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MISHA KNEE SYSTEM FOR MILD-TO-MODERATE MEDIAL KNEE OSTEOARTHRITIS

EXECUTIVE SUMMARY

Medial knee osteoarthritis (OA) is more commonly affected among tri-compartmental OA, owing to the forces transmitted across the knee joint are greater in the medial compartment compared to the lateral compartment even during normal walking, and excessive loading is observed in a diseased state, leading to chronic pain and long-term disability. The MISHA Knee System is a novel, implantable shock absorber placed subcutaneously superficial to medial collateral ligament, indicated for mild-to-moderate medial knee OA who had failed surgical or non-surgical treatment modalities. It reduces a portion of the weight-bearing load exerted on the medial knee during physical activity thereby, reducing the mechanical stress imposed on a degenerative joint and therefore it is claimed to relieve pain, preserve function, and offer a treatment option that could potentially delay arthroplasty.

Keywords: implantable shock absorber, degenerative disease, orthopaedic surgery, medical device

INTRODUCTION

Osteoarthritis (OA) is a degenerative, chronic joint disease characterised by clinical symptoms and distortion of joint tissues[1], as a leading cause of adult chronic pain and long-term disability.[2] It is the most common chronic articular disease and remains one of the few chronic aging disorders with few effective treatments, none of which have been proven to delay disease progression.[1] Osteoarthritis commonly affects the hip, knee, and hand joints, but most joints can be involved.[2] The knee is most frequently affected in up to 10% of men and 13% of women aged above 60 years, with evidence of symptomatic OA of the knee in the United States.[1]

Osteoarthritis can be defined pathologically, radiographically, and clinically. The most common method for radiographic definition is the Kellgren–Lawrence (KL) radiographic grading system and atlas, which has been used for more than 40 years. This overall joint

scoring system grades OA into five levels from 0 to 4, defining OA by the presence of a definite osteophyte (Grade ≥ 2), and more severe grades by the presumed successive appearance of joint space narrowing, sclerosis, cysts, and deformity. However, all patients with radiographic OA do not have a clinical condition, and all patients with joint symptoms do not demonstrate radiographic OA. Therefore, OA must be diagnosed using a variety of pathological, clinical, and radiological methods.[1]

The global disease burden of OA in 2019 were about 414.7 million (95% uncertainty interval (UI): 368.8 to 464.4 million) OA incident cases, with an age-standardised incidence rate (ASR) about 492.21 (95% UI: 438.66 to 551.5) per 100000.[2] Globally, 595 million (95% UI: 535 to 656) people had OA in 2020, equal to 7.6% (95% UI: 6.8 to 8.4) of the global population, and an increase of 132.2% (130.3–134.1) in total cases since 1990.[2] According to one Malaysian data obtained from greater Klang Valley, the crude and weighted prevalence of knee pain and self-reported knee OA symptoms were 33.3% and 30.8% respectively.[3]

Osteoarthritis is a major source of health expenditure. In the United States of America, osteoarthritis was responsible for an estimated USD 80 billion in healthcare spending in 2016, whereas in Hong Kong, osteoarthritis was responsible for more than USD 400 million in direct and indirect spending in 2003.[2]

The medial compartment of the knee is overall more affected than the lateral compartment of the knee. “Unicompartmental” arthritis of the knee is a degenerative condition characterised by abnormal articular cartilage in the medial part of the tibiofemoral joint, which may be associated with meniscal disruption, ligamentous instability, and limb malalignment. The most common symptom is pain confined to the medial compartment, which may be associated with other symptoms of OA.[4] Knee OA may in part be due to excessive loading of the articular cartilage. During walking, the forces transmitted across the knee joint are greater in the medial compartment compared to the lateral compartment, and increased medial compartment loading has been observed in patients with knee OA.[5] Isolated medial tibiofemoral OA, isolated patellofemoral OA, and combined medial tibiofemoral and patellofemoral OA were more common than tricompartmental disease, occurring in 27% (15.2–31.1%), 18% (9.9–22.7%) and 23% (14.1–27.3%) of people respectively. Single/bicompartmental patterns of disease involving the lateral tibiofemoral compartment were less common, summing to 15% (8.5–18.7%).[6]

