Patient Oriented and Performance Based Outcomes following Knee Autologous Chondrocyte Implantation: a time line for the 1st year of recovery

Context: It is well established that autologous chondrocyte implantation(ACI) can require extended recovery postoperatively; however, little information exists to provide clinicians and patients with a timeline for anticipated function during the first year following ACI. **Objective:** To document the recovery of functional performance of activities of daily living following ACI. **Patients:** ACI Patients(n=48, 29 males, 35.1±8.0yrs). **Intervention:** All patients completed functional tests (Weight Bearing Squat, Walk Across, Sit-to-Stand, Step Up/Over, and Forward Lunge) using the NeuroCom Long Forceplate(Clackamas, OR), and completed patient reported outcome measures (IKDC, Lysholm, WOMAC, and SF-36) preoperatively and 3, 6, and 12 months postoperatively. **Main Outcome Measures:** A covariance pattern model was used to compare performance and self-reported outcome across time and provide a time line for functional recovery following ACI. **Results:** Participants demonstrated significant improvement in Walk Across stride length from baseline(42.0±8.9 % height) at 6 (46.8±8.1%) and 12 months(46.6±7.6%). Weight bearing on the involved limb during squatting at 30°, 60°, and 90° was significantly less at 3 months as compared to pre-surgery. Step Up/Over time was significantly slower at 3 months(1.67±0.69) compared to baseline(1.49±0.33s), 6 months(1.51±0.36s), and 12 months(1.40±0.26s). Step Up/Over, lift-up index was increased from baseline(41.0±11.3 %BW) at 3 (45.0±11.7%BW) 6 (47.0±11.3 %BW) and 12 months(47.3±11.6 %BW). Forward lunge time was decreased at 3 months(1.51±0.44s) compared to baseline(1.39±0.43s), 6 months(1.32±0.046s), and 12 months(1.27±0.056). Similarly,

Forward Lunge impact force was decreased at 3 months(22.2±1.4 %BW) compared to baseline (25.4±1.5 %BW). The WOMAC demonstrated significant improvements at 3 months. All patient reported outcomes were improved from baseline at 6 and 12 months post-surgery.
Conclusions: Patients' perceptions of improvements may outpace physical changes in function. Decreased function for at least the first 3 months following ACI should be anticipated, and improvement in performance of tasks requiring weight bearing knee flexion, such as squatting, going down stairs, or lunging, may not occur for a year or longer following surgery.

Autologous chondrocyte implantation (ACI)[1] has become an acceptable and common treatment approach for the management of symptomatic articular cartilage defects.[2] As research regarding ACI has advanced sizable efforts have been made to evaluate both disease and patient oriented outcomes following ACI. Numerous studies have evaluated the utilization of patient reported outcome measures (PROs) to document the recovery of function and return to activity following ACI.[3-5] Meta-analyses of more than 43 studies have revealed large effect sizes demonstrating significant improvement for a variety of PRO scores following ACI.[5] PROs provide reliable and valid information regarding patients' perceived function and health related quality of life (HRQL).[6-13] An alternative to PROs is the use of performance based assessments (PBAs) to document outcomes. PBAs provide a direct, objective measure of patient function and involve measures of performance such as time, distance, or force for specified tasks or movements. The relationship between PROs and PBAs has previously been reported as low to moderate among a variety of knee patients.[14-19] This discordance may be due in part to the strong influence perceived pain may have on PROs. For example, PRO scores may increase even in the absence of improved function if a patient's pain has been resolved.[19-22] Recent research involving total joint arthroplasty patients has provided further support for the inclusion of PBAs as part of a detailed outcomes assessment protocol.[18-20] Combining PROs with PBAs may provide a more complete picture of clinical outcomes after ACI than the utilization of either type of outcome in isolation.

Few studies have utilized PBAs to document the return of function following ACI. Most of those that have, have either examined very low demand activity such as the 6 minute walk test,[23-27] or very high demand activity via the single-limb hop.[28] No known studies have examined the timeline for return to function following ACI using low to moderate demand PBAs that recreate the demands and stresses of common activities of daily living such as squatting, rising from sitting, or going up and down stairs, in addition to walking. A description of functional recovery during the first year following ACI is imperative to provide evidence for prescription of appropriate patient education, rehabilitation protocols, and understanding of the recovery process. Therefore, the purpose of this study was to document serial changes in knee function over one year following ACI using both PROs and PBAs. It was hypothesized that PROs would demonstrate significant improvement from baseline at all postoperative time points. It was also hypothesized that PBA measures for walking, rising from sitting, stepping up/over, and lunging would demonstrate no improvements at the 3 month time point followed by progressive improvement at 6 months and 12 months as compared to baseline measures of function.

