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Original Research

Total Joint Arthroplasty Is a Viable Treatment Option for Patients With Osteonecrosis and Osteoarthritis After Bone Marrow Transplantation

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ABSTRACT

Background: Long-term survival in patients who receive bone marrow transplantation (BMT) is increasing. However, osteonecrosis and secondary osteoarthritis (OA) of the hip and knee are common complications in this population due to post-transplant steroid treatment to prevent graft vs host disease. The purpose of this study was to evaluate the outcomes of total joint arthroplasty (TJA) in patients with prior BMT and compare them to those of patients undergoing TJA for primary OA.

Methods: Patients with a history of BMT undergoing primary TJA from 2013 to 2021 were retrospectively reviewed. Patients were matched 1:1 by surgical site, sex, age, body mass index, American Society of Anesthesiologists score, and Elixhauser Comorbidity Index to patients undergoing TJA for primary OA. Demographics, intraoperative blood loss, perioperative transfusion requirements, hospital length of stay, 90-day emergency department visits and readmissions, all-cause revisions, and 2-year mortality were compared between cohorts.

Results: There were 17 patients undergoing total knee arthroplasty (TKA) after BMT (TKA-BMT) and 43 patients undergoing total hip arthroplasty (THA) after BMT (THA-BMT). More TKA-BMT and THA-BMT patients were immunosuppressed preoperatively compared to 17 matched TKA-OA and 43 THA-OA patients ($P = .018$ and $P < .001$). There were no other significant perioperative differences between BMT and OA groups. Two-year patient and implant survivorship for TKA-BMT and THA-BMT patients were high and not statistically different from TKA-OA and THA-OA cohorts.

Conclusions: TJA after BMT provides satisfactory perioperative and short-term outcomes and is a viable treatment option for patients with osteonecrosis and secondary OA after BMT treatment.

Introduction

In patients with hematopoietic malignancies, bone marrow transplantation (BMT) is a well-established treatment to increase survivorship [1]. From 2016-2020, over 22,000 patients underwent BMT treatment annually in the U.S., and with improving long-term outcomes following BMT, the number of BMT survivors is projected to surpass 500,000 by 2030 [2,3]. However, these patients are at risk of several post-transplantation complications with one of the most severe post-BMT skeletal complications being osteonecrosis. Osteonecrosis occurs in approximately 5%-19% of BMT patients secondary to radiation and high-dose steroid therapy for treatment of graft vs host disease post-BMT [4-10].

Osteonecrosis most commonly affects bones making up the hip and knee joints and can lead to the early development of end-stage arthritis [11]. Notably, the native femoral head has been found to have poor 5-year survivorship after diagnosis of post-BMT osteonecrosis [12,13]. Total joint arthroplasty (TJA) for the hip and knee is a safe and effective procedure with excellent results, reliably improving quality of life in patients with osteoarthritis (OA) [14,15]. However, similar predictable outcomes may be less likely in BMT patients, as poor bone quality from osteonecrosis and immunosuppressed states can increase their risk of medical and surgical complications after TJA [16,17]. Few studies have reported outcomes on total hip arthroplasty (THA) and total knee arthroplasty (TKA) indicated for patients with osteonecrosis and secondary OA after BMT. Current literature regarding THA and TKA outcomes in

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this subset population varies in regards to complication rates, implant survivorship, and patient survivorship [18-23]. Thus, the purpose of this study was twofold: 1) to report TKA and THA outcomes in patients with a history of BMT, and 2) to compare these outcomes to those of patients who undergo TKA and THA for primary OA. We hypothesize that despite the theoretical risks mentioned, BMT patients have similar TJA outcomes compared to primary OA patients.

Material and methods

Institutional review board approval was obtained prior to initiation of the study. An institutional database at a tertiary referral center was retrospectively reviewed from January 1, 2013, to December 31, 2021, to identify patients undergoing primary THA or TKA for degenerative joint disease, a history of prior BMT, and minimum 2-year postoperative follow-up. Revision, conversion, unicompartmental, and fracture-related arthroplasty procedures were excluded. All surgeries were performed by high-volume fellowship-trained orthopaedic arthroplasty surgeons of the adult reconstruction division at the institution.

