Title: Total Osteo-Cartilage Replacement for the treatment of Osteoarthritis of Knee

Dated: 27th July 2026

3. Study Protocol

Total Osteo-Cartilage Replacement for the treatment of Osteoarthritis of Knee

Protocol Number:	113110 Version 105
Version Date:	January 2026
Investigational Product:	Total Osteo-Cartilage Replacement
IND Number:	
Development Phase:	Phase I
Sponsor:	Prof Sadat A AlAli, Dr Hussain K AlOmar Dr Omar Dahluli.
Funding Organization:	None
Principal Investigator:	Name: Dr Jamal Saleh AlSalam Specialist Hospital, Bahrain Telephone: +97336599999 E-mail: drjsaleh@gmail.com
Medical Monitor:	
Coordinating Center:	

.

Approval:

Principle Investigator: Dr Jamal Saleh.

Sponsors Signatures :

Dr Sadat A AlAli

Dr Hussain AlOmar.

Dr Omar Dahluli

This confidential information about an investigational product is provided for the exclusive use of investigators of this product and is subject to recall at any time. The information in this document may not be disclosed unless federal or state law or regulations require such disclosure. Subject to the foregoing, this information may be disclosed only to those persons involved in the study who have a need to know, with the obligation not to further disseminate this information.

5. Study Protocol

Total Osteo-Cartilage Replacement for the treatment of Osteoarthritis of the Knee

Protocol Number: 113110 Version 105
Version Date: January 2026
Investigational Product: Total Osteo-Cartilage Replacement
IND Number:
Development Phase: Phase I
Sponsor: Prof Sadat A. AlAli,
Dr Hussain K AlOmar
Dr Omar Dahluli.

Funding Organization: None
Principal Investigator: Name: Dr Jamal Saleh
AlSalam Specialist Hospital, Bahrain

Telephone: +97336599999
E-mail: drjsaleh@gmail.com

Medical Monitor:
Coordinating Center: RCSI, Bahrain
.

Approval:

Principal Investigator: Dr Jamal Saleh.

Sponsors Signatures :
.

Dr Sadat A AlAli

Dr Hussain AlOmar.

Dr Omar Dahluli :

Date: March 2026

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PROTOCOL AGREEMENT

I have read the protocol specified below. In my formal capacity as Investigator, my duties include ensuring the safety of the study subjects enrolled under my supervision and providing [Dr Jamal Saleh] with complete and timely information, as outlined in the protocol. It is understood that all information pertaining to the study will be held strictly confidential and that this confidentiality requirement applies to all study staff at this site. Furthermore, on behalf of the study staff and myself, I agree to maintain the procedures required to carry out the study in accordance with accepted GCP principles and to abide by the terms of this protocol.

Protocol Number: 113110 Version 105

Protocol Title: Total Osteo-Cartilage Replacement in the Treatment of Osteoarthritis of the Knee

Protocol Date: March, 2026

Investigator Signature Date March 2026

Print Name and Title: Dr Jamal Saleh
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LIST OF ABBREVIATIONS

OAK
NSAIDs
Osteoarthritis of the Knee
Non Steroidal Anti-Inflammatory drugs

TKR	**Total Knee Replacement**
KL	**Kellgran and Lawrence**
VAS	**Visual Analogue Scale**
IKDC	**International Knee Documentation Committee**
TOCR	**Total Osteo-Cartilage Replacement**
NHRA	**National Health Regulatory Authority**

PROTOCOL SYNOPSIS

Title: Total Osteo-Cartilage Replacement in the Treatment of Osteoarthritis of the Knee

Sponsors:	**Prof Sadat A. Al-Ali,** **Dr Hussain K AlOmar** **Dr Omar Dahluli.**
Funding Team:	**Prof Sadat A. Al-Ali,** **Dr Hussain K AlOmar** **Dr Omar Dahluli.**
NUMBER OF SITES	**1**

Background:

Overview of Non-Clinical Studies:

There are no animal studies, but the author has performed cadaveric surgeries using TOCR.