THE TECHNOLOGY

The MISHA Knee System (previous named Atlas and Calypso)[7] is a novel, implantable shock absorber (ISA) developed by Moximed based in Carlifornia.[8] This class II medical device is indicated for younger patients with symptomatic mild-to-moderate medial knee osteoarthritis (OA) who have failed surgical and/or non-surgical treatment modalities.[9] It

is designed to absorb excess forces when the leg is extended (during stance phase of gait), where the knees support most of body weight, therefore it is claimed to relieve pain, preserve function, and offer a treatment option that could potentially delay arthroplasty.[8]

Figure 1. The MISHA Knee System

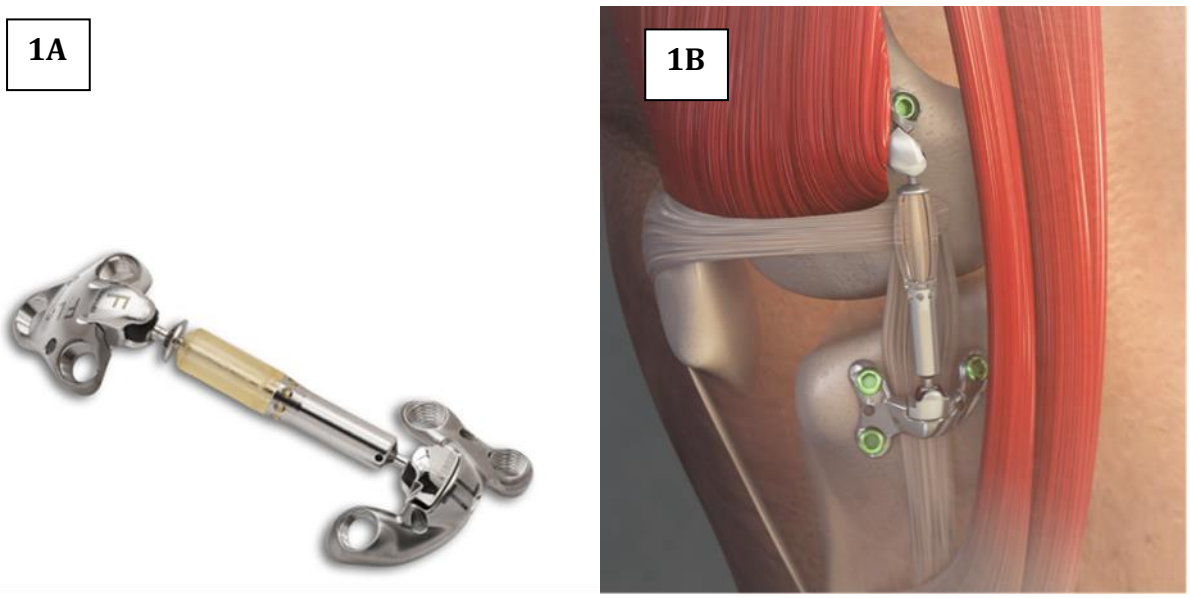

Figure 1A: A single unit of implantable shock absorber. 1B: The position of the device being placed surgically.

It consists of a capsule containing polycarbonate urethane, a springy biocompatible plastic, with titanium brackets at either end that screw into the sides of the tibia.[8] The size of cylindrical shock absorber is 0.8 cm × 5 cm and is fixed by 2.5 cm × 4.0 cm titanium plates to the distal femur and proximal tibia[10] as shown in Figure 1. This mechanical system, in conjunction with the ability of the device to lengthen and shorten via PCU-absorber compression and distention, enables the knee to move in 6 degrees of freedom (DOF). During the stance phase of gait, the absorber will engage and gradually compress to unload the medial knee. As the knee moves into swing phase, the piston and absorber will separate until the device becomes disengaged to maintain a smooth gait pattern.[11] It reduces peak forces on the medial compartment by 32%.[10,11] This medial unloading is equivalent to high tibial osteotomy (HTO) and does not transfer load to the lateral compartment. Load management leads to symptomatic relief because repetitive overload of the joint changes the knee's mechanical environment and often initiates degeneration, interrupting this cascade via unloading may allow the knee to adjust to a new, less symptomatic environment.[10]

The ISA is placed subcutaneously, outside the joint capsule, and superficial to the medial collateral ligament (MCL) in an outpatient-compatible setting using surgical techniques familiar to orthopaedic surgeons.[10]

However, it was not indicated for patients with excessive medial osteophytes or meniscal extrusion; refinement of surgical instrumentation for technique repeatability; and

modification of material selection and dimensions of the implant for robustness and manufacturability.[10]

This technology had just recently been approved on the 10th of April 2023 by US Food and Drug Administration (USFDA).[12] Currently, a MISHA™ Post-Market Clinical Study (NCT06118892) are recruiting participants.[13]

PATIENT GROUP AND INDICATION

The MISHA knee system is proposed to be used for patient with mild-to-moderate medial knee OA who have failed surgical and/or non-surgical treatment modalities.

