Effects of Unloader Bracing in Clinical Outcome and Articular Cartilage Physiology Following Microfracture of Isolated Chondral Defects

Study Protocol

NCT02016300

December 13, 2011

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Background

The management of articular cartilage defects continues to be one of the most challenging clinical problems for orthopaedic surgeons. Articular cartilage is a highly organized tissue with complex biomechanical properties and substantial durability. However, it has a poor intrinsic capacity for healing, and defects resulting from trauma can result in considerable functional impairment and lead to subsequent joint degeneration and osteoarthritis. [1]

Bone marrow stimulation through 'microfracture' is the most frequently used technique for treating small symptomatic defects of the articular cartilage in the knee. It is a technically straightforward procedure, and the costs are low compared with those of other treatment modalities. Microfracture involves perforation of the subchondral plate in order to recruit mesenchymal stem cells from the bone marrow space into the lesion[2]. The formation of a stable blood clot that maximally fills the chondral defect is important, and it has been correlated with the success of bone marrow stimulation procedures[1].

Two aspects of post-operative rehabilitation are thought to be critical to the success of microfracture. First, protected weight-bearing for 8 weeks post-operatively protect the clot from shear forces, which may disrupt the clot and prevent healing.[3,4] Second, continuous passive motion is believed to encourage stem cell differentiation along a chondral pathway.[4,5]

During rehabilitation following microfracture, an unloading valgus brace may further enhance clot stability by protecting it from disruptive shear forces during motion. Unloader braces apply an external, valgus force by creating a three-point bending moment along the knee, which decreases the force on the medial compartment.

The aim of this pilot study is to determine whether the use of post-operative unloading brace will improve outcomes of the microfracture procedure for treatment of isolated cartilage lesions.

Study Design (Pilot Study)

Recruitment

A pilot study will be carried out at two centers. 20 patients will be enrolled at each center and be randomized to 2 groups. Patients will be identified from preoperative clinical and radiographic evaluation as potential candidates for the study, however as eligibility will depend on arthroscopic assessment of the cartilage lesion at the time of surgery final enrollment will occur immediately post operatively.

Inclusion criteria include a discrete, contained chondral defect less than $2cm^2$ in size located on the medial or lateral femoral condyle, age between 18-40 years, and overall neutral lower limb mechanical alignment (<5 degrees varus or valgus). Exclusion criteria include previous chondral procedures, osteoarthritis (Kellegren-Lawrence Grade ≥2), or significant concomitant knee pathology such as a meniscal tear requiring treatment or a ligamentous instability. Patients who have previously undergone ACL reconstruction or meniscal repair will still be eligible for inclusion in the study.

Initial post-operative protocol

All patients will participate in physical therapy two times per week, use a continuous passive motion device for eight weeks and will have no ROM restrictions. Following enrollment, 10 patients will be randomized into one of two groups at each center. Group 1 will be fitted with the Ossur Unloader One brace. Group 2 will be treated without a brace. At Center 1 (USA), patients will be initially kept non-weight bearing for a period of 8 weeks prior to applying an unloader brace. At Centre 2 (Japan), patients will wear an off-loading brace and commence weight bearing immediately post-operatively. Non-bracing group will be NWB for 8 weeks at both centers.

Outcome Measures

Radiographic outcome will be assessed using baseline, 6 month, and one and two year MRI scans which will assess the quality of the cartilage repair. T1 Rho and T2 mapping will be used to assess regenerate cartilage composition compared to surrounding normal cartilage, surface integrity, average cartilage thickness and the percentage to which the defect is filled. MRI mapping protocols investigate cartilage health by looking at glycosaminoglycan (GAG) concentration. Higher concentrations of GAG generally indicate healthier cartilage. Moreover, correlations have been found between T2 values and cartilage hydration, collagen fiber orientation, and loss of type 2 collagen, suggesting some degree of specificity for targeting the spatial collagen architecture of the matrix.[6]

Clinical outcome will be assessed at MRI follow-up time points using: The **Knee injury and Osteoarthritis Outcome Score (KOOS)** questionnaire is a standard clinical tool used to evaluate short-term and long-term symptoms and function in subjects with knee injury and osteoarthritis. It is broken up into five subcategories: Knee symptoms, knee pain, Function in daily living (ADL), Function in Sport and Recreation (Sport/Rec), and knee-related Quality of Life (QOL). The KOOS is a validated, reliable and responsive self-administered instrument that can be used for short-term and long-term follow-up of osteoarthritis and will given to our patients to evaluate the effect of the unloading braces. The KOOS incorporates the commonly used WOMAC survey.