Overview of Clinical Studies

1.2 Overview of Clinical Studies

History of Allograft Use in Joint Replacement.

The use of allografts in joint replacement is not new. The clinical use of allograft joint transplants was first introduced by Lexer in 1908[1], which was converted to total joint transplantation as early as 1925.[2] Allograft tissue works through a process called "osteoconduction." Imagine a vine growing through and around a trellis. Allograft tissue works in a similar fashion. An allograft is like a scaffold that supports the bone-forming cells as they grow new bone over time. Allografts have a 90.9% survival rate.[3] In 1972, Gross and Colleagues from Toronto[4] replaced 50% of the tibial plateau with success in 72-year-old women with bilateral osteoarthritis of the knee. In 9 patients in whom the part of the femoral condyle was replaced by allografts, there was a good range of movements with no collapse of the joint. Histopathological analysis revealed cartilage viability. Two years of interim observations are encouraging enough to continue with this technique in the knee with a severe enough disease not to be helped by osteotomy but not so diffusely damaged as to require total knee arthroplasty.[4] Volkov (1970)[5] reported Allotransplantation of joints in 142 patients from partial to total joints with reasonable success. Gross et al. (2005)[6] reported the long-term results of allograft transplant, with a 10-year survival rate of 80%. In the last few decades, the improvement of the harvesting and processing of the allograft has made the option of TOCR on a routine basis an excellent option for patients who want to lead an active life post-knee replacement.

In the latter part of the last century, in 1984, the first meniscus transplantation was performed. A review after five years gave an excellent outcome.[7] Allograft meniscus transplantation outcomes were reported as acceptable, with reported significant improvements in clinical outcome and a low failure rate.[8]

Meniscal transplants are reported to heal the knee capsule completely or partially in close to 100% of cases when assessed arthroscopically.[9-11] Recently, Gelber et al. (2018)[12] performed an allograft of the tibial plateau in significant post-traumatic osteochondral defects of the proximal tibia to avoid partial arthroplasties. The transplantation of the osteochondral graft with the meniscus improved the final outcome.

2.0 Study Rationale:

Osteoarthritis of the Knee (OAK) is mostly due to the aging process, and as suggested, many factors influence the severity of the disease. The prevalence of OAK in the knee is unknown, but with a prevalence of 365 million people suffering from OAK[13] and the knee being the most frequently affected joint, 344 million people living with osteoarthritis experience severity levels (moderate or severe) that could benefit from treatment.[14] OAK contributes >$27 billion annually in health care expenditures in the USA.[15] The incidence of OAK, but recent reports indicate the prevalence of clinical OAK increased many-fold to 13% and radiological OA of the knee to 52% in males and 60.9% in females.[16-18] The incidence of OAK in Bahrain is reported to be 37.9%.[19] The management of the OAK has been with non-steroidal anti-inflammatory drugs NSAIDs, physical therapy, and nutritional supplements.[20-25]

Even though the prevalence has increased, no new treatments have been added apart from NSAIDs and physical therapy, and the OAK progresses slowly till the joint is destroyed and

quality of life is severely affected. The knee joint is still the most common affected joint with osteoarthritis.[26] Some patients only require non-steroidal anti-inflammatory drugs (NSAIDs) and physical therapy, and in certain groups of patients, the disease progresses, leading to severe disability. Many patients do not respond to the conservative therapies and require steroids and hyaluronic acid injections, arthroscopic joint washout, with varying degrees of pain relief. [23]

