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REVIEW

Bridging the osteoarthritis treatment gap with the KineSpring Knee Implant System: early evidence in 100 patients with 1-year minimum follow-up

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Abstract: Almost 4 million Americans are within the knee osteoarthritis (OA) treatment gap, the period from unsuccessful exhaustion of conservative treatment to major surgical intervention. New treatment alternatives for symptomatic knee OA are greatly needed. The purpose of this report was to assess outcomes of a joint-unloading implant (KineSpring® Knee Implant System) in patients with symptomatic medial knee OA. A total of 100 patients enrolled in three clinical trials were treated with the KineSpring System and followed for a minimum of 1 year. All devices were successfully implanted and activated, with no operative complications. Knee pain severity improved 60% ($P < 0.001$) at 1 year, with 76% of patients reporting a minimum 30% improvement in pain severity. All Western Ontario and McMaster Universities Arthritis Index (WOMAC) subscores significantly improved at 1 year, with a 56% improvement in pain, 57% improvement in function, and a 39% improvement in stiffness (all $P < 0.001$). The percentage of patients experiencing a minimum 20% improvement in WOMAC subscores was 74% for pain, 83% for function, and 67% for stiffness. During follow-up, six (6%) patients required additional surgery, including four total knee arthroplasties and two high tibial osteotomies. The KineSpring System effectively bridges the treatment gap between failed conservative care and surgical joint-modifying procedures.
Keywords: implant, KineSpring, knee, medial, osteoarthritis, unloading

Introduction

Osteoarthritis (OA) is an irreversible joint disease characterized by progressive articular cartilage loss, often resulting in crepitus, pain, and joint dysfunction.[1] OA affects 27 million adults in the US[2] alone, with approximately one in four reporting that OA symptoms require altering their living arrangements, necessitate special transportation accommodation, or influence their paid employment.[3] Older age[4] and obesity[5] are primary risk factors for the development of OA. Given the aging of the population and the increasing rates of obesity, the burden of OA is expected to increase dramatically and will remain a major medical problem for decades to come.[6]

Knee OA is the most prevalent form of the disease, representing the leading cause of disability in the adult population.[7–9] Despite the numerous treatments that are available for management of knee OA symptoms, no known therapy can significantly slow the progression of this disease.[10] Mild or moderate symptomatic knee OA is initially managed with conservative treatments, such as weight reduction, physical activity restriction, physical therapy, orthotics, and/or bracing.[11] Nonsteroidal anti-inflammatory and/or analgesic medications, intra-articular hyaluronic acid and/or corticosteroid

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injections, and arthroscopic lavage and debridement are often attempted for cases that are resistant to initial treatments. Unfortunately, the long-term effectiveness of conservative knee OA treatments is poor.[12–16]

As the disease progresses and knee pain and/or disability become more severe, the only widely available treatments are total or unicompartmental arthroplasty or high tibial osteotomy (HTO), all of which are bone- and joint-altering surgical interventions. The period from unsuccessful exhaustion of conservative treatment to major surgical intervention, referred to as the "treatment gap," represents a protracted period in which the patient endures debilitating pain, reduced quality of life, and a significant financial burden.[17] The duration of this period often spans decades, due to the lack of safe and effective treatments to bridge the gap from ineffective conservative care to invasive operative interventions, as well as the unwillingness of patients to undergo major and irreversible surgery. A great need clearly exists for improved knee OA treatments that address patients in this treatment gap.

Chronic excessive and/or abnormal joint-loading is a major modifiable risk factor in the development of knee OA.[18,19] The medial knee compartment endures over two-thirds of the loads across the knee joint,[20] which explains the higher prevalence of knee OA in the medial compartment compared to the patellofemoral and lateral compartments.[21] Joint unloading relieves OA symptoms and may even stimulate cartilage healing.[22,23] However, the utility of common joint-unloading therapies such as bracing and orthotics is limited by poor patient compliance. Characteristics of an ideal knee OA treatment for patients in the treatment gap include clinically significant improvement in knee pain and knee function, reduction in medial compartmental loading with no adverse load transfer to the lateral or patellofemoral compartments, high patient acceptance, low complication rates, and the ability to delay the need for more invasive surgery such as knee arthroplasty. With this concept in mind, a joint-sparing, extracapsular, medial compartment-unloading implant was developed. The purpose of this report is to summarize outcomes from three prospective human clinical trials that provide early evidence of the effectiveness and safety of this joint-unloading implant to bridge the treatment gap in patients with symptomatic medial knee OA.

