.0001	(0.0, 17.0, 84.0)	≤.0001	(0.0, 14.5, 87.0)	≤.0001	(0.0, 18.0, 93.0)	≤.0001

As of August 2019, the Kaplan-Meier survival estimate for the Trabecular Metal Ankle System when used in primary cases was 97.33% at 3 years.

Table 4: Kaplan-Meier Survivorship for TM Ankle PMCF

Outcome	N At Risk	N Revised (Cumulative)	Survival Estimate	95% Confidence Interval
1 Year	121	2	0.9832	0.9345, 0.9958
2 Year	114	3	0.97333	0.9191, 0.9913
3 Year	90	3	0.97333	0.9191, 0.9913

Conclusion

At 6 weeks, 6 months, 1 year, 2 year, and 3 year follow-up, the functional outcomes measured in this study of the Trabecular Metal Ankle System indicated that subject well-being significantly increased following total ankle arthroplasty using the Trabecular Metal Ankle implant. Pain measures, functional measures, and health status measures all exhibited statistically significant improvement maintained through the 3 year visit. Radiographic parameters also presented a low incidence of findings. Overall, treatment of irreparable ankle impairment using the Trabecular Metal Ankle System resulted in reliable functional and radiological outcome improvement at short-term follow-up in this series. Longer-term follow-up will be required to determine long-term survivorship and performance of the Trabecular Metal Ankle System.

[1] *Prospective Post Market Clinical Follow-Up Study of the Trabecular Metal Total Ankle System's protocol was based on 120 subjects, but 121 subjects were enrolled.*