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Does irradiation affect the clinical outcome of patellar tendon allograft ACL reconstruction?

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Abstract The clinical implications of using irradiation to sterilize allograft bone–patellar tendon–bone (BPTB) remains unknown. The purpose of this study was to compare the clinical outcome of anterior cruciate ligament (ACL) reconstruction with irradiated allograft versus autograft BPTB. We hypothesized that patients undergoing ACL reconstruction with irradiated BPTB allograft would have no significant differences in patient-reported and objective parameters compared to those undergoing autograft BPTB reconstruction. Patients who underwent ACL reconstruction with either irradiated allograft or autograft BPTB from 1996 to 2002 were eligible for this study. One hundred and two patients (39 allograft, 63 autograft) met the study criteria and were available for follow-up. The BPTB allografts were obtained from a single tissue bank and were sterilized with 2.5 Mrad of irradiation prior to distribution. Participants completed the International Knee Documentation Committee (IKDC) subjective knee form and returned for physical and radiographic examinations, instrumented measurement of laxity, and functional testing. Patients were evaluated at an average follow-up of 4.2 years (range 1.8–8.4). Those undergoing allograft reconstruction were older (44 ± 8.4 vs. 25.3 ± 9.3 years, $p < 0.001$) and had a longer median time from injury to surgery (17.1 weeks vs. 9.7 weeks, $p = 0.04$). There was no difference in IKDC Subjective Knee Scores between groups (86.7 allograft vs. 88.0 autograft, $p = 0.65$). The average maximum manual KT-1000 side-to-side difference was 1.3 and 2.2 mm for allograft and autograft, respectively ($p = 0.04$); however, after adjusting for age, this difference was no longer significant. 90.6% of the allograft and 82.8% of the autograft had normal/nearly normal overall IKDC physical examination rating ($p = 0.37$). 66.7% of the allograft and 77.8% of the autograft returned to the same or more strenuous level of sports ($p = 0.25$). Patients undergoing ACL reconstruction with irradiated allograft BPTB had similar clinical outcomes compared to those reconstructed with autograft BPTB. These data suggest that irradiation can be used to sterilize BPTB allograft without adversely affecting clinical outcome.

Keywords ACL · Allograft · Irradiation · Patellar tendon · Autograft

Introduction

Allograft tissue is routinely used to treat a broad spectrum of knee pathology, the most common of which is injury of anterior cruciate ligament (ACL). Although autograft bone–patellar tendon–bone (BPTB) remains the gold standard, allograft BPTB has become an increasingly popular graft choice for ACL reconstruction over the past several years. Allograft tissue has several advantages including decreased operating time, no donor site morbidity, and increased availability of tissue in complex revision or multi-ligament cases. Its most notable disadvantage is the risk of disease transmission. Use of musculoskeletal allograft has been associated with transmission of HIV, hepatitis C, and most recently, a series of bacterial infections with significant morbidity and mortality [2–5, 25, 27]. Donor screening, aseptic harvesting techniques, and various methods of tissue processing minimize the risk of disease transmission by allograft tissue. These techniques do not necessarily, however, provide a ''sterile'' graft that is devoid of all living entities such as bacterial spores and viruses.

Tissue banks implement sterilization techniques, including ethylene oxide and gamma irradiation, to ensure graft sterility. Gamma irradiation, which has known bactericidal and virucidal properties, is currently the most popular option for sterilization of soft tissue allograft [29]. Studies have shown, however, that gamma irradiation significantly alters the initial biomechanical properties of soft tissue allograft in a dose-dependent manner. Doses as low as 2 Mrad have been shown to reduce the initial stiffness and strength of tendon allograft [6–8]. It is unknown whether or not this alteration in biomechanical properties has an effect on clinical outcome.

The purpose of this study was to determine if the clinical outcome of patients who underwent ACL reconstruction with irradiated BPTB is similar to those who underwent ACL reconstruction with autograft BPTB. We hypothesized that patients undergoing ACL reconstruction with irradiated allograft BPTB will not have statistically or clinically meaningful differences in patient-reported, objective, and functional outcomes when compared with those receiving autograft BPTB.

Methods

Patients

Patients who underwent reconstruction of the ACL using either an autograft BPTB or an irradiated allograft BPTB between 1996 and 2002 were recruited to participate in this study. Allografts were obtained from a single tissue-processing company and were sterilized with 2.5 Mrad of gamma irradiation prior to distribution. Subjects who had prior ACL surgery, bilateral ACL injury, history of a cartilage procedure (microfracture, HTO, or mosaic-plasty), underwent ACL reconstruction with an alternative graft choice, or who had concomitant knee ligament injury were excluded from the study. The ACL reconstruction in all subjects was performed by one of the two senior authors using an arthroscopically assisted technique described in previous publications [10]. A similar postoperative program was used for both graft types [14]; however, progression to full weight bearing was delayed by approximately 1 week and return to running and return to sports were delayed by approximately 1 month when reconstruction was performed with allograft BPTB graft. The decision to use an irradiated allograft BPTB graft was determined by the patient after discussion of the benefits and risks of allograft with the surgeon. Generally, allograft was recommended for those who were 35 years of age or older or those with a history of patellofemoral symptoms.

