MISHA®
KNEE SYSTEM

Instructions for Use

Read this entire Instructions for Use (IFU) document carefully prior to use.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.
Additional information is included in the MISHA Knee System Surgical Technique Guide.

GENERAL

Before any surgery, the surgeon must be familiar with the product, available literature and operative technique and must carefully read these instructions for use. Patient selection can be as important as the implantation procedure itself. The warnings and precautions must be heeded, and the instructions for use must be strictly followed.

PRODUCT DESCRIPTION

The MISHA® Knee System includes an extra-capsular implant intended to reduce loads on the medial knee. The implant consists of an absorber located between bases fixed with locking screws to the medial cortices of the distal femur and proximal tibia. The implant shares the load with the medial knee joint and articulating ball-and-sockets allow the device to accommodate the natural motions of the knee.

The device is implanted through a single incision in the subcutaneous tissue of the medial extra-capsular space. The compressible load absorber spans the joint, superficial to the medial collateral ligament. It is designed to be implanted without resection of bone, muscle, or ligaments, and without disrupting the joint capsule. Surgical implantation is completed using standard orthopedic tools and techniques in conjunction with supplied single-use, sterile instruments unique to the MISHA Knee System. Review the MISHA Knee System Surgical Technique Guide for additional details.

The single-use left or right MISHA Knee System is provided terminally sterilized (gamma irradiation). Locking Screws are provided as a 6-pack.

Figure 1: MISHA Implant

The MISHA Knee System implant and instrument components are listed in **Table 1**.

Table 1: MISHA Knee System Components

Item	Catalog Number	Description
MISHA Implant	2-1001	Left
	2-1002	Right
MISHA Locking Screw, 5.0 x 46 mm	1-3016	6 Pack
MISHA Targeting Instruments	2-3002	Collar (qty 2)
		Targeting Tool
		Feeler Gauge
		K-wires, Ø1.6 x 127mm (qty 5)
		Shims (qty 2)
MISHA Trialing Instruments (includes spacer)	2-2001	Trial, Left
	2-2002	Trial, Right
MISHA Fixation Instruments	2-3001	Ø2.4 x 127mm Steinmann Pins (qty 5)
		Ø4.3mm Drill Bit
		Drill Guide (qty 2)
		3.5mm Hex Screwdriver Bit
MISHA Torque Limiting Driver	1-4039	Torque Limiting Driver

INDICATIONS FOR USE

The MISHA Knee System is indicated for patients with medial compartment knee osteoarthritis that have failed to find relief in surgical and/or non-surgical treatment modalities and are still experiencing pain that interferes with activities of daily living and are also unwilling to undergo or ineligible for total knee replacement due to age or absence of advanced osteoarthritis.

CONTRAINDICATIONS

The MISHA Knee System is contraindicated for use in any patient with

- large medial osteophyte(s) or considerable extruded meniscus that may interfere with the placement or function of the device
- poor bone quality e.g., osteopenia, osteoporosis
- ligamentous instability
- active or recent knee infection
- inflammatory joint disease, including sequalae of viral infections
- suspected or documented allergy or hypersensitivity to cobalt, chromium, nickel or other metals
- history of keloid, hypertrophic or contracture scaring
- propensity for restrictive scar formation or adhesions with prior procedures (may lead to stiffness and adhesions leading to removal)
- known or suspected rapidly destructive OA (RDO)

- complex regional pain syndrome or reflex sympathetic dystrophy (RSD)
- body dysmorphic disorder characterized by a preoccupation with appearance
- history of intolerance or dissatisfaction with prior orthopaedic hardware implant procedures
- any other reason the physician deems the product or procedure inappropriate for a patient

WARNINGS (STERILITY AND HANDLING)

- For single patient use only.
- Strict aseptic technique is mandatory to minimize the risk of infection. Follow sterile procedures used for orthopedic implant procedures, including proper sterile surgical technique and handling of implants and instruments. An infection involving the implant is highly likely to require removal.
- Avoidance of periprosthetic local injections at any time after implantation is strongly recommended. Local periprosthetic injections can introduce pathogens to the implant site and increase the risk of post operative infection.
- The MISHA Knee System is supplied sterile using gamma irradiation. DO NOT reuse, reprocess or re-sterilize this product. Reuse, reprocessing or re-sterilization may compromise the structural integrity of the implant and/or create a risk of contamination of the device, which could result in patient injury, illness or death.
- Handle Carefully – Protect from damage and contamination. Inspect packages for punctures or other damage prior to surgery. If the sterile barrier is suspected of being broken, do not use the product, and instead return it to Moximed.