In the recent past, cell-based therapies, particularly Mesenchymal Stromal Cells (MSC) for the repair of damaged cartilage and relief of pain, have been tried in experimental animals with excellent results. Cells (MSC) for repair of damaged cartilage and relief of pain in rabbits and sheep.[27-28] Recently, Jo et al (2014)[29] conducted a phase I/II A Proof-of-Concept clinical trial, in which they injected MSCs into the osteoarthritic knee. Post-injection analysis at 3, 6, and 12 months showed improved function and total relief of pain in the knee joint without causing adverse events and reduced cartilage defects by regeneration of cartilage, which was similar to hyaline cartilage histologically. Soler et al (2016)[30] used autologous MSCs in patients with Grade II and III of Kellgren and Lawrence grading and found that a single intra-articular injection of the MSCs was safe and provided complete pain relief, improved quality of life up to 4 years, and radiological signs of cartilage repair. Recently, Sadat-Ali et al (2021)[31] reported the first study in the Middle East with a clear benefit of autologous bone marrow-derived chondrocytes in reversing the OAK if treated early.

There are clear indications that there is an increasing prevalence of OAK among the Gulf population, with the number of Total Knee arthroplasties on the rise even in young patients. The management of OAK by way of arthroplasty is expensive and complicated. Complications of TKR include vascular and neural injury, instability, malalignment, stiffness, joint infection, tibiofemoral dislocation, wear and tear of the polyethylene insert,

osteolysis, implant loosening, revision, and amputation.[32] Apart from the surgical complications, there is a clear limitation of cultural activities like praying and kneeling on the ground with the regular TKR added to the shorter life span of the implants, making revision more dangerous and expensive. Among the possible complications associated with TKR, infection is the most serious and occurs in up to 9-21% percent of the cases; the resulting consequences include postoperative prosthesis failure, chronic pain, and immobility. An infection after knee replacement surgery can be a serious complication. Treating an infection can include multiple surgeries, and still, the infection is quite hard to eradicate. Infection happens due to the metallic implants. Bacterial biofilms, which are adherent to the implants, can be reduced by surface coating or micro-structuring; it is difficult to eliminate adhesion completely, and some bacteria may still attach to the implant surface. Once bacteria adhere, a biofilm may develop on the implant surface, which is difficult to treat. Once bacteria adhere, a biofilm may develop on the implant surface, which is difficult to treat. Subacute infections occur 3 to 24 months postoperatively (2 to 10 weeks for osteosynthesis) and are caused by low-virulence pathogens contaminating the implant during surgery. Late infections occur more than two years after surgery (more than ten weeks for osteosynthesis) and usually result from blood-borne dissemination.

It is reported that 2.2 million bone grafts are used in orthopaedic surgeries in the world yearly, and it is extrapolated that this will increase by 13% yearly. Allografts reported an infection rate was reported as 1.2%[33] compared to regular TKR of 9% and higher in patients undergoing revision 21%.[34]

The reported complications of revision TKR include:

Issues with wound healing at the operative site.

Stiffness and decreased range of movements.

Infection in the new prosthesis.

Secondary hemorrhage.

Deep vein thrombosis and pulmonary embolism)

Bone fracture during surgery.

In another study, 225 revision TKAs were performed from 2003 to 2012, and 120 had complications (53.33%). The indication of revision TKA were septic complications in 120 and aseptic complications in 86. The main aseptic complication was a periprosthetic fracture in 36, followed by 25 loosening, 13 polyethylene wear, and nine unstable knees. During the final follow-up, there were improvements in the range of movements and Knee scores and WOMAC scores. In seven patients who had re-revision due to reinfection in 6 and periprosthetic fracture in 1.[35-36] In the last decade, bi-cruciate retaining TKR was introduced and showed promising results in younger patients. [37-38]

Colangeli et al (2007)[39] compared TKR with allograft in patients with different pathologies, not osteoarthritis, and found that patients in the TKR group suffered from extension lag and knee stiffness when compared to the allograft knee, which had a significantly higher proportion of patients with a normal knee pattern. Even the functional gait was abnormal in TKR patients while in allograft patients had more of normal walking. It was concluded that an allograft gives better functional results. Even in complicated cases of revision TKR allograft is routinely used. It was concluded that a structural allograft is the only method to combat the loss of bone stock and can restore the lost bone due to infection or any other cause. Moreover, allograft reconstruction is indicated in young patients and not in the less demanding elderly patients. On the whole, the use of allografts gives good outcomes in the literature.[40,41]