Subject recruitment procedures

Following approval by the Institutional Review Board (IRB), potential subjects were identified by searching the Medical Archival and Reporting System (MARS). Operative notes were reviewed to obtain information regarding the surgical procedure and to ensure that patients met the inclusion criteria for the study. This information included graft type, injuries to associated structures including the menisci, articular cartilage, and ligaments, and associated surgical procedures. Patients deemed eligible were provided, via mail, information about the study and an invitation to participate. Those who agreed to participate in the study signed an IRB-approved informed consent form. Participation required the completion of several health status questionnaires and an office visit for a detailed physical examination and radiographs.

Patient-reported measures of health status

Subjects completed several patient-reported measures of health status including the International Knee Documentation Committee (IKDC) Subjective Knee Form [12, 13, 15], Activities of Daily Living Scale (ADLS) and Sports Activity Scale (SAS) of the Knee Outcome Survey (KOS) [16], and the Medical Outcomes Study Short Form-36 (SF-36) [19, 20, 30]. The IKDC Subjective Knee Form is a knee-specific measure of symptoms, function, and sports activities in patients with a variety of knee impairments including ACL injury. The KOS consists of two separate scales. The ADLS includes

items related to symptoms and functional limitations experienced during activities of daily living (ADL) and the SAS consists of items related to symptoms and functional limitations commonly experienced during sports activities. The SF-36 is a general health status measure that is applicable to diverse populations of individuals with a variety of conditions. The SF-36 has been used to measure general health status for a variety of orthopedic conditions, including ACL reconstruction [22].

Physical examination

The follow-up physical examination was performed by a research assistant and a physician (i.e., orthopedic sports medicine fellow) who was not involved in the operative procedure. This exam included an assessment of effusion, joint line tenderness, crepitus, range of motion (ROM), laxity, and a series of functional tests. Knee effusion and crepitus of the anterior, medial, and lateral compartments were graded as present or absent. The ROM of the knee was measured with a goniometer with the patient supine. When measuring passive extension, the heel was elevated on a bolster to allow for hyperextension of the knee if present. The ROM was recorded for both the involved and non-involved knees and the side-to-side differences in knee flexion and extension were calculated.

Examination of knee laxity included the Lachman, pivot shift, posterior drawer, and varus/valgus stress tests. Laxity was graded relative to the non-involved side according to IKDC guidelines. The following definitions were used: normal (< 3 mm side-to-side difference), nearly normal (3–5 mm side-to-side difference), abnormal (6–10 mm side-to-side difference), and severely abnormal (> 10 mm side-to-side difference). Both 30 lb. and maximum manual KT-1000 (MedMetric Inc., San Diego, CA) tests were performed to assess anterior laxity with the knee positioned in 25–30° of flexion. Side-to-side differences in anterior laxity were determined.

Functional tests included the vertical jump and one-legged hop tests. The Vertec unit (Sports Imports Inc., Columbus, OH) was utilized to perform the one-legged vertical jump test and a tape measure affixed to the floor was used to measure the one-legged hop. The subject performed three trials on each leg. The average of the three trials was used to determine the vertical jump and hop indices by dividing the involved leg by the non-involved leg and multiplying by 100.

Radiographs

Radiographs obtained during the follow-up visit included a standing anterior–posterior long cassette, posterior–anterior 45° flexion weight bearing, lateral, and Merchant views. Alignment was measured on the standing long cassette radiograph as the angle between a line drawn from the center of the femoral head to the center of the femoral condyles and a line drawn from the center of the femoral condyles to the center of the ankle joint. Radiographs were scored according to IKDC [11]. Separate grades were determined for the medial and lateral tibiofemoral compartments and the patellofemoral joint.

Data management and analysis

All data were entered into a computerized database. Statistical analyses were performed with SPSS Version 12.0.1 for a personal computer (SPSS Inc., Chicago, IL). We began the data analysis by calculating descriptive statistics including frequencies for categorical and ordinal variables and means, medians, standard deviations, and ranges for continuous variables. To test the null hypothesis that there would be no differences in clinical outcome between the irradiated allograft and autograft groups, we initially performed univariate analyses using procedures that were dependent on the nature of the data (e.g., independent *t*-tests for the continuous outcome measures and Chi-squared tests for categorical outcome measures). Following this, we used general linear models to account for potential confounders that may have affected the results. Potential confounders were included as covariates in the general linear model if there was a significant difference between groups in the potential confounding variable and if the confounding variable was significantly ($p < 0.10$) related to the outcome of interest. After entering the covariates that met these criteria to the general linear model, we added group membership to the model to determine if graft type (irradiated allograft versus autograft BPTB) had a significant effect on outcome after statistically controlling for the confounding variables. To implement these procedures, we used analysis of covariance for continuous outcome measures and logistic regression for dichotomized categorical outcome measures. The alpha level for all statistical tests was set at 0.05 a priori.