Demographic data were collected consisting of patient age at time of TJA, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) score, modified van Walraven Elixhauser Comorbidity Index (ECI), BMT indication, and time from BMT to TJA [24]. Perioperative data was collected on immunosuppression status (ie, being prescribed an immunosuppressive agent) in the month immediately before and after surgery, operating room (OR) time, perioperative blood loss and transfusion requirements, whether a medical or transplant team was consulted, hospital length of stay (LOS), discharge disposition, 90-day emergency department (ED) visits and readmissions, all-cause revisions at 2 years, and 2-year mortality. Patients undergoing TKA or THA after BMT were matched by surgical site (hip or knee), gender, age, BMI, ASA, and ECI to cohorts of patients undergoing TKA or THA for primary OA. Continuous variables were analyzed by Mann-Whitney test and are presented as medians (lower quartile, upper quartile). Categorical variables were analyzed by chi-square or Fisher exact test and are presented as count (percent). Statistical analysis was conducted with RStudio version 4.2.2 (Posit Software, Boston, MA). A *P*-value of $< .05$ indicates statistical significance.

Results

Demographics for TKA

In total, there were 17 TKAs performed in 12 patients with a history of BMT. Patients who underwent TKA after BMT (TKA-BMT) had a median age of 65 years (51, 69) at the time of surgery. There were 7 (41.2%) women. All patients received BMT for hematopoietic cancer or disease except 1 patient who received it as treatment for other oncologic disease. Median time from BMT to TKA was 3.8 years (2.1, 14.4). Median BMI was 29.3 (27.5, 33), and 11 (64.7%) patients had an ASA score >2. Median ECI was 0 (−1, 10). There were 6 (35.3%) patients taking immunosuppressive therapy within a month of TKA.

In comparison, a 1:1 matched cohort of 17 TKAs in patients with primary OA (TKA-OA) had a median age of 67 years (60, 68) ($P = .653$) at the time of surgery. Median BMI was 29.2 (29, 34.3) ($P = .480$), and 12 (70.6%) patients had an ASA score >2 ($P = .714$). Median ECI was 8 (−1, 12) ($P = .653$). No patients were taking immunosuppressive therapy within a month of TKA ($P = .018$). Demographics of TKA-BMT and TKA-OA patients are shown in Table 1.

Demographics for THA

In total, there were 43 THAs performed in 36 patients with a history of BMT. Patients who underwent THA after BMT (THA-BMT) had a median age of 47 years (28, 61) at the time of surgery. There were 27 (62.8%) women. All patients received BMT for hematopoietic cancer or disease except 2 patients who received it as treatment for other oncologic disease. Median time from BMT to THA was 3.6 years (2.1, 7.7). Median BMI was 24.7 (22.8, 27.8), and 28 (65.1%) patients had an ASA score >2. Median ECI was 5 (0, 15).

Table 1
Demographics and perioperative outcomes for TKA-BMT and TKA-OA groups.

Variable	TKA-BMT (n = 17)	TKA-OA (n = 17)	*P*-value
Age (y)	65 (51, 69)	67 (60, 68)	.653
Women	7 (41.2)	7 (41.2)	1
Time BMT-TJA (y)	3.8 (2.1, 14.4)		
BMI	29.3 (27.5, 33)	29.2 (29, 34.3)	.480
ASA >2	11 (64.7)	12 (70.6)	.714
Elixhauser	0 (−1, 10)	8 (−1, 12)	.653
Immunosuppression	6 (35.3)	0 (0)	.018
OR time (min)	93 (84, 100)	91 (77, 97)	.480
Cemented implants	15 (88.2)	17 (100)	.495
Liner type			.464
Cruciate − Retaining	10 (58.8)	13 (76.5)	
Cruciate − Sacrificing	6 (35.3)	4 (23.5)	
Hinged	1 (5.9)	0 (0)	
Total blood volume loss (mL)	100 (50, 150)	100 (50, 150)	.727
Intraoperative transfusion	1 (5.9)	0 (0)	.317
Postoperative transfusion	2 (11.8)	0 (0)	.157
LOS (h)	51 (31, 56)	34 (32, 49)	.850
SNF/rehab disposition	0 (0)	3 (17.6)	.227
90-d ED	3 (17.6)	0 (0)	.227
90-d readmission	3 (17.6)	0 (0)	.227
1-y revision	0 (0)	0 (0)	1
Medical/transplant consultation	2 (11.8)	3 (17.6)	.655
2-y patient mortality	2 (11.8)	0 (0)	.485

Data as median (lower quartile, upper quartile) or count (percent) with Mann-Whitney and chi-square or Fisher exact test as appropriate.
P-value <.05 indicates statistical significance.