Methods

Device description

The KineSpring® Knee Implant System (Moximed, Hayward, CA, USA) (Figure 1) is an implantable, joint-unloading prosthesis consisting of titanium alloy, low contact, femoral and tibial bases, and a cobalt chrome alloy absorber that reduces loading at the medial knee compartment during the stance phase of the gait cycle. The femoral and tibial bases are attached to the bone with compression and locking screws, and three undersurface standoffs allow bone contact at discrete locations, eliminating the need to elevate or remove the periosteum. The single-spring absorber is compressed by a piston during stance and offloads up to 30 lb from the medial knee compartment through 0°–30° knee extension without transferring forces to the lateral or patellofemoral compartments. Because the center of device rotation is offset from the knee center of rotation during surgery, the piston does not compress the spring during flexion >30°, and the device remains passive. The KineSpring System is implanted in the subcutaneous tissue on the medial aspect of the knee and does not involve resection of bone, muscle, or ligaments (Figures 2 and 3). The device accommodates normal knee motions, with the capability of 155° of flexion/extension, >60° internal/external rotation, and 50° of varus/valgus angulation.

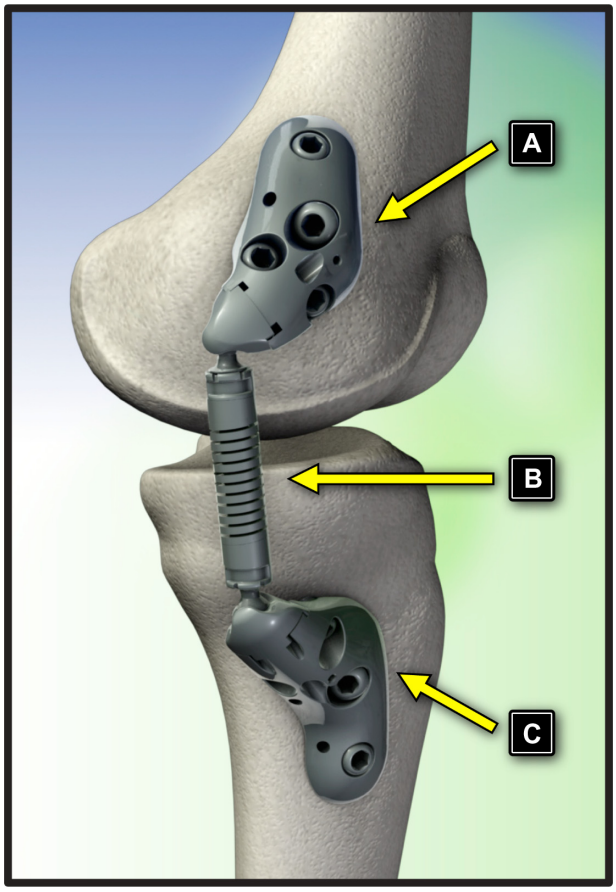

Figure 1 The KineSpring® Knee Implant System. Femoral base (**A**), absorber unit (**B**), and tibial base (**C**).