Sample size was determined a priori by estimating the number of subjects that would be needed to detect a 2 mm between-groups difference in anterior tibial translation as measured with the KT-1000. We chose to estimate the sample size required to detect a 2 mm between-groups difference because we believed that a difference less than this was not clinically relevant. Assuming a common standard deviation of 3 mm with a two-tailed alpha level of 0.05, we determined that 40 subjects per group would be needed to have power greater than 80%.

Table 1 Demographic characteristics of subjects

	Allograft ACL reconstruction ($n = 39$)	Autograft ACL reconstruction ($n = 63$)	p value
Age at surgery (years)[a]	44.0 ± 8.4	25.3 ± 9.3	< 0.001
Height (cm)[a]	175.6 ± 9.2	175.5 ± 10.7	0.95
Weight (kg)[a]	85.6 ± 20.4	80.4 ± 17.6	0.18
Percent females	30.8%	31.7%	0.92
Percent Caucasian	94.9%	98.4%	0.28
Follow-up (years)[a]	4.2 ± 1.8	4.6 ± 1.5	0.22

[a]Number ± standard deviation

Results

Subjects

Thirty-nine allograft and 63 autografts met the study criteria and were available for a follow-up visit. Subjects in each group were similar in terms of height, weight, and race (Table 1). However, subjects undergoing allograft reconstruction were older (44 ± 8.4 years vs. 25.3 ± 9.3 years, $p < 0.001$) and had a longer median time from injury to surgery (17.1 weeks vs. 9.7 weeks, $p = 0.04$). The average length of follow-up was 4.2 years (range 1.8–8.2 years) for those undergoing reconstruction with an allograft and 4.6 years (range 2.1–8.4 years) for those undergoing reconstruction with autograft ($p = 0.22$). Prior to injury, 69.2% (27/39) of the allografts and 85.7% (54/63) of the autografts participated in recreational or competitive sports that involved jumping, hard pivoting, and cutting ($p = 0.08$). The majority of subjects in each group (89.7% of the allografts and 93.7% of the autografts) were injured during sports ($p = 0.59$).

Findings at arthroscopy

In the allograft group, ten patients had a partial medial meniscectomy, four had a medial meniscus repair, two had debridement of the medial meniscus, and the medial meniscus was rasped in one patient. On the lateral side, three patients had a partial meniscectomy, three had debridement of the meniscus and the meniscus was rasped in one patient. In the autograft group, two patients had a medial meniscus repair, one had a partial lateral meniscectomy, two underwent lateral meniscus repair, and one had debridement of the lateral meniscus. Patients undergoing reconstruction with allograft had a higher incidence of medial meniscus injury requiring surgery ($p < 0.001$). The difference in lateral meniscus surgery was not significant.

In the allograft group, 20 patients had medial femoral chondral lesions (grade 1–five, grade 2–eight, grade 3–five, grade 4–two), 12 had lateral femoral chondral lesions (grade 1–six, grade 2–four, grade 3–two), and 11 had patella lesions (grade1–one, grade 2–six, grade 3–one, grade 4–three). In the autograft group, one patient had a grade 3 medial chondral lesion, one patient had a grade 3 lateral chondral lesion, and one patient had grade 2 patellar chondrosis. The proportion of patients having chondrosis in the medial ($p < 0.001$), lateral ($p < 0.001$), and patellar ($p = 0.002$) compartments was significantly higher in those undergoing allograft reconstruction.

Patient-reported measures of health status

The knee-specific and general health status measures by graft type are reported in Table 2. Overall, patients had high levels of function during ADL and sports activities following ACL reconstruction. There were no significant differences in the knee-specific or general measures of health status between those undergoing allograft and autograft ACL reconstruction. Age at the time of surgery was only related to the SF-36 bodily pain score. Correcting for age only resulted in a slight adjustment of the estimated means but it did not change the statistical conclusion regarding the effect of graft type on bodily pain. Time from injury to surgery was related to the SAS ($p = 0.08$) and IKDC Subjective Knee ($p = 0.08$) scores, but adjusting for time from injury to surgery did not change the conclusion regarding the effect of graft type on either of these scores. Medial meniscus surgery and medial compartment chondrosis were not related to any of the knee-specific or general patient-reported outcome measures. Patellofemoral chondrosis was related to the ADLS ($p = 0.08$), SAS ($p = 0.07$), and IKDC Subjective Knee ($p = 0.10$) scores and lateral compartment chondrosis was related to the ADLS ($p = 0.007$), SAS ($p = 0.004$), IKDC Subjective Knee ($p = 0.02$), and SF-36 physical function ($p = 0.06$) scores. Inclusion of either patellofemoral or lateral compartment chondrosis did not change the conclusions regarding the effect of graft type on these scores.