There were 14 (32.6%) patients taking immunosuppressive therapy within a month of THA.

In comparison, a 1:1 matched cohort of 43 THAs in patients with primary OA (THA-OA) had a median age of 57 years (47.5, 60.5) (P = .055) at the time of surgery. Median BMI was 25.9 (23.5, 28.9) (P = .346), and 19 (44.2%) patients were ASA score >2 (P = .083). Median ECI was 0 (0, 8.5) (P = .109). No patients were taking immunosuppressive therapy within a month of THA (P < .001). Demographics of THA-BMT and THA-OA patients are shown in Table 2.

Perioperative outcomes for TKA

Perioperative outcomes were not statistically different between TKA-BMT and TKA-OA patients (Table 1). Median OR time for TKA-BMT was 93 minutes (84, 100) compared to 91 minutes (77, 97) for TKA-OA (P = .480). Cemented implants were used in 15 (88.2%) TKA-BMT cases compared to 17 (100%) TKA-OA cases (P = .495). For TKA-BMT, 10 (58.8%) liners were cruciate-retaining, 6 were cruciate sacrificing, and 1 was hinged. This was not statistically different (P = .464) from TKA-OA, of which 13 (76.5%) were cruciate-retaining and 4 (23.5%) were cruciate sacrificing. No TKA-BMT or TKA-OA patients had intraoperative complications. Median operative blood loss was 100 mL (50, 150) for both TKA-BMT and TKA-OA (P = .727). No TKA-OA patients required an intraoperative or postoperative blood transfusion. There was 1 (5.9%) TKA-BMT patient who required intraoperative blood transfusion (P = .317), and 2 (11.8%) required postoperative transfusion (P = .157). A medical or transplant team was consulted for 2 (11.8%) TKA-BMT and 3 (17.6%) TKA-OA patients (P = .655). Median hospital LOS was 51 hours (31, 56) for TKA-BMT and 34 (32, 49) for TKA-OA (P = .850). No TKA-BMT patients were discharged to either a skilled nursing facility (SNF) or rehabilitation facility. There were 3 (17.6%) TKA-OA patients who were discharged to either a SNF or rehabilitation facility (P = .227). In the first 90 days postoperatively, no TKA-OA patients had ED visits or readmissions. There were 3 (17.6%) TKA-BMT patients who presented to the ED (P = .227) and 3 (17.6%) who were readmitted (P = .227) in the first 90 days postoperatively. Reasons for all ED presentations and admissions are shown in Table 3.

Table 2
Demographics and perioperative outcomes for THA-BMT and THA-OA groups.

Variable	THA-BMT (n = 43)	THA-OA (n = 43)	*P*-value
Age (y)	47 (28, 61)	57 (47.5, 60.5)	.055
Women	27 (62.8)	27 (62.8)	1
Time BMT-TJA (y)	3.6 (2.1, 7.7)		
BMI	24.7 (22.8, 27.8)	25.9 (23.5, 28.9)	.346
ASA >2	28 (65.1)	19 (44.2)	.083
Elixhauser	5 (0, 15)	0 (0, 8.5)	.109
Immunosuppression	14 (32.6)	0 (0)	<.001
OR time (minutes)	102 (88.5, 127)	95 (81, 106.5)	.153
Cemented implants	2 (4.7)	0 (0)	.494
Total blood volume loss (mL)	250 (200, 325)	200 (225, 300)	.196
Intraoperative transfusion	2 (4.7)	1 (2.3)	.564
Postoperative transfusion	6 (14.0)	1 (2.3)	.110
LOS (hours)	52 (32, 59)	36 (31.5, 56)	.394
SNF/rehab disposition	3 (7.0)	3 (7.0)	1
90-d ED	6 (14.0)	7 (16.3)	.763
90-d readmission	10 (23.3)	4 (9.3)	.144
1-y revision	2 (4.7)	1 (2.3)	.557
Medical/transplant consultation	22 (51.2)	14 (32.6)	.126
2-y patient mortality	4 (9.3)	0 (0)	.116

Data as median (lower quartile, upper quartile) or count (percent) with Mann-Whitney and chi-square or Fisher exact test as appropriate.
P-value <.05 indicates statistical significance.

Table 3
Emergency department visit and readmission causes and outcomes for bone marrow transplant patients after total joint arthroplasty.