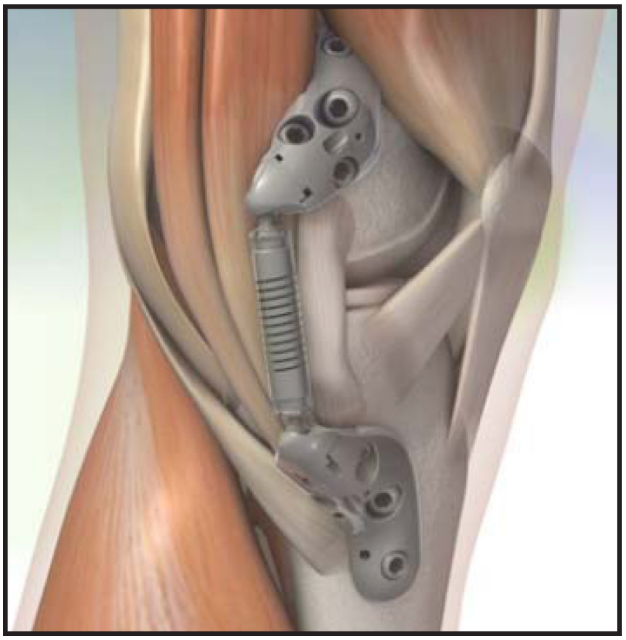

Figure 2 Schematic of the KineSpring Knee Implant System in relation to key anatomical structures. The KineSpring bases are implanted on the anteromedial aspects of the distal femur and proximal tibia. The absorber resides superficial to the medial collateral ligament, with no penetration of the joint capsule or bone resection required.

Preclinical testing

The KineSpring System has undergone extensive preclinical testing that demonstrated excellent mechanical durability, absence of pathologic soft tissue response to the implant, and physiologically relevant reductions in medial knee compartment loading.

The mechanical durability of the KineSpring System was determined in an in vitro study where five tibial and femoral bases were fixed to composite sawbones and the constructs oriented to simulate 0° knee flexion.[24] Cyclic fatigue testing was sinusoidally applied at 10 Hz between 6 and 60 lb per cycle for 10 million cycles, after which each construct was statically loaded to failure. All test constructs survived 10 million cycles of fatigue loading, with no evidence of implant damage or deformation. Static loading construct strength was 911 ± 47 lb. The failure mode was consistently due to fracture of the bone analog, with no damage to the KineSpring System.

Simulated-use testing of the KineSpring System consisted of 15 million flexion/extension movements between 0° and 68° ± 4° applied at 2 Hz, which replicates the in vivo

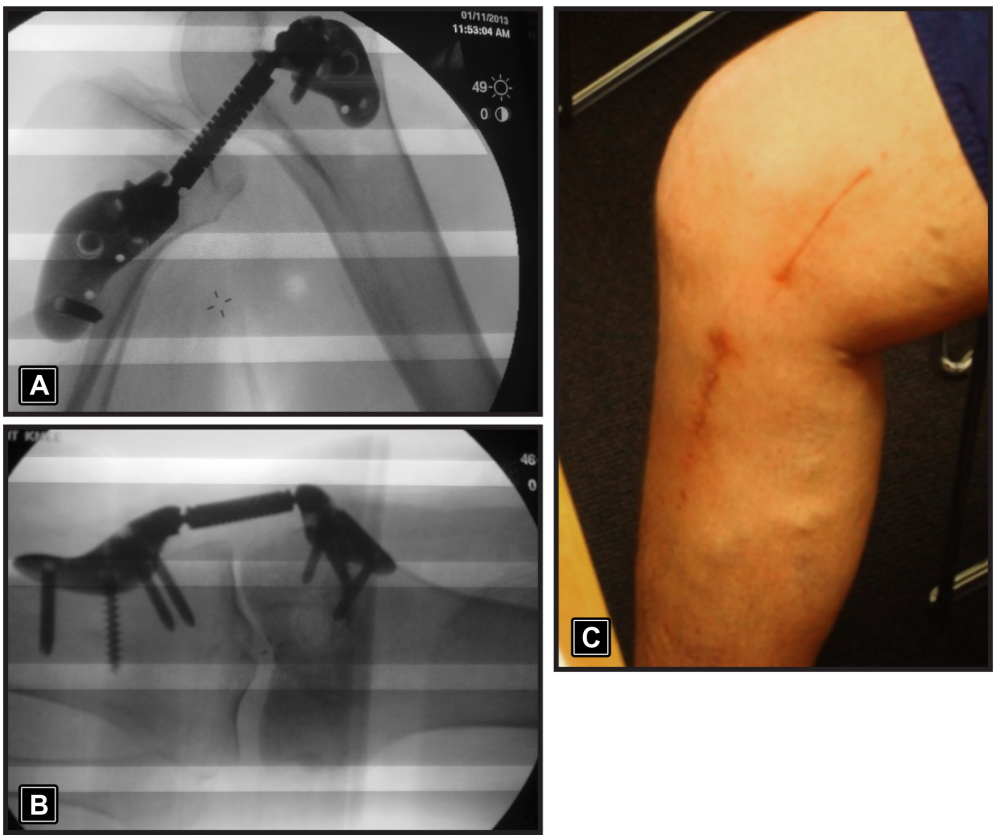

Figure 3 (**A**–**C**) Medial view of the KineSpring Knee Implant System. (**A**) Intraoperative fluoroscopy with knee flexed and absorber unit in a passive state; (**B**) intraoperative fluoroscopy with knee extended and absorber unit in a compressed state; (**C**) 6-week post-treatment "implant profile."