Tegner activity level scale will be used to establish standardized activity levels pre and post treatment. **VR-12** quality of Life questionnaire will be used to establish changes in quality of life. **Lysholm** score will be used to reflect symptoms with activities of daily living. **VAS (Visual Analog Scale)** will be used to determine the level of patient pain at each visit.

Schedule of Appointments

Visit 1 (T=0)

Visit 1 will be the baseline visit and will take place at the first post operative visit. Participants will undergo the informed consent process. Once signed, participants will answer standardized questionnaires (see above), get fitted for the brace (if in bracing group), and undergo baseline MRI scans and x-rays to evaluate alignment. Wearing of the brace will commence at the time of weight bearing, which will occur immediately post-operatively in Centre 2 (Japan) and 8 weeks post operatively at Centre 1 (USA).

Brace fitting

Each participant will be fitted by a licensed orthotist for the Unloader brace.

Imaging

Each participant will undergo a pre-study series of X-rays that are standard for osteoarthritis examination. This series consists of a front-view (AP) X-ray of the knees, a sideways (lateral) view, and a one with the knee flexed at 45° (Rosenberg). There will also be a long standing X-ray (36") that will film the lower extremities. These films will measure any mal-alignment present.

A MRI scan during the first visit will examine cartilage physiology. The scans will take place at the Stanford Medical Outpatient Center or Stanford Medical Lucas Imaging Center with a 3T scanner. Subjects will undergo 2D-T2 mapping, 3D-T2 mapping, and 3D-T1rho mapping. These scans take approximately 12, 10, and 6 minutes, respectively. The total time for the first visit will last approximately 2 hours.

Brace wear and documentation

All patients will be provided with a hard copy bracing diary for the 6-month study duration. Patients will be instructed to document the number of hours for which they wear the brace each day. Diaries will be collected at Visit 2 and daily and weekly averages will be calculated for all patients.

Each Unloader brace will be equipped with an iButton temperature sensor that acquires temperature readings every 20 minutes to objectively document brace wear. The temperature threshold to determine brace wear is set at 25C. The iButton captures and stores these measurements for 1 month after which it must be reprogrammed; all participants will therefore undergo five iButton swaps. These visits will be managed by the orthotist who performs the initial brace fitting. The final iButton will be obtained at Visit 2. iButton data files will be post-processed by Duane Romo and daily and weekly averages calculated for each participant. These values will be compared with the bracing diaries completed by each patient.

Visit 2 (T=6 Months)

Visit two will consist of quantitative MRI scans conducted at the Stanford Medical Outpatient Center or the Stanford Lucas Imaging Center. The patient will also complete the same standardized questionnaires as in the first visit.

Visit 3 (T= 12 months)

The patient will return for another quantitative MRI scan and to answer the standardized questionnaires.

Visit 4 (T= 24 months)

The patient will come back again for a final MRI mapping scan and to answer the standardized questionnaires.

Benefits

All subjects requiring bracing will receive a fitted Unloader One off the shelf brace as compensation for their participation in the study.

Budget

Standard treatment costs, which the study sponsor will NOT be responsible for, include:

1. office visits

2. standard x-ray series
3. off-loader bracing (insurance reimbursement portion)

Sponsor study costs (per study site):

Year 1:

1. Any patient costs for Unloader brace NOT covered by insurance (unknown)
2. Biologic MRI scanning and T2 mapping analysis of 20 patients @ 4 scanning sessions @$600/scan [redacted]
3. MRI analysis (post doc radiologist @ 50% effort)= [redacted]
4. Study coordinator [redacted]

[redacted]

Year 2: [redacted] (MRI analysis and study coordinator only)

References

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