Procedure	Reason for presentation	Course/Outcome
TKA (N = 14)	Cough	Discharged from ED
	Pulmonary embolism	Admitted from ED
	Cataract surgery	Direct admission
	Cataract surgery	Direct admission
	Thrombocytopenia	Discharged from ED
	Thrombocytopenia	Discharged from ED
	Osteosarcoma	Direct admission
	Osteosarcoma	Direct admission
	Osteosarcoma	Direct admission
	Osteosarcoma	Direct admission
	Osteosarcoma	Direct admission
	Osteosarcoma	Direct admission
	Osteosarcoma	Direct admission
	Osteosarcoma	Direct admission
THA (N = 20)	Contralateral THA	Direct admission
	I&D hip	Direct admission
	Hip dislocation	Discharged from ED
	PJI	Direct admission
	PJI	Direct admission
	PJI	Direct admission
	PJI	Direct admission
	PJI	Direct admission
	Total shoulder arthroplasty	Direct admission
	Total shoulder arthroplasty	Direct admission
	EGD	Direct admission
	EGD	Direct admission
	Abdominal pain	Admitted from ED
	Mediastinal lymphadenopathy	Direct admission
	GVHD	Direct admission
	Mouse bite	Discharged from ED
	SOB	Discharged from ED
	SOB	Admitted from ED
	Dysphagia	Direct admission
	Suprapubic pain	Admitted from ED

SOB, shortness of breath; EGD, esophagogastroduodenoscopy; I&D, incision and drainage; GVHD, graft vs host disease.

Perioperative outcomes for THA

There were no significant differences in perioperative outcomes between THA-BMT and THA-OA patients (Table 2). Median OR time for THA-BMT was 102 minutes (88.5, 127) compared to 95 minutes (81, 106.5) for THA-OA (P = .153). Cemented implants were used in 2 (4.7%) THA-BMT cases compared to 0 THA-OA cases (P = .494). There was 1 (2.3%) THA-BMT patient who sustained an intraoperative fracture. No THA-OA patients had intraoperative complications. Median operative blood loss was 250 mL (200, 325) for THA-BMT and 200 mL (225, 300) for THA-OA (P = .196). There were 2 (4.7%) THA-BMT patients who required intraoperative blood transfusion compared to 1 (2.3%) THA-OA patient (P = .564). There were 6 (14%) THA-BMT patients who required postoperative blood transfusion compared to 1 (2.3%) THA-OA patient (P = .110). A medical or transplant team was consulted for 22 (51.2%) THA-BMT and 14 (32.6%) THA-OA patients (P = .126). Median hospital LOS was 52 hours (32, 59) for THA-BMT and 36 (31.5, 56) for THA-OA (P = .394). Both THA-BMT and THA-OA groups had 3 (7.0%) patients who

Table 4
Causes of death of BMT-TJA patients.

Procedure	Cause of death	N	Implant failure at time of death
TKA	Heart failure	1	N
	Unknown	2	N
THA	Liver failure	1	N
	Pneumonia	1	N
	Unknown	3	N

were discharged to either a SNF or rehabilitation facility. There were 6 (14%) THA-BMT patients who presented to the ED and 10 (23.3%) who were readmitted in the first 90 days postoperatively. In comparison, THA-OA patients had 7 (16.3%) ED visits ($P = .763$) and 4 (9.3%) readmissions ($P = .144$) in the first 90 days postoperatively. Reasons for all ED presentations and admissions are shown in Table 3.

Patient and implant survivorship in TKA

Median postoperative follow-up was 57 months (46, 75) for TKA-BMT and 54 months (47, 78) for TKA-OA. At a minimum 2-year follow-up, 2 TKA-BMT patients had died from unknown causes compared to 0 TKA-OA deaths ($P = .485$). At the most recent follow-up, 1 additional TKA-BMT patient had died from heart failure (Table 4). One TKA-OA patient died of an unknown cause 5 years after surgery. Implant survivorship, which was defined by no return to the OR for any prosthetic joint concern, was 100% for both TKA-BMT and TKA-OA patients at 1-year, 2-year, and most recent follow-up timepoints. Patient and implant survivorship at 2 years for TKA-BMT and TKA-OA patients are shown in Figure 1a.