The physical and mental components summary scores are transformed scores that combine all eight SF-36 scale scores into a single score that represents physical and mental function, respectively. In the US population, these scores have a mean of 50 and standard deviation of 10. The physical component summary scores for those undergoing irradiated allograft and autograft ACL reconstruction were 53.5 and 54.4, respectively ($p = 0.43$). The mental component summary scores were 55.9 and 55.4, respectively, for those undergoing irradiated allograft versus autograft ACL reconstruction ($p = 0.55$). The physical and mental component summary scores indicate that on average, the health status of individuals following ACL reconstruction is above the

Table 2 Knee-specific and general health status measures by graft type

	Allograft reconstruction ($n=39$)	Autograft reconstruction ($n=63$)	p value[f]
IKDC subjective knee form	86.7 ± 15.5[e]	88.0 ± 13.3	0.65
ADLS[a]	93.4 ± 10.2	92.7 ± 10.5	0.72
SAS[b]	90.1 ± 17.1	90.1 ± 12.8	0.99
SF-36 physical function	93.8 ± 13.2	94.5 ± 13.8	0.81
SF-36 role physical	96.2 ± 17.7	96.0 ± 13.6	0.97
SF-36 bodily pain	82.4 ± 15.7	84.9 ± 16.5	0.44
SF-36 general health	83.5 ± 16.8	86.0 ± 12.7	0.41
SF-36 vitality	71.3 ± 13.2	72.6 ± 16.4	0.67
SF-36 social function	98.1 ± 5.4	96.6 ± 7.8	0.27
SF-36 role emotional	100.0 ± 0	99.5 ± 4.2	0.43
SF-36 mental health	83.9 ± 8.7	83.1 ± 12.5	0.73
SF-36 PCS[c]	53.5 ± 6.1	54.4 ± 5.4	0.43
SF-36 MCS[d]	55.9 ± 3.0	55.4 ± 5.3	0.55

[a]Activities of daily living scale score of the knee outcome survey
[b]Sports activity scale of the knee outcome survey
[c]Physical components summary score of SF-36
[d]Mental components summary score of SF-36
[e]Values in cells represent means and standard deviations
[f]p Values are two-sided values from independent t-test

US population average. Lateral compartment chondrosis was related to the physical components summary score; however, adjusting for lateral compartment chondrosis did not change the conclusions regarding the effects of graft type on the physical components summary score.

Symptoms

Relatively few patients had symptoms during ADL. Based on individual items from the IKDC Subjective Knee Form, 99.0% of the patients did not have pain during ADL. No patients had swelling or instability during ADL. Eighty-four percent could participate in strenuous or very strenuous sports without pain or swelling and 86.3% could participate in these activities without instability. There were no significant differences in symptoms during ADL and sports between those undergoing allograft versus autograft ACL reconstruction. None of the potential confounding variables were related to symptoms during ADL and sports.

Activity level

Current overall level of function and activity are reported in Table 3. Of those who reported that their current levels of function or activity were lower than they were before surgery, 45.7% stated it was due to their knee, 8.7% stated it was due to lifestyle changes, and 45.7% stated it was due to a combination of their knee and lifestyle changes. Eighty percent of the patients reported they could participate in strenuous or very strenuous sports activity. There was no difference in the ability to participate in very strenuous or strenuous sports activities between those undergoing allograft versus autograft ACL reconstruction. Five allograft patients (12.8%) and two autograft patients (3.2%) were limited to light activities such as walking, housework, or yard work. None of the potential confounding variables were related to the highest level of activity that an individual was able to participate in on a regular basis.

The IKDC Subjective Knee Form includes 11-point rating scales to rate knee function prior to injury and at the current time. The scale is anchored on either end with the phrases "inability to perform any usual daily activities that may include sports" (0) and "normal, excellent function" (10). The average rating of knee function prior to knee injury was 9.9 ± 0.4. The current rating of knee function was 8.9 ± 1.6. There was no significant difference in the rating of current knee function between groups ($p=0.74$). The change in the rating of knee function from before injury to the current time was not significant ($p=0.85$). None of the potential confounding variables were related to current function of the knee or the change in rating of knee function from before injury to the current time.

Table 3 Rating of current function of knee and activity level by graft type

		Allograft reconstruction ($n=39$)[a]	Autograft reconstruction ($n=63$)[a]	p value
Current function of knee	Normal (same or better than before injury)	23 (59.0%)	38 (60.3%)	0.59
	Nearly normal (a little bit worse than before)	14 (35.9%)	24 (38.1%)	
	Abnormal (quite a bit worse than before)	2 (5.1%)	1 (1.6%)	
	Severely abnormal (a great deal worse than before)	0 (0%)	0 (0%)	
Current activity level including sports	Normal (same or better than before injury)	25 (64.1%)	39 (61.9%)	0.89
	Nearly normal (a little bit worse than before)	12 (30.8%)	20 (31.7%)	
	Abnormal (quite a bit worse than before)	2 (5.1%)	3 (4.8%)	
	Severely abnormal (a great deal worse than before)	0 (0%)	1 (1.6%)	