CURRENT PRACTICE

The management of OA involves a multidisciplinary approach with the aim to relieve symptoms and improve joint function. It involves nonpharmacological and pharmacological treatment. Non-pharmacological treatment includes patient education on awareness, lifestyle modification such as weight reduction, improving physical function with exercise programmes, physiotherapy, occupational therapy and orthoses usage to help supporting the joint.[14,15] Pharmacologically, treatments are available in oral (painkillers and/or nutraceutical), intra-articular (such as corticosteroid or viscosupplementation) and topical form (such as NSAIDs, capsaicin and methylsalicylate).[14,15]

Surgery is considered if the symptoms of the affected joints significantly affect the quality of patients' life and interfere with activities of daily living (ADL). The types of surgery that can be offered are arthroscopic surgery, high tibial osteotomy, total joint replacement, partial joint replacement and arthrodesis.[14]

Traditionally, the treatment of choice would be a total knee arthroplasty; however, this involves removing healthy joint surfaces. Arthroscopic debridement in the osteoarthritic knee has fallen out of favour due to poor clinical results.[15]

Recently, a trend has developed towards less invasive surgery; with uni-compartmental knee replacement (UKR) and high tibial osteotomy (HTO) has gained increasing popularity.[15] Uni-compartmental knee replacement will correct an intra-articular deformity caused by cartilage loss with the aim of restoring collateral ligaments to their normal tension. Whereas, an HTO differs in the sense that it aims to alter the mechanical axis of the limb. For this reason, UKR is contraindicated in large deformities (>15 degrees), as they will not be corrected by the intra-articular procedure.[15]

EFFICACY AND SAFETY

Systematic search was conducted from scientific databases such as Medline, EBM Reviews, EMBASE via OVID, PubMed and from the general search engines [Google Scholar and US Food and Drug Administration (US FDA)] on The MISHA knee system.

There was only one published scientific evidence on effectiveness and safety of MISHA knee system.

Efficacy

An open-label cohort study (clinicaltrials.gov; NCT03671213 and NCT03838978; pooled result) conducted in ten centers in the United States and Europe, recruited 81 participants aged between 25 to 65 years old with radiographic evidence of medial OA with Kellgren and Lawrence (KL) grade 1-4 who had failed more than 6 months nonsurgical treatment. The cohort (n=81) received ISA treatment and were compared to 81 historical control who underwent opening-wedge HTO. The primary endpoint was a composite variable combining pain, function, specific adverse events, integrity of implant or hardware, and conversion to subsequent surgery. The secondary endpoint includes days to full weightbearing post-surgery, Western Ontario and McMaster Universities Arthritis Index score (WOMAC) for pain at 3 months, WOMAC function at 3 months, WOMAC pain at 24 months, and WOMAC function at 24 months. Patients were followed-up till 24 months.[10]

The clinical composite primary endpoint at 24 months was met by 85.6% of the subjects in the ISA arm and 65.5% of the subjects in the HTO arm as shown in Figure 2. At 24 months, the mean pain rating in the ISA arm was 14.2 (±16.36) with a 76.0% improvement, and the pain rating in the HTO arm was 19.9 (±19.84) with 64.7% improvement, as shown in Figure 3.[10]

Figure 2 Primary endpoint Composite Variable.[10]

	ISA Arm			HTO Arm		
Variable	*N*	*n*	%	*N*	*n*	%
Enrolled subjects	81	81	100	81	81	100
WOMAC pain responder	72	69	95.8	58	51	87.9
WOMAC function responder	72	66	91.7	64	52	81.3
No subsequent surgical intervention	81	80	98.8	81	80	98.8
No device-related SAE	81	77	95.1	81	76	93.8
Maintenance of implant or hardware integrity	81	80	98.8	81	80	98.8
Overall composite clinical success	81	—	85.6	81	—	65.5

Figure 2 showing overall composite clinical success which was greater among ISA arm as compared to HTO arm, with greater proportion of participants had improvement in their pain and function score in ISA group.

