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Study Title: Clinical and Economic Comparison of Robot Assisted Versus Manual Knee Replacement

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PROTOCOL W/O TRACKING

MAKO SURGICAL CORP.

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Title: Clinical and Economic Comparison of Robotic versus Manual Knee Arthroplasty

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Background and Significance:

The primary indications for joint replacement surgery include severe lower extremity pain that prevents individuals from performing normal daily activities. The level of pain experienced by these patients cannot be managed successfully with oral medications, physical therapy, or joint injections of steroids or hyaluronic acid. The source of the pain most commonly is a result of arthritic changes in the joint; the arthritis may be due to osteoarthritis, rheumatoid arthritis, or traumatic arthritis. Patients who are appropriate candidates for partial joint replacement surgery also may experience joint stiffness that interferes with their normal daily activities. In addition, there usually is radiographic evidence of changes in the joint caused by the arthritic process. Joint damage is evaluated radiographically in order to classify the severity of the joint disease. Partial joint replacement surgery is performed to replace the diseased parts of the joint with prosthesis. There are a variety of options that surgeons and patients can choose for their joint replacement surgery. There are many different joint replacement component systems manufactured by several different companies; some systems are recommended for particular types of patients while others can be used in a greater number of patients. Recently, new techniques have been introduced that are classified as minimally invasive because they require smaller surgical incisions to implant standard joint prostheses. Patients who are younger, thinner, and in better overall health are usually the best surgical candidates for minimally invasive procedures.

Osteoarthritis affects 40 million Americans and 15 million people in the United States suffer from degenerative arthritis of the knee. Unicondylar knee arthroplasty (UKA) was introduced as a treatment option for degenerative arthritis of the knee in the early 1970's[1]. The procedure initially yielded variable results and this unpredictability resulted in broadly low levels of usage[1]. Recent improvements in the surgical techniques and technology used for UKA have increased the effectiveness of this surgery. As the average age of the United States population increases, this surgical procedure will become even more common. It is estimated by the Miliennium Research Group that there will be 55,100 unicondylar knee procedures in 2010 and the compound annual growth rate from 2009 to 2014 will be 8.3%.

UKA can be viewed as an attractive alternative to total knee arthroplasty (TKA) assuming the patient's osteoarthritis has remained isolated in a single compartment. UKA is generally a less invasive procedure than TKA. Since the procedure is less invasive there is usually less blood loss; more cartilage, tissue, and bone is sparred, which results in shorter recovery times than TKA. This procedure is attractive to adults who are interested in remaining active pain-free lifestyles as they age.

Medical Need:

The cost-effectiveness of healthcare interventions, especially new technology, is becoming essential. Comparing the procedural costs of robotic-assisted surgery and the outcomes of the patients versus TKA, the gold standard, will help substantiate whether robotic-assisted surgery from an economic

viewpoint is a cost-effective treatment. In addition the rehabilitation after knee replacement surgery is critical to achieving proper functional outcomes. Information pertaining to knee replacement post discharge costs has been limited. Due to the lack of studies and the continued growth in the number of knee arthroplasty surgeries it is imperative to track post discharge costs of all variables.

Specific Aim:

To document and compare the procedural and postoperative costs, recovery time, and outcomes of two procedure types:

- Robotic assisted unicompartmental knee arthroplasty
- Manual total knee arthroplasty

Methods Overview:

Objectives:

To quantify the procedural costs and clinical outcomes of knee replacement surgery.

- To quantify the costs associated with each type of discharge status of the patients (Home Care [HC], Skilled Nursing Facility [SNF], Inpatient Rehabilitation Unit)
- To compare clinical outcomes of the patients based on discharge status
- To report on postoperative length of stay for each type of knee arthroplasty
- To present the quality of adjusted life years of the patients using questionnaire EQ-5D
- To quantify the costs of postoperative medications prescribed to the patient during the rehabilitation period (name, refills, dosage, and manufacturer)
- To quantify the costs of postoperative therapy for the patients (facility and regimen)
- To quantify the indirect medical costs associated with DME (Walkers, Canes, etc.)
- To measure the increase in functional scores preoperatively and at the completion of physical therapy
- To compare the length of time for a patient to return to work
- To compare the length of time for the patient to return to driving

Endpoints:

- The costs related to each type of discharge status will be summarized per procedure type. The analgesic use, physical therapy, durable medical equipment, and postoperative visits will be used to calculate the total costs. The data will be tracked for 1 year.
- The clinical outcomes of the patients will be assessed using the Knee Society Score, KOOS, reduced WOMAC and Forgotten Joint Score. The results from these questionnaires may be compared preoperatively, postoperatively at 2 weeks, 6 weeks, 3 months, 6 months, and 1 year, depending on the surgeons regular post-operative visit schedule. The surveys will be reported by procedure type and by discharge type.
- The length of stay for each procedure type will be reported and compared.
- Each patient's quality of life will be assessed using the EQ-5D. It will be recorded preoperatively, postoperatively at 2 weeks, 6 weeks, 3 months, 6 months, and 1 year. These data will be compared by procedure type.
- The physical therapy regimen, number visits, and costs associated with each session will be recorded and reported on for each procedure type. Patients will be measured on how quickly they complete the physical therapy regimen prescribed.