To fulfill the limitations of TKR, Total Osteo-Cartilage Replacement (TOCR) is proposed. With TOCR and with this procedure, it is expected that there will be an increase in the range

of movements near normal, allowing the performance of religious and cultural obligations, continuation of regular physical activities and exercises, and, moreover, operation in young patients. The allografts that will be used are from donors of <35 years and impending OAK to develop in the circumstances that take place around 55 years of age, giving a window of survival of the graft for OAK >20 years as per the literature.

3.0 Study Objectives:

Primary Objectives: Assessment of Allograft in osteoarthritis of knee

Time Frame: 36 months

3.1 primary Safety Endpoint.:

The primary end point is to assess the whether the allograft can be used in the osteoarthritis of knee.

Secondary End Points:

Assessment of range movements using WOMAC (Western Ontario University McMaster Osteoarthritis Index) In a standard total knee replacement there is restricted range of movements and the implants does allow to kneel or sit on the ground for muslim prayers.

Time Frame: 3,6,9,12, 18, 24 and 36 months. pain=0-20, stiffness=0-8, physical function=0-68. a total WOMAC score is created by summing the items for all three subscales (max score 96).

4.0 Study Design:

Prospective: This is an open-label, non-randomized study with Total Osteo-Cartilage Replacement (TOCR) in Osteoarthritis of the knee requiring Total Knee Replacement.

In the procedure 9 mm thickness of cartilage of the femoral condyle and up to 13 mm of the proximal tibia will be replaced. The study will assess the safety and feasibility of this type of surgery. Once this is successful, then a comparative study will be performed with a control arm. The control arm will be of patients who had undergone TKR and this group will be matched with age and gender.

5.0 Number of Subjects: TEN (10)

1. Rule of Thumb Method: This method is based on the experience and judgment of experts in the field. It is typically used when there is limited information available on the intervention being tested. A commonly used rule of thumb is to enroll between 6 and 15 subjects in phase 1 trials.
2. Power Analysis Method: This method is based on statistical calculations and requires a priori assumptions about the parameters of interest (e.g. effect size, variance). It is used when there is more information available on the intervention being tested. The sample size is estimated based on the desired level of power and the statistical significance level.
3. While early, ultra-small studies (10–15 patients) exist, they are often exploratory "phase 0" trials, not full Phase 1 studies. Once this trial is successful a full Phase I trial with 20 patients could be performed.

Teresi JA, Yu X, Stewart AL, Hays RD. Guidelines for Designing and Evaluating Feasibility Pilot Studies. Med Care. 2022 Jan 1;60(1):95-103

6.0 Study Population and Subject Selection Criteria:

6.1 Ten Healthy male or female patients with grade KL III and IV OAK.

6.2 Inclusion Criteria:

The inclusion criteria:

- Being between 45 and 70 years of age of either gender. (OAK is common in this Age group)
- Diagnosed with OAK with Kellgren and Lawrence Grading III and IV.
- No ligamentous laxity and varus or valgus deformity. (In standard TKR patients with ligamentous laxity Constrained Condylar Knee (CCK) with intramedullary stem is used).
- Patients who wish to have an active lifestyle.
- Agreeing to participate and signing informed consent voluntarily.
- The patients will be assessed at Salmaniya Hospital and AsSalam hospitals and the cost of XRays, Blood tests and MRI if required will be born by the Hospitals and Sponsors.

6.3 Exclusion Criteria:

- Previous knee surgery within six months.
- Uncontrolled Diabetes Mellitus
- Chronic Kidney Disease. (Patients on hemodialysis)
- Metabolic bone disease. (Severe osteoporosis with T Score of -<3.5)
- Patients who will not consent to follow-up.