Figure 3 Secondary endpoints.[10]

Secondary Endpoints	ISA Arm			HTO Arm			P Value
	N	M	SD	N	M	SD	
Time to full weightbearing (days)	81	13.4	10.12	77	58.7	39.91	<0.001
WOMAC pain percentage change at 3 months	81	−55.5%	29.3%	72	−33.4%	35.8%	<0.001
WOMAC pain percentage change at 24 months	72	−76.0%	28.2%	58	−64.7%	33.0%	0.014
WOMAC function percentage change at 3 months	81	−52.2%	32.0%	75	−25.2%	37.0%	<0.001
WOMAC function percentage change at 24 months	72	−73.9%	29.6%	64	−58.8%	35.8%	0.011

Figure 3. At 24 months, the mean pain rating in the ISA arm was greater than the pain rating in the HTO arm.

Figure 4 showed pain score from baseline up to 24 months follow-up comparing ISA and HTO group.[10]

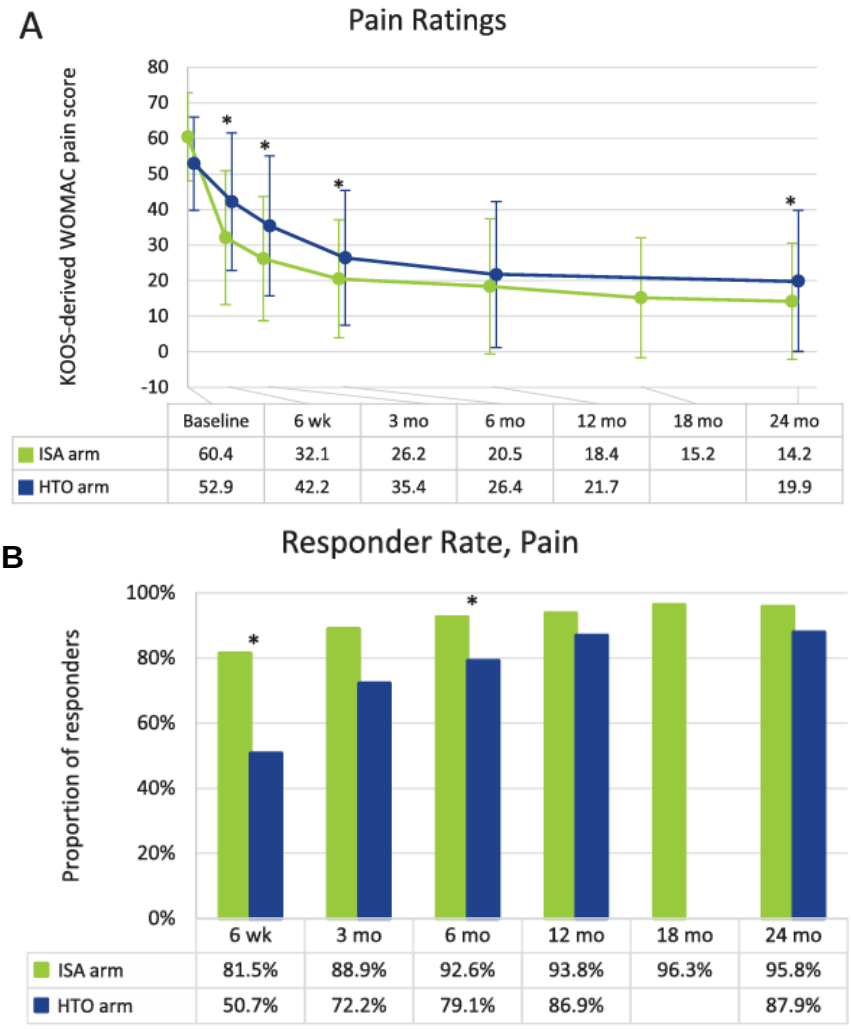

Figure 4 A: reduction of pain score rating among ISA and HTO arms. 4B. The proportion of subjects considered responders at 24 months.