PRECAUTIONS

- The MISHA Knee System should only be used by a licensed physician trained in knee surgery and the use of the device and the surgical procedure.
- Use the MISHA Knee System prior to the expiration date specified on the package.
- Correct selection and implantation of the implant is important to success of the implant.

POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Prior to implantation of the MISHA Knee System, the surgeon is responsible for informing the patient of the risks associated with the treatment and the possibility of complications or adverse reactions. Additional surgery, including removal or reconstruction, may be required to address some of the adverse effects.

Below is a list of the potential adverse effects (e.g., complications) specifically associated with use of the MISHA Knee System.

- Patient dissatisfaction or implant failure to improve osteoarthritis symptoms
- Loss of implant integrity
- Nerve or ligament injury
- Infection

- Adverse tissue reaction to the device
- Soft tissue discomfort around the device

STORAGE REQUIREMENTS

Store the MISHA Knee System at room temperature. Avoid excessive heat, humidity or exposure to sunlight.

MRI SAFETY INFORMATION

MRI Safety Information

A person with Moximed's MISHA® Knee System may be safely scanned anywhere in the body under the following conditions. Failure to follow these conditions may result in injury.

Parameter	**Condition**
Device Name	MISHA Knee System
Static Magnetic Field Strength (B_0)	1.5 T or 3 T
MR Scanner Type	Cylindrical
B_0 Field Orientation	Horizontal
Maximum Spatial Field Gradient	30 T/m (3,000 Gauss/cm)
RF Excitation	Circularly Polarized (CP)
RF Transmit Coil Type	Integrated Whole Body Transmit Coil
Operating Mode	Normal Operating Mode
Maximum Whole-Body SAR	2 W/kg
Maximum Head SAR	3.2 W/kg
Scan Duration	2 W/kg whole-body average SAR for 60 minutes of continuous RF (a sequence or back-to-back series/scans without breaks)
Scan Regions	Any landmark is acceptable
Image Artifact	In non-clinical testing, the image artifact caused by the device extends approximately 37 mm from the implant when imaged with a gradient echo pulse sequence and a 3 T MRI system.

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Surgeons should be trained on patient selection and surgical technique. Review the current MISHA Knee System Surgical Technique Guide before using the product.

The MISHA Knee System is intended to relieve pain and improve function in osteoarthritic knees; it is not a cure for osteoarthritis. As part of the patient selection process, the treating surgeon or medical staff should educate the patient about expected outcomes, contraindications and warnings.

Characteristics considered positive for patient selection include:

- Activity exacerbated knee pain isolated to medial compartment and not global in nature that is nonresponsive to non-surgical management options.
- An understanding of the extra-articular nature of the implant and the potential to be able to palpate the implanted device, especially in patients with minimal adipose tissue around their knee.
- Acknowledgement that some patients may not be fully satisfied with the results in which case implant removal may occur.
- Willingness to follow the surgeon's prescribed post-operative rehabilitation program. Adherence to such a program provides the best potential for success.

Preoperative

1. The MISHA Knee System Instruments, provided separately, are required to complete this surgery. Review the surgical technique guide for the correct use and handling of these instruments.
2. Strict aseptic technique is mandatory to minimize the risk of infection. Follow sterile procedures used for orthopedic implant procedures, including proper sterile surgical technique and handling of implants and instruments. An infection involving the implant is highly likely to require removal.

Intraoperative

1. Prior to use, visually inspect each implant and screw for possible imperfections.
2. Follow the implant instructions as described in the surgical technique guide. The guide describes acceptable device placement and functional evaluation.
3. Steps in the procedure rely on closing the medial joint space by holding a varus stress on the knee. Refer to the surgical technique guide to confirm the specific instances in the procedure. This is mandatory to ensure proper operating performance and avoid premature failure of the implant.
4. Use only screws provided by Moximed to ensure proper fit, and to avoid improper mixing of metals. Fixation screws should be fully seated in the bases to assure stable fixation.
5. Ensure that all packaging materials have been removed and reconciled.
6. Prior to closure, the surgical site should be thoroughly cleaned.

Postoperative

1. Instruct the patient to follow a prescribed post-operative protocol. As with all surgeries, wound healing is a priority.
2. Periodic X-rays are recommended to detect any progressive changes in implant position or loosening.
3. Return to daily activities and exercise will be patient specific. Discuss individual expectations prior to surgery.
4. Post-operative patient care is important. The patient should be encouraged to promptly report any unusual changes in the operative extremity or changes in the performance of the device to his or her physician.