- Durable medical equipment such as canes, walkers, etc. will be tracked. Each patient will record how long each device was used. The costs of each device will be obtained from the facility or manufacturer. The data will be compared per procedure type.
- Patients will be given a functional test by a physical therapist preoperatively to get an initial starting point. The physical therapist will create a regimen for the patient to complete post operatively with an end point that is reachable based on the starting point. The length of time associated with reaching the end point will be captured.
- Patient employment will be documented. In addition a patient's leave from work will be recorded which may include things such as; short-term disability, vacation, or unpaid leave from work. The patient's salary will be requested and used to track the cost of missed time. If a patient elects not to disclose salary his or her zip code will be requested in order to find the median salary per that area. Worker's compensation claims may or may not factor into rehabilitation adherence and recovery time and will therefore be excluded from this study.
- A patient's return to work and function at work will be logged. The information will be compared based on procedure type.
- The time it takes a patient to return to driving will be tracked. In addition if the knee replacement procedure was a performed on the left leg or right leg will be documented because this could factor into time it takes to return to driving. The length of time to return to driving will be reported by procedure type.
- The procedural costs of the different type of knee replacement allocated into different cost centers. The charges, costs, and reimbursements will also be examined and the data be gathered from the hospital accounting software.

Inclusion Criteria:

Study Design Patients will be recruited into the study under the direction of one of the principal investigators or qualified team members during regularly scheduled clinic visits. All patients over 21 years of age who require knee replacement surgery will be asked to participate in the study. These patients will have failed non-operative management of their joint disease and are candidates for partial joint replacement because of pain and joint stiffness that interferes with their performance of normal daily activities.

- Age, 21-80 years
- Sex, males and females will be included
- BMI less than or equal to 39
- Stable health, the patient would be able to undergo surgery and participate in the follow-up program based on physical examination and medical history
- Patient is willing and able to cooperate in follow-up therapy at Rebound facilities
- Patient has stable and functional collateral ligaments
- Patient or patient's legal representative has signed the Informed Consent form
- Failed non-operative management of their joint disease
- Need to obtain pain relief and improved function
- Moderate or severe pain with either walking or at rest
- Diagnosed with osteoarthritis in one or more compartments of the knee and non-surgical treatment options have failed to provide relief for symptoms

- Patient exhibits preoperative radiographic evidence of joint degeneration that cannot be treated in non-operative fashion

Exclusion Criteria:

Patients will be excluded from study participation if they are cognitively unable to complete study health-related quality of life forms and pregnant women are also excluded from participation in this study.

- Patients who, in the opinion of the Investigator, have an existing condition that would compromise their participation and follow-up in the study
- Patients with pre-op flexion contracture greater than 10 degrees, overall flexion less than 115 degrees, and varus/valgus greater than 10 degrees
- Patient who is on workmen's compensation
- Patients who are on chronic long acting preoperative narcotic pain medication
- Patients with inflammatory polyarthritis
- Women who are pregnant
- Subjects who are known drug or alcohol abusers or with psychological disorders that could affect follow-up care or treatment outcomes
- Subjects who are currently involved in another clinical study with the exception to an outcomes study
- Patients with a pathology which, in the opinion of the Principal Investigator, will adversely affect healing
- A diagnosed systemic disease that would affect their welfare or the overall outcome of study (i.e. Paget's disease, renal osteodystrophy)
- Patients receiving an isolated patellofemoral UKA, lateral UKA, or bi-compartmental arthroplasty
- Patients with significant medical condition preventing a well-functioning contralateral knee

Risk/Benefits:

This is a minimal risk study which involves collection of data. The purpose of this study is for research purposes only. There is no direct benefit to the patient to participate in this study. The results of this research study may contribute to clinical research overall and may be published.

Study Enrollment Procedure:

The study investigator will evaluate the patients for study inclusion/exclusion at their perioperative consultation visit. The surgeon will describe the various surgical options that he believes to be appropriate for each individual patient. The patient and surgeon then will determine which prosthesis is most appropriate for their surgical procedure. Then the surgeon or his assistant will explain the study to the prospective participant. Prospective participants will be encouraged to ask questions regarding study participation. Once they are fully informed about the study, the interested patients will be asked to sign a consent form.