Figure 5 Percentage improvements relative to baseline in function and pain for the ISA and HTO arms at 3 months (A) and 24 months (B).[10]

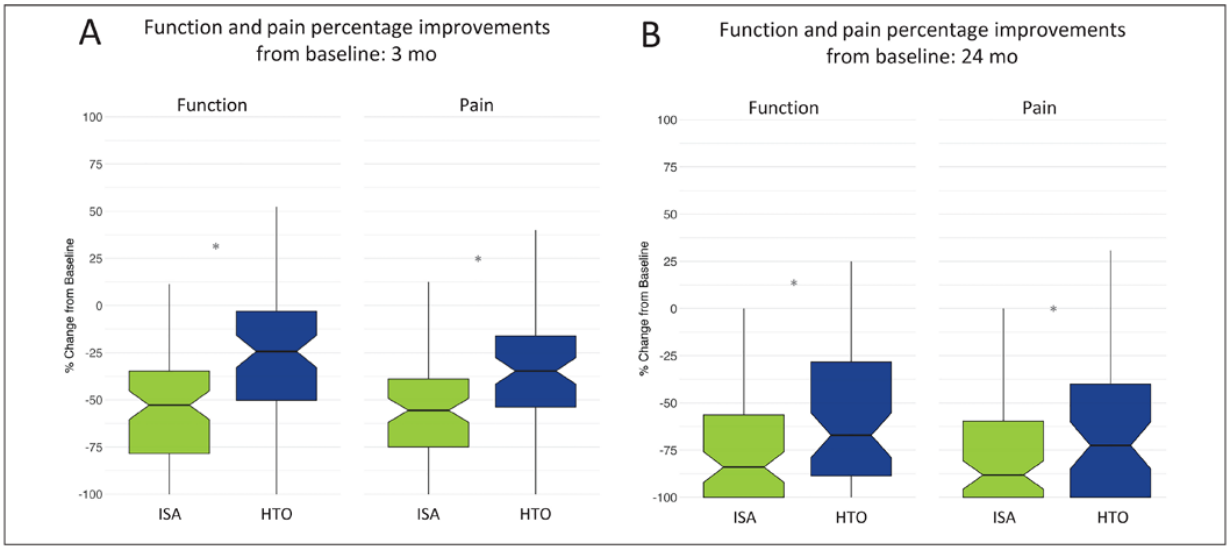

Figure 5: Boxplot indicates median (notch) and interquartile range (IQR), with whiskers identifying the highest and lowest data point within 1.5x IQR, and * indicates a statistically significant difference between the arms.[10]

The proportion of subjects considered responders at 24 months was 95.8% in the ISA arm and 87.9% in the HTO arm, as shown in Figure 4. Pain and function improved more in the ISA arm as compared to HTO arm as shown in Figure 5.[10]

Figure 6 Comparison of time to full weight bearing after procedure.[10]

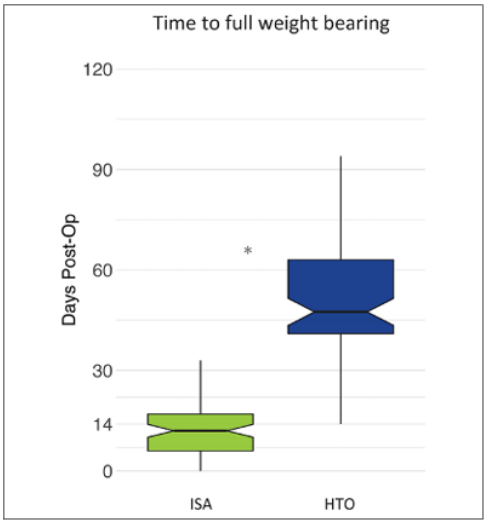

Figure 6 has shown that patients undergoing ISA procedure were able to fully weight bearing earlier as compared to HTO groups. The time to full weightbearing on the operated leg was 13.4 days (±10.12 [SD]) in the ISA arm and 58.0 days (±39.91) in the HTO arm (P < 0.001).[10]

Other positive finding includes the time to full weightbearing on the operated leg was 13.4 days (±10.12 [SD]) in the ISA arm and 58.0 days (±39.91) in the HTO arm (P<0.001), as shown in Figure 6. Percentage changes in pain and function relative to baseline at both 3 and 24 months were also larger in the ISA arm than in the HTO arm (all P values <0.02).[10]

Societal/ethical

There was no retrievable evidence on societal or ethical issue on MISHA Knee System. This technology might reduce the need for admission as in the previous study mentioned, 90.5% of the subjects in the United States were treated on an outpatient basis.[10]