CLINICAL SUMMARY

Study Design

The MISHA Knee System was studied in a prospective, multicenter clinical study (Calypso Study) comparing the MISHA Knee System to a historical cohort of subjects treated with High Tibial Osteotomy (HTO). A total of 81 treatment arm subjects were enrolled in the study at 10 investigational sites located in Europe and in the United States (U.S.) and propensity-matched with 81 HTO subjects enrolled at eight sites in Europe.

MISHA Knee System subjects, age 25 to 65 years, with a diagnosis of medial knee osteoarthritis and study knee pain with an overall WOMAC pain score ≥ 40 (scale 0-100) were enrolled in the study.

Patient Population and Baseline Demographics

The primary analysis population was the propensity-trimmed modified Intent-to-Treat (mITT) population.

Key baseline demographic characteristics are presented (**Table 2**). There were no significant differences between the treatment groups at baseline for these key variables.

Table 2: Key Subject Demographics at Baseline, mITT Population

	MISHA Knee System (N=81)	Control (HTO) (N=81)	p-value
Age (years)			
Mean ± SD	51.2 ± 7.71	52.5 ± 7.58	0.857
Median (Min, Max)	52.0 (33.0, 64.0)	52.0 (34.0, 71.0)	
Height (inches)			
Mean ± SD	68.4 ± 3.72	68.7 ± 3.02	0.829
Median (Min, Max)	68.9 (59.8, 74.4)	69.3 (61.4, 74.4)	
Weight (lbs)			
Mean ± SD	189.5 ± 30.68	196.6 ± 33.32	0.983
Median (Min, Max)	189.6 (125.7, 251.3)	189.6 (112.4, 282.2)	
BMI (kg/m2)			
Mean ± SD	28.4 ± 3.44	29.3 ± 4.36	0.895
Median (Min, Max)	28.1 (21.4, 34.7)	29.2 (20.9, 38.9)	
Sex = Male n/N (%)	60.5% (49/81)	65.4% (53/81)	0.942

The **primary endpoint** at 24 months was achieved in this study. Both non-inferiority and superiority of the MISHA Knee System to HTO have been demonstrated.

A subject was a responder in the study if all the following components were met at 24 months:

- Clinically significant improvement of at least 20% from baseline on the WOMAC pain questions in the KOOS Knee Survey with a change of ≥10 points
- Clinically significant improvement of at least 20% from baseline on the WOMAC function questions in the KOOS Knee Survey with a change of ≥10 points
- Freedom from the following device-related serious adverse events:
  - deep infection requiring surgical intervention (Both arms)
  - damage to adjacent neurovascular or ligament structures necessitating reconstruction (Both arms)
  - non-union (HTO only)
- Maintenance of implant integrity as evaluated by radiographic assessment

NOTE: A subject was considered a non-responder if they had a conversion to arthroplasty or loss of implant integrity of the MISHA Knee System at 24 months.

Primary Endpoint

The primary composite clinical success rate (CCS) at Month 24 was 83.5% for the investigational arm and 57.2% for the control arm (p=0.015), demonstrating both statistical non-inferiority and superiority. There was a high Month 24 responder rate in the MISHA Knee System arm for pain and function at 95.8% and 91.7%, respectively.

Table 3: Primary Endpoint Responder Rates

Outcome	MISHA Knee System			Control (HTO)			p-value
	N	n	%	N	n	%	
Enrolled	81	81	100.0%	81	81	100.0%	
WOMAC Pain endpoint responder	72	69	95.8%	58	51	87.9%	
WOMAC Function endpoint responder	72	66	91.7%	64	52	81.3%	
No Safety Endpoint Event (CEC)	81	77	95.1%	81	76	93.8%	
No Endpoint Implant Integrity Failure	81	80	98.8%	81	80	98.8%	
No Endpoint Subsequent Surgical Intervention	81	80	98.8%	81	80	98.8%	
Composite Clinical Success (CCS)	**81**	**--**	**83.5%**	**81**	**--**	**57.2%**	**0.015**

The **secondary endpoints** included the following measures of recovery and early and sustained pain and function improvement as tabulated below.