[a]Values in cells represent number (percent within graft type)

Overall patient rating

Overall, 77.5% of the patients described themselves as greatly improved and 14.7% rated themselves as somewhat improved as the result of surgery. Of the remaining patients, one allograft and one autograft patient were slightly improved, two autograft patients were neither improved nor worse, two autograft patients were slightly worse, and two autograft patients were somewhat worse. No patients reported themselves to be greatly worse. There was no difference in the rating of change from surgery between groups ($p = 0.21$). One hundred percent of the allograft patients and 83.3% of the autograft patients would undergo the procedure again ($p = 0.006$). None of the potential confounding variables were related to the subject's perception of progress since surgery. Only age at the time of surgery was related to the subject's willingness to undergo the surgery again ($p = 0.01$); however, entering this as a covariate in the model did not change the statistical conclusion regarding the effect of graft type on the subject's willingness to undergo surgery again.

Findings from physical examination

Ninety-one percent of the allografts and 85.5% of the autografts had no effusion ($p = 0.75$). Patellofemoral crepitus with moderate patellofemoral pain was present in 15.4 and 11.1% of the allografts and autografts, respectively ($p = 0.55$). Three patients (two allograft and one autograft) had medial compartment crepitus with mild pain and three patients (two allograft and one autograft) had lateral compartment crepitus with mild pain. The remaining patients had either no or mild crepitus without pain in the patellofemoral, medial, and lateral compartments. Ninety-one percent of the patients had no patellar tenderness. Three (7.7%) allograft and four (6.3%) autograft patients had mild tenderness with palpation and two (3.2%) autograft patients had moderate patellar tenderness. Incisional tenderness was reported by 21.1% of patients that underwent allograft reconstruction and by 21.7% of patients that underwent autograft reconstruction ($p = 1.00$). Individuals that had an autograft reconstruction had significant numbness and dysesthesia in the area of the incision than individuals that underwent reconstruction with an allograft (80.0% vs. 25.6%, $p < 0.001$); however, there was no difference with difficulty kneeling on the front of the knee (46.7% vs. 43.6%, $p = 0.84$).

Average flexion of the involved knee for all patients was $143 \pm 8°$ (range 118–158°). The average loss of flexion compared to the non-involved knee was $3 \pm 4°$ for those undergoing allograft reconstruction and $2 \pm 4°$ for those undergoing autograft reconstruction ($p = 0.14$). Average extension of the involved knee for all patients was $-1 \pm 4°$ (range 10° flexion contracture to 9° of hyperextension). The average loss of extension compared to the non-involved knee was $2 \pm 3°$ for those undergoing allograft reconstruction and $3 \pm 2°$ for those undergoing autograft reconstruction ($p = 0.07$). Medial meniscus surgery was associated with the side-to-side difference in passive extension; however, inclusion of medial meniscus surgery as a covariate did not change the statistical conclusion regarding the effect of graft type on side-to-side difference in passive knee extension. None of the other potential confounding variables were associated with the side-to-side difference in passive extension or flexion.

The majority of patients had −1 to 2 mm of laxity compared to the non-involved knee for the Lachman test (Table 4). There was a significant difference between groups in the Lachman test ($p = 0.02$); however, post hoc testing could not identify significant differences in the proportion of individuals with −1 to 2 mm of laxity (allograft 41.0% vs. autograft 60.3%, $p = 0.07$) or in the proportion of individuals that had 6–10 mm of laxity (allograft 0% vs. autograft 6.3%, $p = 0.30$). Age ($p = 0.04$) and medial compartment chondrosis ($p = 0.02$) were associated with the Lachman test. Inclusion of age as a covariate reduced the significance of graft type to $p = 0.56$ and inclusion of medial compartment chondrosis reduced the significance of graft type to $p = 0.61$. None of the other potential confounding variables were associated with the Lachman results.

The majority of patients also had a pivot shift that was equal to the non-involved side (Table 4). The difference in the proportion of a normal pivot shift test between groups approached significance ($p = 0.06$). Ninety-two percent of the allografts and 74.2% of the autografts had pivot shifts equal to the contralateral side. The pivot shift was associated with age ($p = 0.01$) and medial compartment chondrosis ($p = 0.01$). Inclusion of age as a covariate reduced the significance of graft type to $p = 0.38$ and inclusion of medial compartment chondrosis reduced the significance of graft type to $p = 0.31$. None of the other potential confounding variables were associated with the pivot shift test.

There was no significant difference in AP translation at 70° of flexion between subjects undergoing allograft and autograft reconstruction ($p = 0.48$) (Table 4). Medial meniscus surgery was associated with AP translation at 70° of flexion ($p = 0.07$); however, inclusion of medial meniscus surgery as a covariate did not change the statistical conclusion regarding the effect of graft type on AP translation at 70° of flexion. None of the other potential confounding variables were associated with AP translation at 70° of flexion.