METHODS

Patients

Between July 2008 and July 2011 patients were prospectively recruited from an active cartilage center. Inclusion criteria were planned ACI surgery to the medial or lateral femoral condyle, trochlea, or patella; willingness to participate; no uncorrectable contraindications to ACI such as extensive degenerative joint disease, insufficient meniscus, or unstable knee; and ability to ambulate without use of assistive devices. There were no exclusions based on limb malalignment if the malalignment was corrected prior to or at the time of surgery via high tibial osteotomy or tibial tubercle transfer. Similarly, patients undergoing concomitant or staged ligament reconstruction to correct joint instability were also eligible for study participation.

A total of 50 patients (31 males, 19 females, 35.0±7.9 yrs, 180.34±30.7 cm, 92.0±20.6 kg) agreed to participate. During the enrollment period four patients were invited to take part of the study, but declined to participate resulting in an enrollment rate of 93% of eligible patients. Of the enrolled patients 24 underwent ACI to the patellofemoral joint with a tibial tubercle transfer and the remaining 26 underwent ACI to the medial femoral condyle, of which 4 also had a concomitant high tibial osteotomy and 2 underwent concomitant meniscal transplantation. Mean number of defects treated per patient were 1.5 ± 0.6 with an average treatment area of 8.7 ± 6.8 cm^2 (range 1.96 to 39.0 cm^2). All participants signed a university approved IRB consent form at the time of enrollment.

Procedures

Surgical Procedures and Rehabilitation

All patients underwent a two-step ACI procedure performed by the same surgeon (CL). During the first procedure a limited chondroplasty was performed and the lesion was evaluated arthroscopically. At this time a biopsy was obtained from the intracondylar notch (100 to 200 mg cartilage). This sample was sent to a commercial laboratory where it was cultured and expanded (Carticel, Genzyme Corp, Cambridge, MA). In a second surgical procedure chondrocyte implantation was performed using a mini-arthrotomy. First the defect or defects were prepared using a curette to debride down to the subchondral plate with stable edges. A type I/III collagen membrane (Bio-Gide (R), Geistlich Biomaterials, Wohousen, Switzerland) was shaped to match the defect. Sutures and fibrin glue (Tisseel, Baxter Healthcare Corp., Deerfield, IL) were used to adhere the membrane over the defect to form a water tight seal. The chondrocytes in suspension were then injected beneath the membrane into the defect through a small portal remaining at the edge of the collagen membrane. The portal was then closed and sealed with sutures and additional fibrin glue.

All patients followed standardized rehabilitation protocols following surgery with considerations for defect location and concomitant procedures.[29] All patients were braced in full extension and were non-weight bearing for 2 weeks postoperatively. Toe-touch weight bearing was permitted from 2 to 4 weeks with partial weight bearing from 4 to 6 weeks and progression to full weight bearing between weeks 6 to 12. Continuous passive motion was prescribed for all patients for 6 to 8 hours per day for 6 weeks. For defects in the tibiofemoral joint, knee braces were gradually unlocked between 2 to 4 weeks as quadriceps control was gained. For defects to the patellofemoral joint, knees were braced in full extension for weight bearing through 4 weeks postoperative and then were gradually unlocked as quadriceps control was gained between weeks 4 and 6. Once good quadriceps control was gained all patients were transitioned to a hinged knee sleeve. All patients were recommended to abstain from high intensity cutting or pivoting activity until at least 12 months post ACI.

Patient Reported Outcomes

The PROs used in this study were the Medical Outcomes Study – 36 Item Short Form Health Survey Physical Component Scales (SF-36 PCS),[11, 30, 31] the Western Ontario and McMaster Osteoarthritis Index (WOMAC),[10] the International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form,[7] and the Lysholm scale.[32] The SF-36,[13] IKDC,[13] Lysholm, [8] and WOMAC[8, 13] have all been evaluated for reliability among cartilage patients. A researcher independent of the treating physician reviewed each instrument with the patients and was available to answer any questions they may have had. All PROs were completed at the following time points: prior to implantation (preoperation), 3 months, 6 months, and 12 months post-surgery.