compression/relaxation cycle of the spring absorber when implanted. All test specimens survived 15 million cycles of simulated-use flexion/extension motion and loading, and no evidence of implant damage was noted.

Soft tissue response to the articulating subcutaneous implant was studied in a chronic ovine model.[25] Eleven sheep were implanted with a custom ovine-specific KineSpring System, and tissue response was characterized by gross and microscopic pathology at 4, 12, 26, and 52 weeks. Macroscopically, an acute inflammatory response was noted at 4 weeks, which resolved at subsequent time points. Skin incisions were completely healed by 26 weeks in all animals. Histological evidence at 4 weeks showed that the device was covered with a soft tissue membrane that was edematous, slightly inflamed, and had surface fibrin deposition. However, this inflammatory response resolved by 12 weeks. At 52 weeks, the histological results were characterized by the formation of a dense, mature fibrous tissue layer around the implant.

A gait simulation study was performed on six cadaver knees tested in each of two configurations: (1) without the implant (untreated) and (2) with the implant (treated).[26] Femorotibial forces in the medial compartment of the knee throughout the stance phase were reduced by 31 ± 11 lb ($P = 0.002$) when the device was implanted. The reductions in peak medial forces were greatest around heel strike (29 ± 18 lb, $P = 0.01$) and around toe-off (44 ± 20 lb, $P = 0.008$). In addition, the total joint load (the sum of medial and lateral forces) was also significantly reduced in the treated knees. These reductions in medial and total intra-articular loads were within the clinically effective ranges of other joint-unloading therapies and provide validation for the clinical usefulness of the KineSpring System[27] (Figure 4).

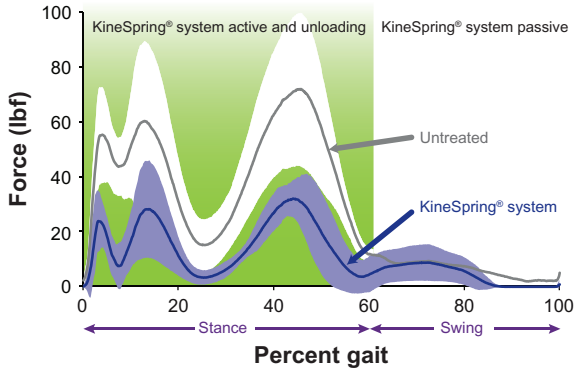

Figure 4 Medial knee joint loading throughout simulated gait cycle. Plot of medial compartment loading during the gait cycle showing reductions with the KineSpring System (green) implanted relative to the untreated knee (blue). Significant differences are noted at heel strike (3% of gait), initial loading (13% of gait), and toe-off (45% of gait).

No significant transfer of load to the lateral compartment was noted compared to the untreated knees.

Clinical trial overview

Clinical outcomes with the KineSpring System are reported from three single-arm clinical trials, each prospectively registered in a public trials registry, namely the OASYS (Safety and Feasibility of a Load Bypass Knee Support System [LBKSS] for the Treatment of Osteoarthritis; ACTRN12608000451303),[28] OAKS (Multi-Center, Open-Label, Interventional Study to Assess Pain Relief in Patients with Medial Compartment Knee Osteoarthritis [OA] Treated with the KineSpring System; ACTRN12609001068257),[29] and COAST (Multicentre Open-Label Interventional Study of Patients with Medial Compartmental Knee Osteoarthritis [OA] Symptoms Treated with the KineSpring Unicompartmental Knee Arthroplasty [UKA] System; ISRCTN63048529)[30] trials. All research procedures performed in these studies followed predefined protocols that were approved by all researchers and the ethics committee at each site. All patients provided written, informed consent before surgery.