- Mental disorders and drug dependency (Patients who cannot understand the consent or the procedure of the TOCR).

7.0 **EFFICACY EVALUATION FOR** Total Osteo-Cartilage Replacement for the knee.

7.1 Primary Endpoint:

The objective of the study is to assess the benefits of TOCR in osteoarthritis of the knee in comparison to the standard TKR in terms of pain, stiffness and range of movements.

Assessment of pain: Intensity/Severity: Pain is assessed using a scale from 0 (no pain) to 10 (worst possible pain), daily, three times a day, and on every visit.

Secondly, use of pain medications postoperatively X 3 days.

Stiffness: Involves evaluating the knee's range of motion (ROM), with common definitions of stiffness including a flexion of less than 75° and a lack of full extension, postoperatively and at every visit. The primary end point is to relieve severe knee pain and improve functional mobility **with** Return back to near normal range of movements and aiming for a significant reduction in discomfort and improved quality of life.

7.2 Secondary Endpoint:

Secondary End Points: often include the range of motion (achieving at least –120°+ flexion) and to reduce the incidence of complications like infection or loosening. To assess the increase in function (range of movement) of the TOCR-replaced knee joint and improvement of normal lifestyle and physical activities prior to TOCR, such as kneeling, regular praying, and recreational sporting activity. Post-TOCR assessment will be made

using a combination of patient-reported outcome measures (PROMs), clinical objective evaluations, and implant survivorship.

To assess the increase in function (range of movement) of the TOCR-replaced knee joint and improvement of normal lifestyle and physical activities prior to TOCR, such as kneeling, regular praying, and recreational sporting activity.

The Comparison with the regular TKR will be made from the reports in the literature,

The objective of the study is to assess the benefits of TOCR in osteoarthritis of the knee in comparison to the standard TKR in terms of pain and stiffness for 3 years.

Post-TOCR assessment will be made using a combination of patient-reported outcome measures (PROMs), clinical objective evaluations, and implant survivorship. The follow-up study will continue for a minimum of three years.

7.3 Safety Evaluations:

7.3.1 Report Incidence of Adverse Events: as per the NHRA guidelines of AE, SAE.

7.3.2 Other Evaluations: X-rays and MRI

8. **Concurrent Medications:** No restrictions whatsoever.

9.0 **STUDY TREATMENTS**

9.1 **Method of Assigning Subjects to Treatment Groups:** Consecutive Patients.

9.2 **Blinding:** None

9.3 **Packaging and Labeling:** Custom Matched Allograft will be imported from the company in USA.

9.4 **Supply of Study Implants at the Site**:

Custom Matched Allograft will be imported from the company in USA.

9.5. **Storage:** Will be stored for 100 hours in the saline and then in -80^0 centigrade as per the requirement of the companies supplying the Allografts.

9.6 Measures of Treatment Compliance: None.

10. **Study Procedures and Guidelines:**

The hospital has a structured consent form that will be utilized in the study.

10.1 Study Overview

The researchers intend to study 10 patients with grade III and IV osteoarthritis (KL grading), who require TKR. This will be an open-label, single-arm clinical trial of TOCR. The endpoints will be based on the core outcome set (COS). The study was based on the IDEAL-D (Idea, Development, Exploration, Assessment, Long-term Follow-up) stages of assessment for interventional therapy innovation. The idea and development have been conducted before, and in the present study, the surgery and its assessment follow-up. Assessment of the surgery and patients' recovery will be measured by the Visual Analogue Scale for pain and mWOMAC score.[20,42]

The stability of the TOCR will be assessed by clinical examination at 3, 6,9, 12, 18, 24 and 36 months and MRI at 6 and 12 months as needed. For the next two years, patients will be followed every 6 months, informed consent will be obtained from the patient, and the patient will follow up for at least 36 months. Pain radiographs will be done, and a custom-built matched allograft will be ordered for individual patients. The patients will undergo the standard cruciate retaining TKR cuts of the distal femur and proximal tibia.