Safety

According to previously-mentioned cohort study, there were 15 device- and procedure-related serious adverse events (SAEs) in 13 subjects in the ISA arm (16.0%). In the HTO arm, there were 42 SAEs in 37 subjects (45.7%). The overall occurrence of SAEs was significantly higher in the HTO arm, with pain (reported by 4.9% in the ISA arm and 35.8% in the HTO arm) being the primary contributor to the group difference ($p < 0.001$) safety of MISHA Knee System. There were zero mechanical device malfunctions in either arm. There was one incidence of a screw partially backed out in ISA subject and one incidence of a screw breakage in HTO group. The ISA arm had 11 of 81 (13.6%) implant removals, of which 7 of 11 (63.6%) were elected by the subject. One subject in the ISA arm (1/81, 1.2%) was converted to unicompartmental knee arthroplasty (UKA). Reasons for removal were infection (n = 4), discomfort/ catching-pulling sensation (n = 2), pain (n = 2), scar formation (n = 2), and dissatisfaction (n = 1). Whereas, the HTO arm had 61 of 81 (75.3%) implant removals.[10]

ESTIMATED COST

The exact price of the device was not revealed by the company. There was no retrievable cost-effectiveness study on this technology. However, one abstract on exploratory analysis of the costs and benefits of implantable shock absorber placement in patients with medial knee osteoarthritis published on 2023 ISAKOS Biennial Congress Paper had shown that ISA placement improved WOMAC pain scores from 60.4 at baseline to 14.2 at 24 months, corresponding to a utility increase from 0.70 at baseline to 0.80, in line with the utility estimate for TKA. At 5 and 10 years, 74% and 55% were projected to remain on ISA treatment. The projected cumulative 10- and 20-year incidences of primary TKR were 24.9% vs. 58.2% (RR=0.42) and 68.6% vs. 82.5% (RR=0.83) for ISA and standard of care, respectively. Over the patients' lifetime, ISA was projected to add 0.23 QALYs (14.45 vs. 14.22 QALYs) at concurrent lifetime cost increase of $8,510 (~RM 40452.28; 1 USD= RM4.75) ($61,339 vs. $52,829), yielding an incremental cost-effectiveness ratio

(ICER) of $36,413 (~RM 173089.20;1 USD= RM4.75) per QALY gained. Incremental costs for the ISA strategy were lowest at 10-year follow-up ($1,610; RM 7653.13) across conducted sensitivity and scenario analyses, they concluded that ISA remained cost-effective.[16]

Comparatively,in the United States, total direct medical costs for other surgical options were $20,436 (RM97142.53; 1 USD= RM4.75) for high tibial osteotomy, $24,637 (~RM117111.98) for unicompartmental knee arthroplasty, and $24,761 (~RM117701.41) for total knee arthroplasty.[17] The average facility payments for those surgical options ranged from $21,306-$30,421 (RM 101278.07 -144606.22) for HTO; $24,332-$28,058 (RM 115662.16 - 133373.70) for UKA and $28,756-$31,670 (RM 136691.65 - 150543.35) for TKA.[18]

In a private hospital in Malaysia, the price of total knee replacement surgery inclusive of 4days-3night ward stay, procedure, medications and physiotherapy is about RM 28998.[19] The cost of osteotomy in Malaysia for medical tourists varies depending on the complexity of the procedure and other factors such as the hospital or clinic chosen, the type of care needed, and the medical team involved. Generally, medical tourists can expect to pay between USD 4,000 (RM 19136.40 ;1 USD= RM4.78) and USD 15,000 (RM 71761.50 ;1 USD= RM4.78) for osteotomy in Malaysia.[20]

POTENTIAL IMPACT

In conclusion, there was limited evidence retrieved on MISHA Knee System. It was claimed to have good safety profile, has the potential to improve pain and function for mild-to-moderate medial knee osteoarthritis in younger population, while delaying the need for TKR. However, cost effectiveness study is needed before its usage in our facilities.

REFERENCES

1. Jang S, Lee K, Ju JH. Recent Updates of Diagnosis, Pathophysiology, and Treatment on Osteoarthritis of the Knee. International Journal of Molecular Sciences. 2021;22(5):2619.
2. Steinmetz JD, Culbreth GT, Haile LM, et al. Global, regional, and national burden of osteoarthritis, 1990–2020 and projections to 2050: a systematic analysis for the Global Burden of Disease Study 2021. The Lancet Rheumatology. 2023;5(9):e508-e522.
3. Mat S, Jaafar MH, Ng CT, et al. Ethnic differences in the prevalence, socioeconomic and health related risk factors of knee pain and osteoarthritis symptoms in older Malaysians. PLoS One. 2019;14(11):e0225075.