Patient and implant survivorship in THA

Median postoperative follow-up was 64 months (53.5, 91) for THA-BMT and 67 months (57, 92.5) for THA-OA patients. At a minimum 2-year follow-up, 4 THA-BMT patients had died, 2 from unknown causes, 1 from liver failure, and 1 from pneumonia, compared to 0 THA-OA deaths ($P = .116$). At the most recent follow-up, 1 additional THA-BMT patient had died from an unknown cause (Table 4). There were 0 THA-OA deaths at the most recent follow-up. Two THA-BMT patients required revision surgery in the first postoperative year, both for periprosthetic join infection (PJI) concern. An additional THA-BMT patient experienced a hip dislocation, for which a closed reduction under sedation was performed in the ED. One (2.3%) THA-OA patient required surgical revision in the first postoperative year for PJI ($P = .557$). At the most recent follow-up, no additional revisions were reported in either group. Implant survivorship was 95.3% for THA-BMT and 97.7% for THA-OA patients at 1-year, 2-year, and most recent follow-up timepoints. Patient and implant survivorship at 2 years for THA-BMT and THA-OA patients are shown in Figure 1b.

Discussion

As survival of hematopoietic disease continues to increase following BMT, more patients will likely require TJA for osteonecrosis and secondary OA of the hip and knee. A study by Niinimaki et al. (2016) found patients with hematopoietic disease, especially those younger than 50 years of age, are already at increased risk of requiring TJA [25]. High-dose steroid and radiation therapies to suppress graft vs host disease following BMT further increases the risk of osteonecrosis and the necessity for TJA. Osteonecrosis most commonly affects the hip, and the presented data suggest this to be true, as there were more THA than TKA after BMT at our institution. This study demonstrates that BMT patients receive TJA at potentially younger ages, especially as the average age of our THA-BMT patients, 47 years, is well below the national average of primary THA patients, 66 years [26]. As chronic immunosuppression following BMT also increases the risk of surgical wound infection and PJI, orthopaedic surgeons should proceed with caution when performing TJA in patients with a history of BMT [16,17]. This study contributes to the body of knowledge on outcomes for patients receiving TJA for osteonecrosis following BMT.

Perioperative outcomes did not differ between TKA-BMT and TKA-OA groups, and prosthetic joint implant selection was also comparable between the 2 groups. Interestingly, 2 TKA-BMT patients received cementless implants. This was decided by the surgeon based on intraoperative evaluation of patient bone stock, and a recent study by Sultan et al. (2018) has also demonstrated excellent 3-year outcomes and survivorship uncemented TKA in patients with knee osteonecrosis [27]. Two-year TKA-BMT patient survivorship in our study was 88%, similar to the 91% reported by Chalmers et al. (2017) on a cohort of 15 TKA in 11 patients [19]. However, they reported higher complication rates from poor wound healing and worse implant survivorship compared to historical controls, whereas TKA-BMT patients in our study were comparable to TKA-OA patients in these regards. Unfortunately, additional research on TKA in patients with prior BMT is scarce.

Perioperative outcomes did not differ between THA-BMT patients and a cohort of THA-OA patients matched by age, sex, BMI, ASA, and ECI. However, our THA-BMT patients were nearly 20 years younger than the average age of primary THA-OA patients nationally, as reported by Patel et al. (2023) [26]. This younger age at the time of TJA was not seen in our TKA-BMT group. This perhaps suggests a different mechanism of disease progression affecting the hip and the knee in BMT patients and should be studied further.

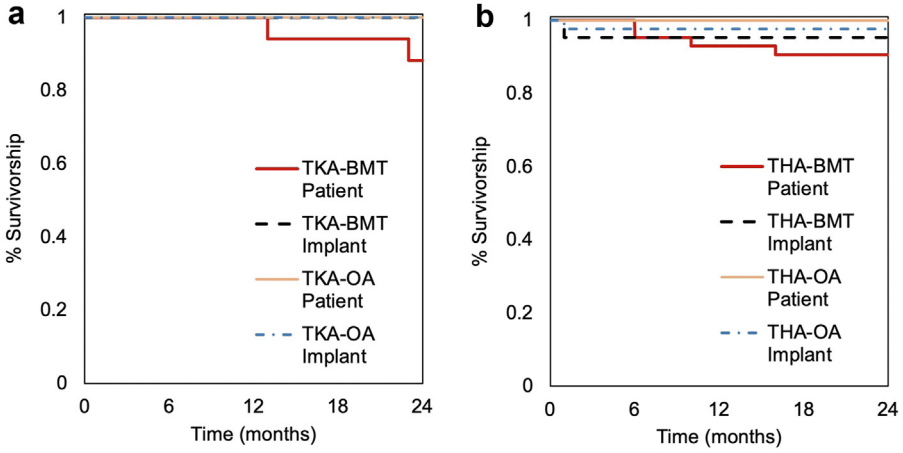

Figure 1. Patient and implant survivorship following TJA. (a) Patient and implant survivorship of TKA-BMT vs TKA-OA. (b) Patient and implant survivorship of THA-BMT vs THA-OA.