Performance Based Assessments

At each time point after completing PROs each participant completed a series of 6 PBAs in a musculoskeletal laboratory setting. All PBAs were completed using the NeuroCom Balance Master® and long forceplate (NeuroCom International, Clackamas, OR). This is a commercially available system designed both as a training and evaluation tool for function and balance tasks, and it has the ability to provide immediate feedback to clinicians and patients regarding quality of task performance for a variety of activities of daily living (ADLs).[33] The only exposure study participants had with the long foreplate was for research testing purposes and they were not provided feedback during testing.

The long forceplate consists of a 45.72 cm x 152.40 cm force plate with data sampled at 100 Hz and a personal computer equipped with data capture software (Balance Master ver. 8.1). These functional tasks were selected because of their direct relationship to activities of daily living and the feasibility of patients being able to complete the task at each testing time point

(Table 1). Tests were completed in the order presented at all time points. This order was subjectively determined during pilot testing to be from least to most demanding. All testing was administered by the same investigator (JSH). For all single limb tests the uninvolved limb was tested first. Three successful trials of each task were performed (except for the Weight Bearing Squat which consisted of a single trial at each joint angle). Approximately 15s of rest was permitted between each trial and 30s of rest between each task. For the purposes of this manuscript all outcome variables are identified using the names assigned to them by the software utilized. Definitions for these variables are presented in Table 1. The six tasks are described below.

Walk Across (Figure 1.)*:* Patients walked across the long forceplate using their freely chosen standard gait speed and pattern.

Weight Bearing Squat (Figure 2.)*:* Patients stood still on the force plate and force was recorded with knee flexion angles of 0˚, 30˚, 60˚, and 90. The percentage of body weight on the involved limb was measured during a single trial with a duration .01s for each position. A standard goniometer was used to verify knee joint angle at each position.

Sit to Stand (Figure 3.)*:* Patients were seated on a 50cm box. Upon both visual and audio signal from the computer they rose to full standing as quickly as possible without using their hands, and then maintained a steady stance for the remainder of the 10 s trial.

Step-Up/Over (Figure 4.)*:* Participants stood behind a 29cm high box and stepped up onto the box with their test leg, then brought their non-test leg up and over the box, and then stepped down with their test leg. Patients were instructed to complete this task as quickly as possible while still maintaining control.

Forward Lunge: Patients in a standing position stepped forward on one leg and squatted down as far as possible, and then returned to the initial standing position as quickly as possible.

Previous research has investigated the global components of function assessed by the long forceplate. Using factor analysis methods, Chong identified the latent functional variables assessed in several of the included tasks.[34] He concluded that the Sit to Stand assessed the underlying factors of both "agility" and "weight transfer", the Step up/Over assessed "force control," and the Forward Lunge assessed the underlying factor of "agility."[34] Additionally, Walk Across stride width and stride length evaluated "walking" factors not well represented in the other functional tasks.[34] Outcomes utilizing the long forceplate have also previously been reported for postoperative recovery following total knee replacement.[19] Finally, the long forecplate has been reported to be sensitive to functional deficits following anterior cruciate ligament reconstruction.[35] This existing literature supports the use of the long forceplate as a useful tool for the assessment of lower extremity function, particularly among postoperative knee patients.

Statistical Analysis

A mixed model analysis using a covariance pattern model with an autoregressive covariance matrix was used to compare changes in PROs and PBAs between preoperative, 3 month, 6 month, and 12 month postoperative evaluations. Significance level was set at $p \leq 0.05$ *a priori* and when a main effect was significant, protected least significant difference pairwise comparisons were used to identify differences between individual time points.

RESULTS

Six participants were declared clinical failures at or before the one year time point and were not medically cleared to complete functional testing at all follow-up time points; however

PRO scores were available for 4 of these patients who had yet to undergo reoperation at the one year time point. An additional five participants were lost to follow-up. All available data for all participants at all time points was incorporated into the statistical analysis.

Patient Reported Outcomes

There was a main effect ($p < 0.001$) for time for all four PRO instruments (Figure 5). The WOMAC ($p=0.050$) was the only instrument to show significant changes between preoperation and the 3 month time point. There were significant improvements from preoperation to the 6 and 12 month follow-ups for the IKDC ($p < 0.001$, $p < 0.001$, respectively), SF36-PCS ($p = 0.002$, $p = 0.001$), Lysholm ($p < 0.001$, $p < 0.001$), and WOMAC ($p < 0.001$, $p < 0.001$).