Patients

Common inclusion criteria among the studies included males and females aged 30–75 years, body mass index <40 kg/m^2, and symptomatic, imaging-confirmed knee OA refractory to conservative therapies. Main exclusion criteria included lateral compartment or patellofemoral OA in the affected knee, varus alignment >10°, clinical joint instability, rheumatoid knee arthritis, prior traumatic injury or joint infection, knee prosthesis in the affected knee, moderate-to-severe osteoporosis, recent arthroscopic surgery, and current smoking.

Pre-treatment procedures

Pre-treatment assessments included inclusion/exclusion criteria evaluation, a complete clinical and orthopedic examination, and medical history. Imaging studies included standing X-rays (anteroposterior, lateral, and sunrise views) and magnetic resonance imaging. Patient evaluations included knee pain severity using a 0–100 visual analog scale, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) version 3.1,[31] and knee joint range of motion.

Treatment

The operative procedures were performed under general or regional anesthesia with the knee fully extended in a true lateral position, and the medial and lateral femoral

condyles coincident under fluoroscopy in both the distal and posterior planes. Standard aseptic precautions were taken, similar to those for knee arthroplasty. Using standard instrumentation, the surgeon inserted a K-wire under fluoroscopic guidance into the medial femoral condyle, and using this K-wire as a reference location, achieved initial access with an incision extending proximally parallel to the femur and then utilized a subvastus surgical approach to the distal femur. The femoral base was attached subvastus to the medial distal femoral cortex using compression screws and locking screws. Next, a second oblique incision was made 5 cm distal to the femoral incision, over the anteromedial aspect of the proximal tibia. A continuous extracapsular tunnel linking the femoral and tibial incisions was created via blunt dissection. The load absorber was inserted into the tunnel via the tibial incision and attached to the femoral base using a Morse-style taper locking device. Next, the tibial base was attached to the proximal tibia, with the knee held in varus, using similar methods as with the femoral base component. Critically, the knee must be placed in just enough varus alignment to close the joint space during tibial base fixation to ensure that the absorber does not compress beyond its working length during normal use. Once fixation of the tibial base was complete, the precompressed load absorber was activated by release of a constraining cable, and the knee was examined through a full range of motion to ensure there was no impingement of the device on surrounding soft tissue structures. Importantly, the procedures were performed with minimal disruption of the knee anatomy, requiring no resection of bone, cartilage, or ligament. In all cases, visualization of the implant was performed in anteroposterior and lateral views using fluoroscopy. The wounds were closed using standard techniques, and postoperative care was provided as per the standards of the institution and at the discretion of the investigators. Patients were encouraged to ambulate immediately following recovery from anesthesia.

Patient follow-up

Patients returned for follow-up visits at 6 weeks, 3 months, 6 months, and annually thereafter. Each visit included a complete clinical and orthopedic examination. Standing X-rays (anteroposterior and lateral views) were performed at discharge, 6 months, and annually thereafter. Magnetic resonance imaging was performed at 1 and 2 years in the OASYS and OAKS trials. The WOMAC questionnaire was administered at 6 weeks and at all subsequent follow-up visits. Patient follow-up is ongoing through 5 years.

Data analysis

Data were analyzed using Predictive Analytics Software (version 18.0, IBM, Inc., Armonk, NY, USA). Continuous data were reported as mean ± standard deviation or median and range, depending on normality assumptions. Categorical data were reported as frequencies and percentages. Longitudinal changes in clinical outcomes were assessed with repeated measures analysis of variance. The minimal clinically important difference (MCID) has been established at ≥30% improvement from baseline for pain severity and ≥20% improvement for WOMAC subscores.[32]

Results

A total of 100 patients enrolled in the single-arm clinical trials with the KineSpring System with a minimum of 1 year follow-up (mean 1.6 years, range 1–3 years) were included in this report. Baseline patient characteristics are presented in Table 1. Patients were mostly (75%) male, with a mean body mass index of 30 kg/m^2. Mean pre-treatment knee pain severity was 59, and WOMAC subscores ranged from 44 to 52, values that are comparable to knee OA patients undergoing total knee arthroplasty (TKA).[33,34]

Procedural success, defined as successful device implant and activation with no operative complications, was 100%. General anesthesia was used in most (77%) but not all patients. The femoral and tibial incisions required for KineSpring System insertion were small (6–7 cm), blood loss was minimal, and patients were discharged in a median of 1 day. One patient remained hospitalized for 13 days due to a wound infection, which resolved with conservative treatment (Table 2).