Procedure for the TOCR:

A cruciate knee replacement requires less bone and soft tissue resection. A more normal transmission of the weight-bearing stresses is possible compared to other knee

replacements.[38] Preserving both cruciate ligaments mandates the correct tension on all ligaments. Bi-cruciate retaining (BCR) TKA is considered to show improved clinical function and kinematics. The standard technique of the Bi-cruciate retaining (BCR) TKA is described. The importance of retaining both the cruciate ligaments cannot be over emphasized. IN TOCR both the cruciate ligaments retained are native. The Cruciate ligaments, particularly the Anterior Cruciate Ligament (ACL), are vital for knee proprioception, acting as specialized sensors that inform the brain about knee position, movement, and load. They contain mechanoreceptors that initiate reflex muscle contractions to stabilize the joint. In standard TKR both the cruciate are removed making the stability on the implants.

the standard cuts of the Femur and Tibia using the routine instrumentation of the Bi-cruciate retaining (BCR) TKA. During regular TKR, the bone segments removed are discarded, and this will follow the same procedure as TOCR.

2. TOCR uses standard instrumentation of the bi-cruciate retaining TKR.

3. All the cuts and procedures are similar to the TKR.

4. Instead of metallic and polyethylene implants, a custom-matched Allograft of the femoral cartilage and Tibial plateau will be performed.

5. The Allograft will be fixed with 2 Acutrak 2, 7.5mm X 120mm long, in the femur and tibia.

6. The menisci will be sutured to the capsule of the native joint.

6. The custom-matched allografts will be obtained by MTF Biologics, New Jersey, USA.

7. The surgeons will carry out the initial 10 cases, and the cost will be borne by the Patent holders.

8. Will take liability medical insurance for the patients to be treated if there are any complications. If the TOCR fails patients will undergo standard TKR and will be covered by the Insurance and Sponsors.

9. The failure of the procedure could be infection which will be treated by antibiotics on out patient basis.

10. As postoperatively patients will have routine physical therapy to strengthen the muscles and proper gait training for one month. On regular assessment if required this period will be

11.The there is a failure of union then a bone graft can be further augmented and worse is to take out the allografts and perform the standard Total knee replacement.

All the additional costs will be covered by the insurance.

All patients will be instructed to report immediately to the hospital if any side effects are noted. Depending on the adverse effects, patients will continue or stop further treatment. All patients without or with adverse events will be followed for 36 months from the time they were operated on. All Adverse Events (AEs) were noted at every visit and were graded based on the intensity (mild, moderate, or severe) and relevance (serious, non-serious).

Post-surgery patients will have the routine mobilization protocol by physical therapy as for standard TKR.

10.2 Clinical Assessments : made at 0, 3, 6, 9, and 12 months. Then every 6 months for 36 months Using modified WESTERN ONTARIO AND MCMASTER OSTEOARTHRITIS INDEX (WOMAC)

10.3 Demographics

Demographic information (date of birth, gender, weight, and height) will be recorded at the

beginning of the study.

10.4 Medical History

Relevant medical history, including history of current disease, other pertinent respiratory history, and information regarding underlying diseases, will be recorded at Screening.

10.5 Physical Examination

A complete physical examination will be performed by either the Investigator or a sub-investigator who is a physician at the start of the study.

Vital Signs: Body temperature, blood pressure, pulse, and respiration will be measured after resting for 5 minutes at the start of the study.

10.6 Oximetry: Not Applicable

10.7 Spirometry: Not Applicable

10.8 Clinical Laboratory Measurements (include sections as appropriate)

10.9 Hematology: Complete blood picture will be done at the start of the study.

10.10 Blood Chemistry Profile: As needed

10.11 Urinalysis: As needed

11 Evaluations By Visit: 0,3,6,9, and 12 months. Every 6 months for 36 months.

11.1 Visit 1 Date:

1. AS per the inclusion criteria.
2. Assign the subject a unique screening number.
3. Consent
4. Record demographics data.
5. Record concomitant medications.
6. Perform a complete physical examination.
7. Perform and record vital signs.
8. Fill out the Modified WOMAC
9. Order X-rays of both Knee joints
10. MRI-affected Knee joint. As needed

11. Treatment of Adverse Events and Side Effects:

11.1. As per the NHRA regulations, all adverse events and the side effects will be communicated to the Sponsors and NHRA within a 7-day period.