Performance Based Assessments

All PBAs demonstrated changes over time (Table 2.). For the Walk Across task there was a significant increase in stride length observed at both the 6 and 12 month time points compared to preoperation (6 month, $p = 0.002$; 12 month, $p= 0.005$) and when compared to 3 month values (6 month, $p < 0.001$; 12 month, $p = 0.001$). There was no main effect for time for stride width ($p= 0.663$) or walking speed ($p=.051$).

For the Weight Bearing Squat a main effect for time was observed for squatting at 30^{o} ($p < 0.001$), 60^{o}, and 90^{o}. Post-hoc analyses revealed decreases in weight distribution on the surgical limb between preoperation (48% body weight) and 3 months (43% body weight, $p = 0.020$) and 6 months (45% body weight, $p = 0.020$) for squatting at 30^{o}. Decreased weight bearing was also observed between preoperation and 3 months ($p < 0.001$) and preoperation and 6 months ($p = 0.048$) for squatting at 60^{o}. Similarly, squatting weight distribution asymmetries were observed at 90° relative to baseline at 3 months (p < 0.001) Although not statistically different from preoperative values, at the 12 month time point mean weight distributions remained below preoperative values at 30°, 60°, and 90°.

The Sit to Stand demonstrated the earliest positive effects of surgery with decreased weight transfer time at 3 months (p=0. 016) compared to preoperation. Weight transfer time continued to improve at 6 months (p=0.05) and 12 months (p=0.002).

For the Step Up/Over there were significant increases in lift-up force between preoperation and the 3 (p=0.003), 6 (p = 0.005), and 12 (p=0.010) month follow-up time points. Time required to complete the Step Up/Over was also increased at 3months (p=0.009), but returned to baseline at later time points. Similarly, Step Up/Over impact index was increased over preoperation values at 3 months (p=0.001) and 6 months (p=0.034), possibly demonstrating a loss of eccentric control when stepping down from the box.

Finally, results for the Forward Lunge showed a significant decrease in impact index (peak vertical ground reaction force) at 3 months (p = 0.007), but returned to preoperative levels and began to increase at the 6 and 12 month time points. Similar to the Step Up/Over, Forward Lunge time was slower at the 3 month time point (p = 0.006) but gradually became quicker at subsequent evaluations.

DISCUSSION

The primary purpose of this study was to provide a timeline for recovery that could be utilized by both patients and clinicians in managing expectations regarding postoperative recovery of function. A summary timeline of the functional recovery observed in the first year following ACI can be seen in Figure 6. Overall, these results suggest that patients may experience physical benefits such as decreased pain and symptoms as early as 3 months following ACI, but some facets of functional performance may initially decline following surgery, with significant improvements in functional performance of complex tasks such as squatting and stepping not occurring until 12 months, or perhaps longer.

Patient Reported Outcomes

PROs have frequently been utilized to document functional outcomes following ACI.[3-5] The observed results suggest that patients may experience functional improvements for simple activities of daily living tasks such as those evaluated by the WOMAC as early as 3 months following ACI. However, data from the other self-reported outcome instruments utilized suggest that patients should not expect significant improvement prior to the 6 month time point. The lack of significant improvement in most PRO scores at the 3 month time point is in agreement with previous research by Henderson and Levigne and Ebert et al. [23, 36] However, both of these authors observed decreases in self-reported function using the IKDC[36] and SF-36 PCS[23, 36] at the three month time point, while we observed slight, but non-significant increases. In contrast Tohyama et al. reported significant improvements in Lysholm scores as early as 3 months following treatment with atelocollagen-associated ACI.[37]

The improvements observed among patients in IKDC, Lysholm, and SF-36 PCS scores at 6 months were similar to the outcomes observed by Niemeyer et al. for the IKDC[38] and both Niemeyer et al. and Kreuz et al. for the Lysholm.[38, 39] Other authors have observed even larger improvements in IKDC[37] and Lysholm[40] scores as early as 6 months following ACI.

Across all PROs we observed improvements when preoperative scores were compared to scores 12 months following ACI surgery. These results are in agreement with the findings of others when utilizing the IKDC,[36, 38, 39, 41-45] Lysholm,[37-39, 41, 42] SF-36 PCS,[36] and WOMAC[46, 47] scores 1-year following ACI. Regardless of which outcome instrument is used, the IKDC, Lysholm, SF-36 PCS, or the WOMAC, both clinicians and patients can anticipate improvements in self-perceived function during the first year following ACI.