Knee pain severity significantly improved following KineSpring System implant, from 59 ± 19 at baseline, 33 ± 22 at 6 weeks, and gradually improving through 1 year (23 ± 22), representing a 60% overall reduction in pain ($P < 0.001$) (Figure 5). The percentage of patients achieving the pain severity MCID

Table 1 Baseline patient characteristics

Characteristic	Values
Demographics and medical history	
Male sex, n (%)	75 (75)
Age, mean ± SD, years	52 ± 9
Body mass index, mean ± SD, kg/m^2	30 ± 5
Knee-specific patient-reported outcomes	
Knee pain severity, mean ± SD	59 ± 19
WOMAC pain, mean ± SD	45 ± 17
WOMAC function, mean ± SD	44 ± 18
WOMAC stiffness, mean ± SD	52 ± 21
Range of motion, mean ± SD, degrees	119 ± 13

Abbreviations: SD, standard deviation; WOMAC, Western Ontario and McMaster Universities Arthritis Index.

Table 2 Procedural data

Characteristic	Values
Anesthesia time, mean ± SD, minutes	104 ± 42
Femoral incision length, mean ± SD, cm	7.4 ± 1.8
Tibial incision length, mean ± SD, cm	6.1 ± 1.4
Operative time, mean ± SD, minutes	67 ± 17
Blood loss, median (min–max), cc	0 (0–500)
Hospital stay, median (min–max), days	1 (1–13)

Abbreviation: SD, standard deviation.

increased throughout the follow-up period, from 60% at 6 weeks to 76% at 1 year (Figure 6). All WOMAC subscores significantly improved over the 1-year follow-up period, with a 56% improvement in pain, 57% improvement in function, and a 39% improvement in stiffness (all $P < 0.001$) (Figure 7). At 1 year, 74% of patients achieved the MCID for pain, 83% for function, and 67% for stiffness (Figure 8). Knee joint range of motion decreased from pre-treatment to the 6-week postoperative period (119° ± 13° to 105° ± 19°). Thereafter, range of motion gradually increased to pre-treatment levels at all subsequent follow-up periods through 1 year (Figure 9). During the follow-up period, six (6%) patients whose knee OA symptoms failed to improve following KineSpring System implant required additional surgery (four TKA, two HTO). Four patients had no pain resolution and underwent explant between 2 and 10 months postimplant. Two patients had recurring pain within 6 months of implant. On explant analysis, no failure of the KineSpring implant was identified in any patient.

Discussion

Knee OA is the leading cause of musculoskeletal pain and disability in the US.[7,9,35] Almost 4 million Americans

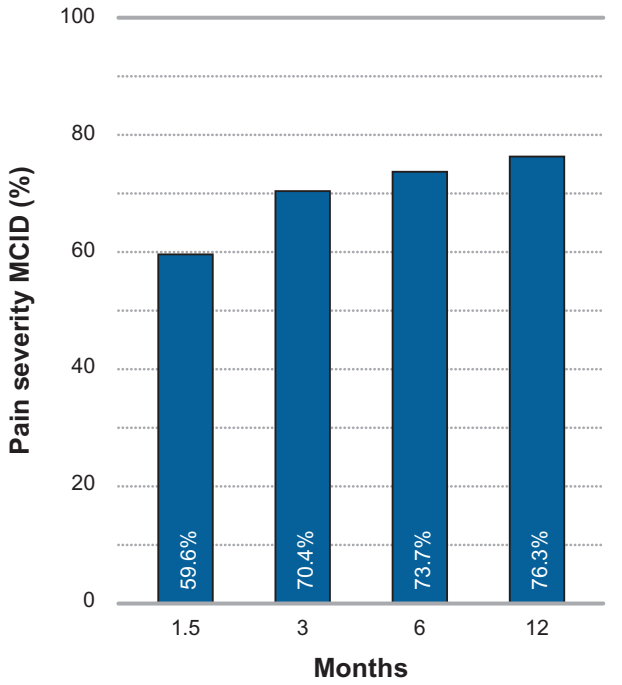

Figure 6 Percentage of patients achieving the minimal clinically important difference (MCID) for pain severity improvement through 1 year following KineSpring System implant.