Evaluation to be used for Knee Replacement Patients:

At each clinic visit which coincides with a study interval (preoperative, 2 weeks postoperative, 6 weeks, 3 months, 6 months and 1 Year) the surgeon or qualified member of the study will

- Assess the function and range of motion of the knee joint
- Document any complications that may have occurred after surgery
- Complete a radiographic assessment of the operated knee post-operatively per surgeon standard of care.
- Complete the Knee Society Score in order to provide a rating of the pain, function, range of motion, and knee joint stability for each patient
- Study participants will be asked to complete standardized health-related quality of life instruments to document their perception of their pain and function. Study participants will complete the following outcome instruments. These instruments can be completed via phone, mail, website, or email if a clinic visit is not required at the study interval per surgeon standard of care.
    a) The American Knee Society Score is subdivided into a knee score that rates only the knee joint itself and a functional score that rates the patient's ability to walk and climb stairs[2].
    b) The EQ-5D is a standardized instrument for use as a measure of health outcome. Patients will be also given a questionnaire with questions pertaining to employment, loss of wages, driving, etc.
    c) The Reduced WOMAC is a truncated version of the Western Ontario and McMasters University Osteoarthritis Index. The questionnaire is patient administered and designed to asses pain, disability and joint stiffness in the OA patient[3].
    d) The KOOS or Knee injury and Osteoarthritis Outcome Score is a patient completed questionnaire to assess the patient's opinion regarding their knee and its associated OA. Poor outcomes are reported with a lower score and good outcomes with a higher score [4-7].
    e) Post-op, the Forgotten Joint Score is a 12-item questionnaire completed by the patient to determine how aware they are of their joint in their everyday life[8].
- Post-op patients will complete a "progress report" regarding their satisfaction and rehabilitation.
- At 6 weeks post-op, patients will also be asked to complete a "return to function" questionnaire regarding their rehabilitation including their return to work and driving and physical therapy regimen. This questionnaire can be completed via phone, mail, website or email if a clinic visit is not required per surgeon standard of care.

In addition to regularly prescribed physical therapy, patients will meet with a physical therapist or qualified member of the study preoperatively for testing to create a starting point. They will also undergo multiple tests/ measurements at 6 weeks and 3-months postoperatively. The physical therapist will create a physical therapy regimen and create an endpoint for the patient. The endpoint will be goals within reach for each patient to complete before the patient can discontinue physical therapy.

- The patient will undergo a series of tests to create an initial starting point preoperatively and post operatively at 6 weeks and 3 months. The tests will be the following:
    - Timed up and Go (TUG) Test: Participants are instructed to stand up from a seated position from a standard chair, walk 3m around a cone and then return to the chair and resume a seated position. Pace is self-selected. The time to complete the test is recorded.

    - 6 Minute Walk Test (6MWT) : Participants are instructed to cover as much distance walking in 6 minutes and can stop and rest if necessary. The course is 30 meters in length, marked at 1 meter intervals with cones marking the turnaround point. Distance measured is rounded up to the nearest meter and recorded.
    - Stair Ascend/Descend Test: Participants are asked to ascend and descend 11 steps using a hand rail if necessary. Stair height is 17.8 cm (7”). Pace is self-selected. The time to ascend/ descend 1 flight of stairs is recorded.
- An achievable endpoint that the patient will need to meet to conclude the physical therapy is described below. The endpoint will include the following goals for the patient and will be assessed at each post-operative physical therapy visit until patient is discharged from physical therapy:
    - Range of motion 5 to 115 degrees
    - Strength 4/5 for flexion and extension, expressed as a percent of maximal isometric contraction.
    - Gait with minimal limp without an assistive device for a distance of 250 feet
    - Able to ascend/ descend a flight of stairs with step over gait with good control (and with use of handrail)
- The number visits and duration to reach the endpoint will be tracked by the physical therapist.
- If patient is unable to reach PT D/C criteria by 8 weeks post-op and is unwilling to continue physical therapy, the patient will be discharged from PT at 8 weeks and their current functional state will be recorded.