Performance Based Assessments

Limited improvements in PBAs were observed 1-year following ACI (Table 2.). In general, a decrease in physical performance was observed at 3 and 6 months postoperatively, followed by a return towards baseline at 12 months following ACI. This pattern of decreased function followed by gradual return/improvement of function was particularly true for the Weight Bearing Squat, Step Up/Over, and Lunge. The only measures to show positive improvements from preoperative levels at or within the 12 month time period were Walk Across stride length , Sit to Stand weight shift time, and Step Up/Over lift-up index. These results suggest that improvements for simpler, less demanding tasks, such as walking or going up steps can be seen as early as 6 to 12 months following ACI. However, for more complex tasks, particularly those that require eccentric quadriceps control - such as squatting, going down steps, or lunging - meaningful changes in function may not be observed within the first year following ACI.

Decreases in physical performance at the 3 month time point have been previously observed with the 6 minute walk-test following matrix-induced autologous chondrocyte implantation (MACI)[23, 25] and characterized chondrocyte implantation (CCI).[24] Similar to our results, other researchers have observed slight improvements in walking performances at the 6 month[25] and 12 month[24, 25] time points that continue to improve at 24 month follow-up.[24, 25] During laboratory gait analysis, improvements in gait speed and stride length, without significant changes in stride width, were observed over 12 months following MACI.[48] These results support our observation that, after an initial decrease in function, both patients and physicians can anticipate improvements in gait beginning around the 6 month time point following ACI.

In examining more dynamic tasks, Van Assche et al. observed deceased functional performance for a series of hopping and strength tasks (single-limb hop, cross-over hop, 6 m timed hop, and isometric knee extension strength) at 6 months following CCI and no significant improvements were observed as late as 24 months after CCI.[28] For example, these authors observed a 9% decrease in the single-leg hopping limb symmetry index through 24 months following surgery.[28] These results are in agreement with our observations demonstrating an initial decrease in function for more dynamic tasks such as squatting and stepping, with few or no significant or measurable improvements in functional performance at the 12 month time point following ACI.

In comparison to normative data[49] it can be observed that some long forceplate variables are below preoperative levels at baseline, but approach or achieve age group normative values during the first year of postoperative recovery. These include the Step Up/Over lift-up index and Forward Lunge distances. However, other variables such as Step Up/Over and Forward Lunge times are below normal at baseline, become more abnormal at the three month time point and despite some improvement continue to be below normative levels at the one year mark. These results suggest that although patients may have improvements in the ability to successfully perform the task, they continue to do so at a slower pace.

Across the literature and within our study sample, improvements in gait relative to presurgery have been observed as early as 6 months following ACI.[25] However, improvements in more dynamic activities such as squatting, lunging, stepping, and hopping have not been observed within the first 12 months following ACI in the present study or elsewhere.[28] These results support existing theory that although improvements in self-report measures may occur early postoperatively, maximal defect healing and functional improvement continues beyond 12 months following ACI. [50-53]

The occurrence of changes in self-report measures of function prior to changes in performance based measures of function may be a result of the large influence pain levels have been observed to have on PRO scores.[19-22] The observed improvement in PRO scores in the absence of improved physical performance supports the importance of incorporating both types of outcome measures when documenting patient outcomes. The importance of a patient's own rating of function and subjective feelings towards joint health cannot be ignored. However, when considering decisions such as ability to return to work or physical activity, or to evaluate postoperative changes in biomechanics, performance based measures provide unique information that cannot be fully and accurately captured by PROs along.

Limitations

A limitation of this study is the inclusion of a diverse ACI patient population. The study sample included individuals undergoing treatment for lesions to the patella, trochlea, and/or femoral condyle many of which also underwent concomitant realignment procedures. Additionally, rehabilitation compliance was not tracked, and all patients were free to work with a physical therapist of their choice. Because of this variability, the presented timeline for recovery is not specific or precise for any one defect location and/or realignment procedure. Instead a broad pattern of recovery has been presented that can be generalized to a variety of defect patterns and sizes.

An additional limitation of this study is the lack of outcomes beyond 12 months post-ACI. However, the purpose of this study was to provide a descriptive time line for changes in self-perceived function and functional recovery in the first year following ACI. This time line is intended to describe when patients can expect improvements in activities of daily living and when patients will perceive a benefit from the surgery, two key pieces of information that may be valuable to patients and physicians when deciding if and when to undergo ACI. Future examination of these outcome variables for a longer period (> 1 year) will provide more information regarding the long term course of recovery following ACI.