are within the knee OA treatment gap, and this number is anticipated to increase to 5 million people by 2025, due to low arthroplasty utilization and increasing life expectancies.[17] The average duration of the treatment gap has been estimated at almost 20 years, with an annual economic burden currently estimated at $17 billion and anticipated to grow to $24 billion by 2025.[17] Since only 9%–33% of patients with severe knee OA are willing to consider knee arthroplasty,[36–38] there is a critical medical and economic need to bridge the

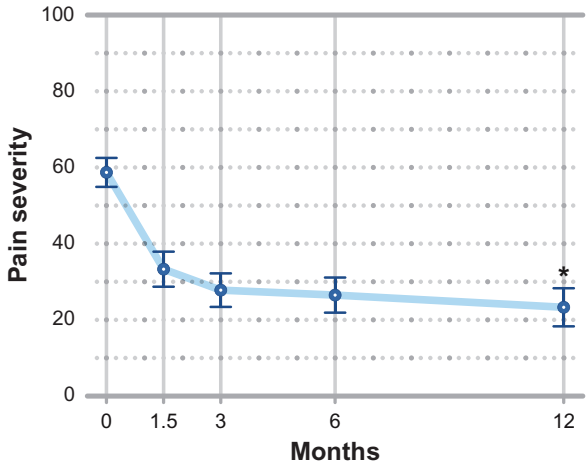

Figure 5 Pain severity improvements over 1 year following KineSpring System implant.
Note: *$P < 0.001$.

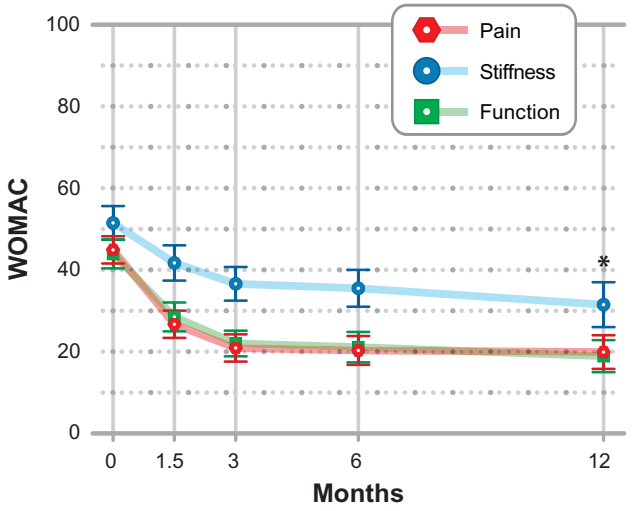

Figure 7 Western Ontario and McMaster Universities Arthritis Index (WOMAC) pain, function, and stiffness improvements over 1 year following KineSpring System implant.
Note: *All $P < 0.001$.

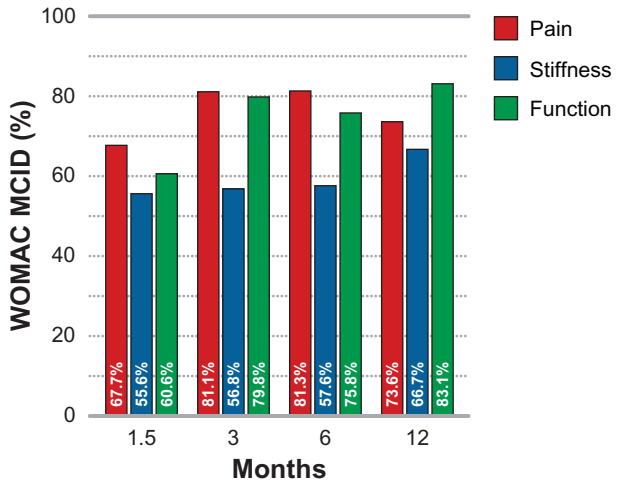

Figure 8 Percentage of patients achieving the minimal clinically important difference (MCID) for Western Ontario and McMaster Universities Arthritis Index (WOMAC) subscore improvement through 1 year following KineSpring System implant

gap between conservative care and joint-modifying surgical procedures.