There was no significant difference in the average 30 lb. KT-1000 side-to-side difference; however, the maximum manual side-to-side difference was significant (allograft 1.3 mm vs. autograft 2.2 mm, $p = 0.04$)

Table 4 Laxity findings by graft type

		Allograft reconstruction ($n=39$)	Autograft reconstruction ($n=63$)	p value
Lachman test	−1 to 2 mm	16 (41.0%)[c]	38 (60.3%)	0.02
	3–5 mm	23 (59.0%)	21 (33.3%)	
	6–10 mm	0 (0%)	4 (6.3%)	
A–P translation at 70°	−1 to 2 mm	33 (84.6%)	47 (74.6%)	0.48
	3–5 mm	5 (12.8%)	14 (22.2%)	
	6–10 mm	1 (2.6%)	2 (3.2%)	
Pivot shift test	Equal	36 (92.3%)	46 (74.2%)	0.06
	Glide	3 (7.7%)	12 (19.4%)	
	Clunk	0 (0%)	4 (6.5%)	
30 lb. KT-1000[a]	< 3 mm	32 (82.1%)	37 (67.6%)	0.03
	3–5 mm	5 (12.8%)	23 (36.5%)	
	> 5 mm	2 (5.1%)	3 (4.8%)	
Maximum manual KT-1000[b]	< 3 mm	30 (76.9%)	37 (58.7%)	0.16
	3–5 mm	8 (20.5%)	24 (38.1%)	
	> 5 mm	1 (2.6%)	2 (3.2%)	
Avg 30 lb. KT-1000[a]		1.1 ± 2.5[d]	1.9 ± 2.3	0.11
Avg maximum manual KT-1000[b]		1.3 ± 2.3	2.2 ± 2.0	0.04

[a]Side-to-side difference of anterior translation for 30 pound KT-1000 test
[b]Side-to-side difference of anterior translation for maximum manual KT-1000 test
[c]Values in cell represent number (percent of sample within graft type)
[d]Values in cells represent mean and standard deviation in millimeters of side-to-side difference in anterior translation

(Table 4). Age ($p=0.003$) and chondrosis of the medial ($p=0.03$) and lateral ($p=0.03$) compartments were associated with the 30 lb. KT-1000 side-to-side difference and age ($p=0.004$), time from injury to surgery ($p=0.01$), and chondrosis of the medial ($p=0.02$) and lateral ($p=0.03$) compartments were associated with the maximum manual side-to-side difference. Analysis of covariance to account for age did not have any effect on the statistical conclusion for the 30 lb. KT-1000 test, but adjusting for age eliminated the significant difference in the maximum manual KT-1000 test (adjusted means allograft 1.8 mm versus autograft 1.9 mm, $p=0.94$). Adjusting for medial and lateral compartment chondrosis did not change the statistical conclusions regarding the effect of graft type on the 30 lb. KT-1000 side-to-side difference. Adjusting for medial and lateral compartment chondrosis eliminated the significant difference in the maximum manual KT-1000 test (adjusted means allograft 1.5 mm versus autograft 1.6 mm, $p=0.88$). Adjusting the maximum manual KT-1000 test for time from injury to surgery reduced the significance of graft type to $p=0.10$.

Most patients had less than a 3 mm side-to-side difference in anterior translation for the 30 lb. and maximal manual KT-1000 tests (Table 4). Eighty-two percent of the allografts and 58.7% of the autografts had less than a 3 mm side-to-side difference for the 30 lb. KT-1000 test ($p=0.02$). For the maximum manual KT-1000 test, 79.9% of the allografts and 58.7% of the autografts had less than a 3 mm side-to-side difference ($p=0.09$). Classification of the side-to-side difference of the 30 lb. ($p=0.001$) and maximum manual KT-1000 ($p=0.02$) tests were related to age, but not to any of the other potential confounding variables. When age was considered, the effect of graft type on classification of the 30 lb. ($p=0.88$) and maximum manual ($p=0.69$) KT-1000 was no longer significant.

The single leg hop and vertical jump tests were $95.4 \pm 11.2\%$ and $93.6 \pm 16.6\%$, respectively, of the non-involved leg. There were no significant differences in single leg hop ($p=0.95$) and vertical jump ($p=0.65$) tests between those undergoing allograft versus autograft ACL reconstruction. Age was related to the single leg hop ($p=0.01$) and vertical jump ($p=0.03$) tests. Lateral compartment chondrosis was related to the single leg vertical jump ($p=0.09$), but not to the hop ($p=0.16$). Inclusion of these variables as covariates did not change any of the statistical conclusions related to the effect of graft type on the single leg hop and vertical jump tests.