11.2: **Safety & Adverse Event Reporting:**

An Adverse Event (AE) monitoring plan:

1. AE will describe the process for identifying, classifying, reporting, and managing

2. AE will be reported by Sponsor-Applicant-CRO and Investigator inform to NHRA/ and Institutional IREC within two working days of any serious adverse event (SAE) occurring the clinical trial/research study, whether expected or unexpected.

3. Action taken on the AE.

SAE: SUSAR monitoring

Serious Adverse Events (SAEs) are any undesirable medical occurrences or effects that result in death, are life-threatening, or require or prolong hospitalization.

SAE will be reported within 2 days to the PI, IRB, and NHRA.

4. Annually, reports of AE, SAE will be sent to the Clinical Trial Section of the National Health Regulatory Authority (NHRA), as well as reports of sentinel events and medical device-related issues or falsified devices, promptly using specific NHRA forms.

Additionally, any complaints/side effects of the implants will be reported via the designated reporting forms to the NHRA.

All adverse events will be appropriately treated at AlSalam Specialist Hospital or any other hospital in Bahrain. All patients will be medically insured for recovery from conditions arising from the TOCR procedure.

12. Discontinuation and Replacement of Subjects:

12.1 Withdrawal of Subjects:

Patients who wish to discontinue the treatment will be allowed and subjects.

Duration of the follow-up will be included in the analysis.

Replacement of Subjects will be done if more than five patients withdraw on the follow up.

12.2: Stopping rules of the Trial:

The trial will be stopped if there is failure primarily to protect patient safety, maintain ethical standards, or due to scientific and operational failures. The decision will be made

jointly by independent Data and Safety Monitoring Boards (DSMBs) (RCSI) committees IRBs based on pre-defined criteria such as increased of SAE if the people taking part are having unexpected and severe side effects.

13. Protocol Violations:

Any protocol violations will be reported in the analysis.

14. Patients Monitoring:

Will be done by RCSI.

15. Statistical Methods:

The data age, duration of the surgery, pain assessment, stiffness, and functional improvement, patient-reported outcome measures (PROMs), and objective clinical assessments will be entered in the database and analyzed using SPSS Ver 25. The data were expressed as a mean ± SD. Statistically significant differences between the different groups were determined using Student's t-test, and $P < 0.05$ was considered to be significant and was ascertained at a CI of 95%.

16. Data Collection and Retention:

The complete data will be collected and retained at AlSalam Specialist Hospital for the next 10 years or any other duration required by NHRA.

17. Subject Confidentiality: Patient confidentiality will be maintained at all cost.

18. Administrative, Ethical, Regulatory Considerations:

18.1 Protocol Amendments.

Every attempt will be made to avoid. If, due to unavoidable circumstances, any protocol amendment needs to be done, prior approval from the Ethical Committee and the NHRA will be obtained.

18.2 Institutional Review Boards and Independent Ethics Committees

All results will be communicated to the IRB, the ethical committee, and NHRA.

18.3 Informed consent will be taken from the patients/caregivers. Informed consent will be available in two languages, Arabic and English.

18.4 Publications

All publications will be submitted to the IRB, the Ethical Committee, and NHRA.

18.5 Investigator Responsibilities

The PI Investigators will be responsible for supervising the proper handling, operation of patients, and their follow-up.

At times, a certain task will be delegated to an appropriately qualified individual, but the ultimate responsibility will be the PIs.

As a PIs I will undertake full responsibility in promoting patient safety and the collection of quality research data.

References:

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