Time and Events Chart:

Action	Pre-operative	Intra-operative	2 weeks	6 Weeks	3months	6 Months	1 year
Issue patient information leaflet	X						
Obtain written informed consent	X						
Complete demography, medical history, medication, coexisting disease	X						
Radiographs collected	X		X				X
Intra-op Data		X					
PT Functional Assessment	X			X	X		
PT DC Criteria (Completed at EVERY PT visit)			X	X			
Return to function				X			
Progress Report			X	X	X	X	X
AKSS knee scores	X		X	X	X	X	X
EQ-5D	X		X	X	X	X	X
Reduced WOMAC	X		X	X	X	X	X
KOOS	X		X	X	X	X	X
Forgotten Joint Score			X	X	X	X	X
Advise patient when they will be seen next	X		X	X	X	X	X
Incentive payment of $50					X		X

Patient Follow-up:

All patients who chose to participate in the study and who undergo knee replacement surgery will be followed according to the "standard of care" follow-up guidelines in order to determine their functional status and health-related quality of life before and after surgery. Patients will be assessed by the surgeon or qualified member of the study before surgery and at postoperative visits scheduled at 2 weeks, and 6 weeks. Per surgeon “standard of care” visits may also be scheduled at 3 months, 6 months, and 1 year. Study questionnaires may be completed by the patient preoperatively, and postoperatively at 2 weeks, 6 weeks, 3 months, 6 months and 1 year.

Cost Data:

Financial data will be obtained from each facilities cost accounting system. If data cannot be attained using this method, CPT codes will be recorded and cross-referenced with the 2010 Medicare Fee Schedule. The financial data will be estimated using this method. The use of Medicare reimbursement rate is reasonable given that more than 60% of arthroplasty cases are reimbursed by this agency. A patient's analgesic use will be recorded by the surgeon and the Average Wholesale Price will be assigned to each script. Discharge data collected in this study will be compared to 2006 National Hospital Discharge Survey (NHDS).

Data Management:

All data will be collected using data collection forms or questionnaires in clinic or via phone, mail, website or email. The data dependent upon the questionnaire or form will be recorded by the patient, investigator, or qualified team member. Information will then be entered into a secure online data entry system by a qualified team member and the data will be stored in a secure database. Numerous business rules ensure that only properly formatted data is submitted. The information undergoes further verification by a human operator, who checks the integrity of each record prior to submitting it to the database. All access to the information- including reports, queries and data tools- is password protected and restricted to users that have the proper credentials. Information pertaining to cost data will be uploaded separately into the database.

Data Analysis:

Descriptive statistics consisting of frequency tables and percent for categorical variables and means, standard deviations, and ranges for continuous variables will be tabulated at the conclusion of the study.

General Statistical Considerations:

Tabulation of summary statistics, graphical presentations, and statistical analyses will be performed using SAS® software. The primary presentations and analyses will be based on data pooled across study centers. Relevant summaries for individual centers, or combinations of centers, may be presented for primary data. All patient data will be presented in separate data listings. All patients who are enrolled in this study and receive any of the treatments as part of this study will be included in the safety analysis. All testing and confidence intervals will use a 0.05 significance level. All testing is two sided unless otherwise noted.

Patient Characteristics:

The number of patients included in the evaluations, patients completing the study, and the reasons for any withdrawals will be tabulated by counts and percent. For all of the treatment groups, demographic data (age, height, and body surface area) will be summarized using descriptive statistics individually for each group and pooled across groups. Race and gender will be summarized using counts and percent. Homogeneity testing will be performed.

Timeline:

Recruitment of research assistant to begin immediately.

Patient enrollment to begin after IRB approval and continue for 18 months or until study participation reaches target enrollment.

Data collection and analysis to continue for 36 months or until 1 year data has been collected from all study participants.

References:

1. Willis-Owen, C.A., et al., *Unicondylar knee arthroplasty in the UK National Health Service: an analysis of candidacy, outcome and cost efficacy.* Knee, 2009. **16**(6): p. 473-8.
2. Insall, J.N., et al., *Rationale of the Knee Society clinical rating system.* Clin Orthop Relat Res, 1989(248): p. 13-4.
3. Whitehouse, S.L., et al., *Development and testing of a reduced WOMAC function scale.* J Bone Joint Surg Br, 2003. **85**(5): p. 706-11.
4. Radford, A., et al., *National surveillance of small animal disease in the UK.* Vet Rec, 2010. **166**(15): p. 471-2.
5. Roos, E.M., et al., *Knee injury and Osteoarthritis Outcome Score (KOOS)--validation of a Swedish version.* Scand J Med Sci Sports, 1998. **8**(6): p. 439-48.
6. Roos, E.M., H.P. Roos, and L.S. Lohmander, *WOMAC Osteoarthritis Index--additional dimensions for use in subjects with post-traumatic osteoarthritis of the knee. Western Ontario and MacMaster Universities.* Osteoarthritis Cartilage, 1999. **7**(2): p. 216-21.
7. Roos, E.M., et al., *Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure.* J Orthop Sports Phys Ther, 1998. **28**(2): p. 88-96.
8. Behrend, H., K. Giesinger, J. Giesinger, M.S. Kuster, *The 'forgotten joint' as the ultimate goal in joint arthroplasty: validation of a new patient-reported outcome measure.* J Arthroplasty, 2011.