Overall IKDC rating

The overall IKDC rating for physical examination of the knee was determined according to the revised guidelines published by the IKDC [11]. The category and overall ratings for the physical examination are reported in Table 5. The IKDC ratings for effusion and ROM between groups were not significantly different. A slightly

Table 5 Group and overall IKDC ratings for physical examination

		Allograft Reconstruction ($n=39$)	Autograft reconstruction ($n=63$)	p value
Effusion	Normal	29 (90.6%)	53 (85.5%)	0.75
	Nearly normal	3 (9.4%)	9 (14.5%)	
	Abnormal	0 (0%)	0 (0%)	
	Severely abnormal	0 (0%)	0 (0%)	
ROM	Normal	21 (53.8%)	28 (44.4%)	0.62
	Nearly normal	14 (35.9%)	29 (46.0%)	
	Abnormal	4 (10.3%)	5 (7.9%)	
	Severely abnormal	0 (0%)	1 (1.6%)	
Laxity	Normal	12 (31.6%)	31 (52.5%)	0.05
	Nearly Normal	25 (65.8%)	24 (40.7%)	
	Abnormal	1 (2.6%)	4 (6.8%)	
	Severely abnormal	0 (0%)	0 (0%)	
Overall rating	Normal	6 (18.8%)	10 (17.2%)	0.73
	Nearly normal	23 (71.9%)	38 (65.5%)	
	Abnormal	3 (9.4%)	9 (15.5%)	
	Severely abnormal	0 (0%)	1 (1.7%)	

[a]Values in cells are numbers (percent of sample within graft type)

higher proportion of individuals undergoing allograft ACL reconstruction had a normal or nearly normal IKDC laxity rating (97.4% vs. 93.2%, $p=0.65$) and normal or nearly normal overall IKDC rating (90.7% vs. 82.7%, $p=0.37$); however, these differences were not statistically significant. Age was related to the IKDC laxity rating ($p=0.09$); however, adding age to the model as a covariate did not change the statistical conclusion regarding the effect of graft type on the IKDC laxity rating. None of the other potential confounding variables were related to any of the IKDC group ratings or the overall IKDC rating.

Radiographic findings

Radiographic findings for the medial, lateral, and patellofemoral compartments according to IKDC guidelines are summarized in Table 6. More patients undergoing autograft reconstruction had normal radiographs of the medial compartment [55.6% vs. 33.3% (13/39), $p=0.04$]. Medial compartment radiographic changes were related to age ($p=0.001$), time from injury to surgery ($p=0.08$), medial meniscus surgery ($p=0.07$), and degree of medial compartment chondrosis at the time of surgery ($p=0.006$). In the model containing all

Table 6 Summary of radiographic findings according to IKDC guidelines by graft type

		Allograft reconstruction ($n=38$)	Autograft reconstruction ($n=63$)	p value
Medial compartment	Normal[a]	13 (34.2%)	35 (55.6%)	0.01
	Nearly normal[b]	17 (44.7%)	22 (34.9%)	
	Abnormal[c]	3 (7.9%)	6 (9.5%)	
	Severely abnormal[d]	5 (13.2%)	0 (0%)	
Lateral compartment	Normal	31 (81.6%)	41 (65.1%)	0.01
	Nearly normal	2 (5.3%)	18 (28.6%)	
	Abnormal	3 (7.9%)	4 (6.3%)	
	Severely Abnormal	2 (5.3%)	0 (0%)	
Patellofemoral joint	Normal	29 (76.3%)	45 (71.4%)	0.21
	Nearly normal	4 (10.5%)	15 (23.8%)	
	Abnormal	4 (10.5%)	2 (3.2%)	
	Severely abnormal	1 (2.6%)	1 (1.6%)	

[a]Normal radiographs indicate no radiographic findings are present
[b]Nearly normal radiographs indicate mild changes are present. Mild changes include small osteophytes, slight sclerosis, or flattening of the femoral condyle and narrowing of the joint space that is just detectable
[c]Abnormal radiographs indicate moderate findings are present. Moderate changes include osteophytes, sclerosis, and/or flattening of the femoral condyles with 2–4 mm of joint space or up to 50% narrowing of the joint space compared to the contralateral knee
[d]Severely abnormal radiographs indicate severe changes are present. Severe radiographic changes indicate there was less than 2 mm of joint space or greater than 50% narrowing of the joint space compared to the contralateral knee
[e]Values in cells are percent of sample

four of these variables as covariates, the effect of graft type on medial compartment radiographic changes was no longer significant ($p = 0.33$).

For the lateral compartment, there was a trend for more patients undergoing allograft reconstruction to have normal radiographs (82.1% vs. 65.1%, $p = 0.07$). Lateral compartment radiographic changes were related to age ($p = 0.07$) and degree of lateral compartment chondrosis at the time of surgery ($p = 0.05$). When both of these variables were entered into the model as covariates, the significance of graft type decreased to $p = 0.12$.

There were no differences in radiographs for the patellofemoral joint (allograft 74.4% normal vs autograft 71.4% normal, $p = 0.82$). Radiographic changes of the patellofemoral compartment were related to age ($p = 0.07$) and chondrosis of the patellofemoral compartment at the time of surgery ($p = 0.09$). When age and patellofemoral chondrosis at the time of surgery were entered as covariates, the risk for radiographic changes of the patellofemoral joint was increased for those undergoing ACL reconstruction with autograft BPTB ($p = 0.01$). After controlling for age and patellofemoral chondrosis at the time of surgery, the odds for radiographic changes of patellofemoral joint were 7.5 times (95% confidence interval, 1.6–33.9) higher for those undergoing autograft BPTB reconstruction.