CONCLUSIONS

This study presents a descriptive timeline for changes in both PROs and PBAs during the first 12 months following ACI. Self-perceived changes in function were observed as early as 3 months following ACI while performance based measures of function demonstrated functional deficits compared to preoperative levels at both the 3 and 6 month time points. Specifically, patients demonstrated increased asymmetry of weight distribution when squatting and rising from sitting, decreased vertical ground reaction force production during lunging, and longer performance times for lunging and stepping activities. At the 12 month time point performance improvements were seen for walking speed, Sit to Stand weight transfer time and Step Up/Over lift-up index: however, Step Up/Over time and Forward Lunge impact index and time remained below previously reported norms. Overall, it was observed that patients' perceptions of functional improvements may outpace true physical changes in function. The present results, combined with those in the literature provide important information for both physicians and rehabilitation specialists to consider when working with cartilage patients who desire to return to high level physical activity. Clearly, recovery can be lengthy, and intense rehabilitation (beyond the existing standard of care) may be necessary to improve beyond or even restore dynamic function to preoperative levels.

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Table 1. Functional tasks evaluated on the NeuroCom Balance Master ® Long Force Plate. All tasks were performed in the order presented by patients treated for articular cartilage defects to the knee.

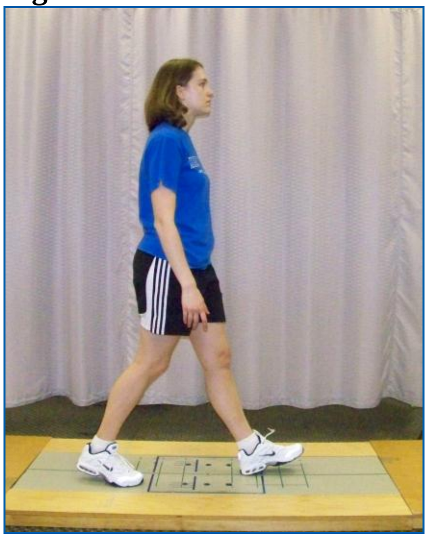
Task	Parameter(s) Assessed	NeuroCom Outcome Variable	Definition
Walk Across	Characterization of Gait	Stride Length (cm)	Distance between contralateral heel strikes
		Stride Width (cm)	Lateral distance between center of pressure of left and right foot strikes
		Walking Speed (cm/s)	Speed of forward progression of the center of gravity (COG)
Weight Bearing Squat	Strength, Weight Distribution	% Body Weight (BW) at 0° (full extension), 30°, 60°, and 90° of knee flexion	% BW on the involved limb at each position (test duration .01s)
Sit To Stand	Strength, Weight Distribution, Performance Time, Double Limb Balance	Weight Transfer time (s)	Time required from start of motion while sitting (i.e. increase in center of pressure(COP) forward velocity by 5% from resting velocity) to achieve full weight bearing standing (i.e. forward velocity drops to within 5% of standing resting velocity)
		Rising Index (%BW)	Peak vertical force exerted through the legs when rising to full standing relative to stationary vertical standing force
		Weight Symmetry	% Difference in weight supported by each limb during the weight transfer phase
Step-up/Over	Concentric Strength, Eccentric Control, Performance Time	Lift-up Index (%BW)	Peak vertical force occurring while stepping up onto the box as a percentage of body weight
		Impact Index (%BW)	Peak vertical force occurring while stepping down off the box as a percentage of body weight
		Movement Time (s)	Time between initial weight shift (i.e. change in COP velocity by 5%) and contact with force plate on opposite side of box (determined by COP velocity dropping to within 5% of post-test resting velocity)
Lunge	Concentric and Eccentric Control, Functional Range of Motion, Performance Time	Distance (% subject height)	Length of lunge step as a percentage of subject height
		Movement Time (s)	Duration of lunge phase during which lead leg is in contact with the force plate. Start and stop of a trial is determined by 5% change in COP velocity from pre-test and post-test resting velocity.
		Impact Index (%BW)	Peak vertical force occurring during lunge maneuver as a percentage of body weight

Table 2. Patient Reported and Performance Based Assessments Over 12 Months Following Autologous Chondrocyte Implantation