4. Hsu H, Siwiec RM. Knee Osteoarthritis. StatPearls. Treasure Island (FL) ineligible companies. Disclosure: Ryan Siwiec declares no relevant financial relationships with ineligible companies.: StatPearls Publishing. Copyright © 2023, StatPearls Publishing LLC.; 2023.
5. Levinger P, Menz HB, Fotoohabadi MR, et al. Foot posture in people with medial compartment knee osteoarthritis. Journal of Foot and Ankle Research. 2010;3(1):29.
6. Stoddart JC, Dandridge O, Garner A, et al. The compartmental distribution of knee osteoarthritis – a systematic review and meta-analysis. Osteoarthritis and Cartilage. 2021;29(4):445-455.
7. Gever J. New Option on Horizon for Younger People With Refractory Knee OA. 2023. Available from: https://www.medpagetoday.com/meetingcoverage/aaos/103486. Accessed on 20 January 2024.
8. Moximed. What Is The Misha Knee System? 2024. Available from: https://mishaknee.com/misha-overview/. Accessed on 3 January 2024.
9. (USFDA) USFDA. MISHA™ Knee System. 2023. Available from: https://www.accessdata.fda.gov/cdrh_docs/pdf22/DEN220033.pdf. Accessed on 3 Jan 2024.
10. Diduch DR, Crawford DC, Ranawat AS, et al. Implantable Shock Absorber Provides Superior Pain Relief and Functional Improvement Compared With High Tibial Osteotomy in Patients with Mild-to-Moderate Medial Knee Osteoarthritis: A 2-Year Report. Cartilage. 2023;14(2):152-163.
11. Morgan OJ, Hillstrom HJ, Ranawat A, et al. Effects of a Medial Knee Unloading Implant on Tibiofemoral Joint Mechanics During Walking. Journal of orthopaedic research : official publication of the Orthopaedic Research Society. 2019;37(10):2149-2156.
12. Moximed. FDA Authorizes Marketing of MISHA™ Knee System for People Suffering from Knee Osteoarthritis. 2023. Available from: https://moximed.com/news/fda-authorizes-marketing-of-misha-knee-system-for-people-suffering-from-knee-osteoarthritis/. Accessed on 3 Jan 2024.
13. Clinicaltrials.gov. MISHA™ Post-Market Clinical Study. 2023. Available from: https://clinicaltrials.gov/study/NCT06118892?term=implantable%20shock%20absorber&rank=1. Accessed on 5 Jan 2024.
14. Ministry Of Health Malaysia. Clinical Practice Guidelines: Management of Osteoarthritis (Second Edition). 2013. Available from: https://www.moh.gov.my/moh/attachments/CPG%202014/Osteoarthritis.pdf. Accessed on 5 Jan 2024.
15. McCormack DJ, Puttock D, Godsiff SP. Medial compartment osteoarthritis of the knee: a review of surgical options. EFORT open reviews. 2021;6(2):113-117.
16. Andreas H. Gomoll, Anne Ryschon, Abigail M Garner, et al. An Exploratory Analysis of the Costs and Benefits of Implantable Shock Absorber Placement

in Patients with Medial Knee Osteoarthritis. 2023. Available from: https://www.isakos.com/2023/Abstract/16276. Accessed on 5 Jan 2024.

17. Konopka JF, Gomoll AH, Thornhill TS, et al. The cost-effectiveness of surgical treatment of medial unicompartmental knee osteoarthritis in younger patients: a computer model-based evaluation. The Journal of bone and joint surgery American volume. 2015;97(10):807-817.
18. Holy CE, Chitnis AS, Escarpeta-Soriano J, et al. Surgical Procedures for Knee Osteoarthritis- Volume and Costs Among the Commercially-Insured Patients in the United States. Value in Health. 2018;21:S177.
19. Hospital KSS. Total Knee Replacement. 2024. Available from: https://www.kpjhealth.com.my/selangor/packages/total-knee-replacement. Accessed on 14 February 2024.
20. MyDocTrip. Osteotomy Cost in Malaysia. 2023. Available from: https://www.mydoctrip.com/treatment/osteotomy-price-malaysia/. Accessed on 14 February 2024.

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