Implantable medical devices are used to treat similar "treatment gaps" across many therapeutic areas, including orthopedics. However, none of these technologies has been applied to management of knee OA. The KineSpring System represents a paradigm shift in knee OA management by addressing the underlying biomechanical cause, excessive joint-loading, with a potentially reversible implantable device that spares the knee joint.

The patients in the current trial presented with knee pain and function levels similar to that of patients undergoing arthroplasty.[33,34] Additionally, patients treated with the KineSpring System yielded similar clinical improvement as those undergoing arthroplasty. WOMAC pain, function, and

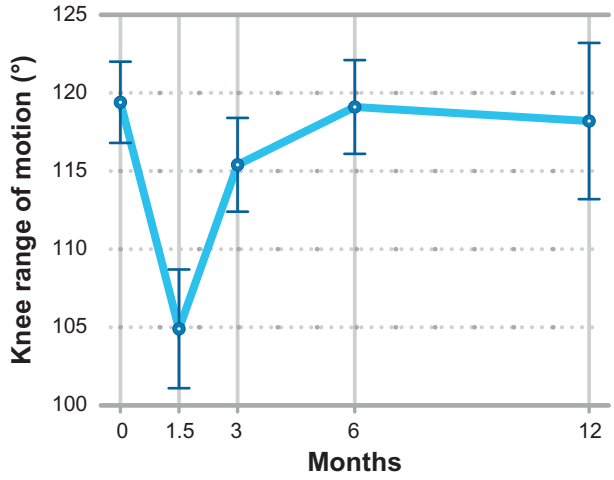

Figure 9 Changes in knee joint range of motion over 1 year following KineSpring System implant.

stiffness scores typically improve by 43%–65% following TKA,[33,34] which is comparable to the 39%–57% improvements in the current study. These data suggest that the KineSpring System improves knee pain and dysfunction in patients with symptomatic knee OA to a similar degree as TKA without the need for permanent surgical alterations to the knee joint.

The KineSpring System has several advantages over HTO or unicompartmental or TKA. First, the less invasive device implantation is extracapsular and performed with no removal of bone, muscle, or ligamentous tissue or alteration in the mechanical axis of the limb. Second, patient acceptance with the KineSpring System may be higher compared to only 9%–33% of patients willing to undergo arthroplasty, given the less invasive, reversible nature of the surgical procedure.[36–38] This aversion to surgery is warranted, since only 43% of patients report being completely pain-free after arthroplasty.[39] Third, the KineSpring System implantation procedure is essentially reversible, making revision surgery simple, utilizing the same surgical incisions as the original procedure. In contrast, revision surgery for joint-modifying procedures is more technically demanding, potentially more expensive, and associated with more complications compared to primary arthroplasty procedures.[40]

There are several limitations associated with this research. The human clinical trials presented herein were uncontrolled case series and were subject to associated bias influences. Second, long-term data with the KineSpring System are currently unavailable, and therefore the results presented herein should be considered preliminary. Lastly, the KineSpring System has very specific indications and contraindications for use, which limits the applications of this implant. Importantly, the KineSpring System is not intended for patients with lateral or patellofemoral knee OA. Additionally, the device is only intended to unload the knee joint during gait, but not during activities such as squatting or stair climbing. Prospective controlled clinical trials with larger sample sizes are warranted to elucidate further the effects of the KineSpring System. The GOAL study (Study of the KineSpring System Versus High Tibial Osteotomy Surgery for the Treatment of Medial Compartment Knee Osteoarthritis; NCT01610505)[41] is one such trial, which is a prospective, nonrandomized, controlled postmarket study that is designed to assess outcomes in 225 patients treated with the KineSpring System or high tibial valgus osteotomy.

Conclusions

Based on the performance of the KineSpring System during extensive preclinical testing and in 100 patients with medial

knee OA followed for at least 1 year, we conclude that the KineSpring System effectively bridges the gap between failed conservative care and surgical joint-modifying treatment. Patients treated with the KineSpring System report symptom improvement similar to that of patients undergoing TKA, but with a less invasive, extracapsular, joint-sparing implant.

Acknowledgment

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Disclosure

NJL, LEM, and JEB are consultants to Moximed, Inc. JS reports no conflicts of interest in this work.

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