Test / Variable	Preoperative Mean (SD)	3 Months Mean(SD)	6 Months Mean (SD)	12 Months Mean (SD)
Walk Across				
Width (% height)	10.1 (2.8)	9.7 (2.5)	9.7 (2.1)	9.5 (2.5)
Length (%height)	42.0 (8.9)	42.1 (10.5)	46.8 (8.1)*†	46.9 † (7.6)*
Speed (cm/s)	82.6 (16.8)	87.7 (24.6)	88.2 (19.3)	94.5 (18.2)
Double Limb Squat (% Body Weight (BW))				
0°	48 (5)	48 (3)	49 (3)	49 (5)
30°	48 (8)	43 (6)*	45 (6)*	46 (5)
60°	47 (8)	42 (7)*	44 (6)*	45 (6)†
90°	48 (6)†	44 (5)*	46† (6)	46 (6)†
Sit to Stand				
Weight Transfer Time (s)	0.51 (0.26)	0.39 (0.32)*	0.36 (0.19)*	0.33 * (0.20)
Rise Index (% BW>100%)	23.3 (9.4)	22.0 (8.5)	24.0 (8.4)	24.6 (8.8)
Inv/Uninv Symmetry (-towards uninvolved)	-6.24 (17.6)	-13.7 (15.2)*	-9.9 (9.8)	-8.37 (12.3)
Step Up/Over				
Lift-up Index (% BW>100%)	41.0 (11.3)	45.0 (11.7)*	47.0 (11.3)*	47.3 * (11.6)
Time (s)	1.49 (0.33)†	1.67 (0.69)*	1.51 † (0.36)	1.40 † (0.26)
Impact (% BW)	47.6 (17.0)†	54.9 (18.2)*	54.1 (19.3)*	50.7 (16.9)
Forward Lunge				
Distance (% height)	44.9 (7.1)	46.8 (19.1)	50.5 (19.0)	51.3 (23.8)
Impact Index (% BW)	24.4 (7.0)†	21.8 (6.7)*	24.4 (7.4)†	27.2 † (10.4)
Time (s)	1.39 (0.43)†	1.51 (0.44)*	1.34 † (0.28)	1.29 † (0.39)
Patient Reported Outcomes				
IKDC	38.43 (12.5)	41.62 (15.68)	51.10 (18.34)*†	56.21 (20.64)*†
SF-36 PCS	37.39 (8.79)	37.98 (9.83)	43.50 (9.16)*†	44.22 (11.28)*†
Lysholm	47 (18)	54 (21)	61 (23)*†	65 (24)*†
WOMAC	33 (17)†	28 (17)*	22 (19)*†	20 (19)*†

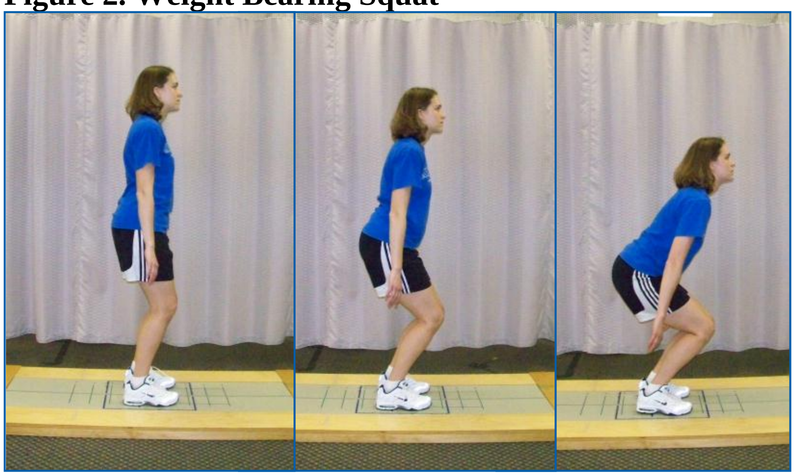
*significantly different from preoperative time point, †significantly different from 3 month time point,