Table 4: Secondary Effectiveness Endpoints

Secondary Endpoints Primary Analysis Set (N=162)									
	MISHA Knee System				Control (HTO)				
	N	Mean	SD	Med	N	Mean	SD	Med	p-value*
Time to Full Weight Bearing (Days)	81	13.4	10.12	12.0	77	58.0	39.91	48.0	<0.0001
WOMAC Pain % change to Month 3	81	-55.5%	29.3%	-55.6%	72	-33.4%	35.8%	-34.7%	0.0001
WOMAC Pain % change to Month 24	72	-76.0%	28.2%	-88.2%	58	-64.7%	33.0%	-72.5%	0.0157
WOMAC Function % change to Month 3	81	-52.2%	32.0%	-52.8%	75	-25.2%	37.0%	-24.3%	0.0001
WOMAC Function % change to Month 24	72	-73.9%	29.6%	-84.0%	64	-58.8%	35.8%	-67.1%	0.0018

*Four of the five secondary endpoints demonstrated superiority. Based on FDA's recommendation for use of a 1-sided α=0.0125 criterion, as the maximum 1-sided p-value = 0.0157 > 0.0125, superiority in WOMAC Pain % Change from Baseline at Month 24 could not be demonstrated.

Safety Results

Adverse events were evaluated throughout the Month 24 follow-up period. There were no significant differences between the two arms for all serious study knee related events, except a higher rate of pain in the control arm. There were no mechanical failures in the investigational arm.

Table 5: Study Knee Related Serious Adverse Events

AE Term	MISHA Knee System #events/#subjects (%subjects) (N=81)	Control (HTO) #events/#subjects (%subjects) (N=81)	p-value
Anesthesia complications: Other, respiratory symptoms	2/2 (2.5%)	0/0 (0%)	NS
Bleeding: Hematoma	0/0 (0%)	1/1 (1.2%)	NS
Discomfort: Catching or pulling sensations	2/2 (2.5%)	0/0 (0%)	NS
Discomfort: Inability to perform certain tasks, such as lifting, exercising, etc.	2/2 (2.5%)	0/0 (0%)	NS
Hospital readmission: Removal of implant due to dissatisfaction	1/1 (1.2%)	0/0 (0%)	NS
Infection: Cellulitis	1/1 (1.2%)	0/0 (0%)	NS
Infection: Deep incisional surgical site infection	4/4 (4.9%)	2/2 (2.5%)	NS
Infection: Superficial incisional surgical site infection	0/0 (0%)	1/1 (1.2%)	NS
Nerve injury (neuropathy): Injury to a nerve resulting in motor or sensory symptoms	1/1 (1.2%)	1/1 (1.2%)	NS
Other: Other, Bone Consolidation	0/0 (0%)	3/3 (3.7%)	NS
Pain	4/4 (4.9%)	30/29 (35.8%)	< 0.001
Phlebitis (Blood Clot) / Thrombophlebitis: Superficial venous thrombosis (Superficial Thrombophlebitis)	0/0 (0%)	1/1 (1.2%)	NS
Psychological event: Other, Kinesiophobia	1/1 (1.2%)	0/0 (0%)	NS
Scar Formation: Other, -MISHA: Periprosthetic adhesions / fibrosis in conjunction with screw loosening -HTO: Neuroma in the area of the scar	1/1 (1.2%)	1/1 (1.2%)	NS
Scar Formation: Periprosthetic adhesions / fibrosis	1/1 (1.2%)	0/0 (0%)	NS
Swelling	0/0 (0%)	2/2 (2.5%)	NS
Wound: Other, Injury	0/0 (0%)	1/1 (1.2%)	NS
Wound: Wound dehiscence (post explant)	0/0 (0%)	1/1 (1.2%)	NS

The rate of secondary operations for implant removal in the investigational arm was significantly lower than the control arm. The investigational arm had 11/81(13.6%) implant removals. Only one subject in the MISHA Knee System arm (1/81, 1.2%) was converted to 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). The control arm had 61/81 (75.3%) implant removals. Only one subject in this arm (1/81, 1.2%) underwent joint modifying surgery after implant removal. Reasons for removal were bone consolidation - prevention of future problems (30), pain (27), swelling (2), bone consolidation with plate pain (1), and nerve injury/neuropathy (1).

Table 6: Study Knee Removals and Conversions

	MISHA Knee System (N=81)	Control (HTO) (N=81)	p-value
Hardware Removal	11	61	<0.001
Endpoint Failure (e.g., Conversion/Joint Altering Surgery)	1	1	NS

Interpretation of Symbols

LOT	Batch code
REF	Catalog number
	Use by
QTY	Quantity
STERILE R	Sterilized using irradiation
	Non-pyrogenic
	Caution
	Do not use if package is damaged
	Consult instructions for use
	Do not reuse
	Do not resterilize
	MR Conditional
	Manufacturer
℞ only	Prescription Use only

REQUESTS FOR INFORMATION

For further information, please contact Moximed Customer Service.

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For the Moximed family of products, including the MISHA Knee System, patents please see: https://moximed.com/patents/