Additionally, there may be a lower clinical threshold for surgeons to perform THA in younger patients compared to TKA. BMT patients undergoing THA at younger ages also increases the risk of requiring revision surgeries in the long-term postoperative period, although this was not seen in our study. Our results agree with many findings in previous research on THA after BMT. Nearly all THA-BMT patients received press-fit prosthetic implants. The reported comparable outcomes support a Kim et al. (2021) finding that press-fit THA in BMT patients was not associated with higher risk or postoperative complications compared to patients with idiopathic osteonecrosis [21]. THA-BMT patients in our study had a 9% complication rate and a 5% revision rate, which is similar to previously reported rates of around 10% and 5%, respectively [20,21,23]. Two-year THA-BMT patient survivorship was 91%, matching a Chalmers et al. (2016) study on 42 THA in 36 patients [20].

Our study has several limitations. While we identified 60 patients who received TJA after BMT, few of these patients had confirmed osteonecrosis via magnetic resonance imaging. However, all patients had radiographic confirmation of severe degenerative joint disease, and we believe BMT-related osteonecrosis contributed to these patients' joint degeneration and secondary arthritis. Additionally, our findings that TJA is a viable treatment option for BMT patients can be useful for orthopaedic surgeons choosing patients in the community setting without access to magnetic resonance imaging. While several studies support TJA after BMT to significantly improve patient function and quality of life, our study did not investigate patient-reported outcomes and therefore cannot make conclusions regarding this [19,21-23]. Furthermore, TJA may not be suitable for all BMT patients. While this study demonstrates comparable postoperative outcomes between BMT and primary OA patients, we did not include BMT patients managed nonoperatively, nor did we investigate how BMT patients were evaluated and selected for surgical management with TJA. Additional research is needed to identify positive outcome predictors in BMT patients, which can inform patient selection for TJA. While our study cohorts were comparable in size to those of prior studies on TJA following BMT, the total patient count was still low and may not be sufficient to detect differences in perioperative outcomes, if they exist. This study analyzing outcomes at a single institution may not be generalizable, and additional research is needed with larger cohorts across multiple centers. Lastly, our analysis was limited to a 2-year follow-up period to maintain reasonable sample sizes. While we reported good outcomes 2 years after TJA, some other studies have demonstrated a significant decline in implant survivorship at 5 and 10 years postoperatively [17,20,21].

Conclusions

Patients at a single institution with a history of BMT who subsequently underwent elective THA or TKA demonstrated comparable perioperative and short-term outcomes compared to patients undergoing the same procedure for primary OA. There were no statistical differences in surgical complications, 90-day ED visits and readmissions, all-cause revisions, and patient mortality at 2-year follow-up. More long-term follow-up is needed to confirm these findings. This research supports previous studies suggesting TJA is a viable option in treating osteonecrosis of the hip and knee in patients with prior BMT, and it can be useful for surgeons evaluating patients with prior BMT considering TJA.

Conflicts of interest

S. Ryan is a paid consultant at Romtech. T. Seyler receives royalties from Restor3d and Pattern Health; is a paid consultant of Heraeus, Peptilogics, and Smith & Nephew; receives research support from Zimmer; receives financial/material support from Lippincott Williams & Wilkins; and is a board/committee member of AAHKS and MSIS. All other authors declare no potential conflicts of interest.

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Authors' contributions

All authors have seen and approved the final version of the manuscript being submitted, and all authors fulfill the Committee on Publication Ethics requirements for authorship.

CRediT authorship contribution statement

Jerry Chang: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Danielle S. Chun:** Writing – review & editing, Methodology, Investigation. **Christine J. Wu:** Writing – review & editing, Investigation, Conceptualization. **Niall H. Cochrane:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Billy I. Kim:** Writing – review & editing, Formal analysis, Data curation. **Sean P. Ryan:** Writing – review & editing, Investigation, Conceptualization. **Thorsten M. Seyler:** Writing – review & editing, Methodology, Investigation, Conceptualization.

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