Figure 1. Walk Across



Walk Across outcome variables included stride width, stride length, and speed

Figure 2. Weight Bearing Squat

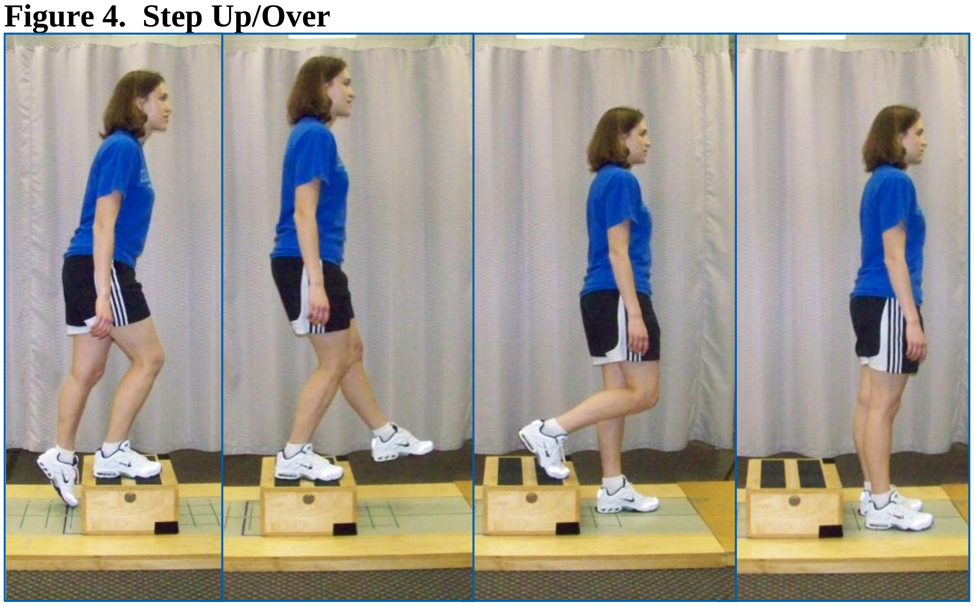


Percentage of body weight on the involved limb was evaluated at 0 (not pictured), 30, 60 and 90 degrees of knee flexion.

Figure 3. Sit to Stand

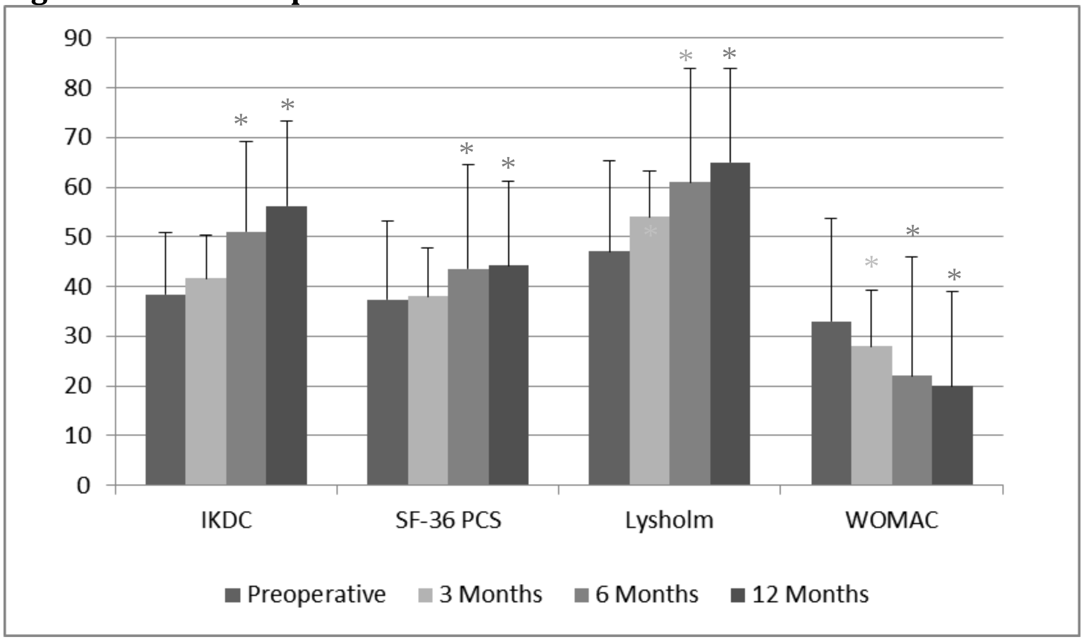
Sit to Stand: Beginning from a sitting position, upon receiving a visual and audio cue participants were instructed to rise from sitting as quickly as possible without using hands to push off the box. Outcome measures included weight transfer time, rising index and weight symmetry.

Figure 4. Step Up/Over



Step Up/Over: Beginning with both feet behind the box, participants were instructed to step up and over the box and return to stationary standing as quickly as they could do so while still maintaining control. Outcome variables were lift-up index, impact index, and movement time.

Figure 5. Patient Reported Outcome Scores



*p ≤ 0.05 compared to preoperative time point. IKDC and Lysholm are scored from 0 to 100 with 100 representing an ideal score. SF-36 PCS uses norm based scoring system where 50 represents a mean score with a standard deviation of 10 and higher scores representing higher levels of function. The WOMAC is scored 96-0 with 0 representing no disability. Error bars represent standard deviation.

Figure 6. Timeline of Functional Recovery Following Autologous Chondrocyte Implantation