Complications

No patients in this study developed an infection or deep vein thrombosis following surgery. None of the allograft patients had loss of motion after surgery; however, three (4.8%) autograft patients developed loss of motion and required arthroscopic debridement and application of a dropout cast to restore motion. There were no allograft graft failures. One autograft patient ruptured the graft as a result of a twisting injury and subsequently underwent revision ACL reconstruction with allograft Achilles tendon. Three (8%) allograft and four (6.3%) autograft patients underwent arthroscopy and debridement for meniscal or chondral lesions.

Discussion

The use of musculoskeletal allograft in orthopedic procedures has increased considerably over the last decade [28]. Allograft tissue, particularly BPTB, has become an increasingly popular graft choice for ACL reconstruction and has been shown to offer results similar to those of autograft tissue [10, 21, 24]. One of the major concerns regarding allograft tissue is the associated risk of disease transmission. Although the risks of transmitting bacterial and viral diseases are low, significant efforts are being made by tissue banks to further minimize this risk. Because certain bacterial spores and viruses are resistant to current processing techniques, aseptically harvested and processed tissue cannot be regarded as sterile. In order to be considered sterile, the probability of a viable microorganism existing within an allograft tissue cannot be greater than one in one million allografts tested (10^{-6}) [1]. For this reason, many tissue banks use sterilizing agents after the tissue has been harvested and processed.

The two primary methods of sterilization that have known bactericidal and virucidal effects are ethylene oxide and gamma irradiation. Because it has been shown to incite a chronic synovitis, ethylene oxide has largely been abandoned as a sterilizing agent for tissue used for reconstruction of intra-articular ligaments [17]. According to a 1996 survey by Vangsness et al. [29], gamma irradiation is used by 80% of tissue banks in doses ranging from 1 to 3.5 Mrad. One of the advantages of gamma irradiation over sterilizing solutions it that is has tremendous penetration that ensures its effect throughout the entirety of the tissue. It is very effective against bacteria at relatively low doses (1.0–2.5 Mrad), but is less effective against viruses. Studies suggest that doses greater than 2.5 Mrad are required to inactivate HIV in allograft tissue [9, 26]. The dose of irradiation that can be administered, however, is limited by the adverse effects that it has on musculoskeletal tissue. According to several biomechanical studies, gamma irradiation has a dose-dependent effect on the biomechanical properties of allograft tissue. Doses as low as 2 Mrad have been shown to reduce the structural properties of BPTB allograft [6–8]. Questions remain regarding the clinical implications of these findings.

The purpose of this study was to compare the clinical outcome of patients undergoing ACL reconstruction with irradiated allograft BPTB versus autograft BPTB. All surgeries were performed by the senior authors using an identical endoscopic technique for ACL reconstruction. All BPTB allografts used in the study were obtained from the same AATB-approved tissue bank and were irradiated with a dose of 2.5 Mrad prior to distribution.

Due to the surgeons' criteria for offering allograft as a graft choice, the population of patients undergoing allograft ACL reconstruction was older and had a longer time from injury to surgery. Furthermore, these patients had more chondrosis of the medial, lateral, and patellofemoral compartments at the time of surgery, and required more medial meniscus surgery compared to the patients receiving autograft. Upon follow-up, we found that irradiated allograft BPTB and autograft BPTB ACL reconstruction provided similar patient-reported and objective results. There were no differences in the knee-specific or general measures of health status between those undergoing irradiated allograft and autograft ACL reconstruction. Statistically adjusting for differences in age, time of surgery, degree of chondrosis,

and medial meniscus surgery did not change this conclusion.

Several studies have evaluated the effect of gamma irradiation on the biomechanical properties of allograft BPTB. In 1995, Fideler et al. [8] demonstrated a dose-dependent effect of irradiation on both the structural and mechanical properties of human BPTB allograft. A dose of 2 Mrad resulted in a statistically significant reduction in four out of seven biomechanical parameters tested, including modulus and maximum stress to failure of the tissue. All seven parameters were reduced in a dose-dependent fashion after 3.0 and 4.0 Mrad of irradiation [8]. More recently, Curran et al. [6] studied the effect of 2 Mrad on the cyclic and failure properties of human BPTB allograft. This low dose of irradiation resulted in a 27% increase in elongation after cyclic loading and a 20% decrease in strength compared to non-irradiated grafts. The authors felt as though these effects may be detrimental to graft function and could lead to graft failure when used to reconstruct the ACL. They suggested the use of non-irradiated rather than irradiated allograft to avoid such problems [6].

We did not find an increase in anterior laxity or rate of graft rupture in patients who underwent reconstruction with irradiated allograft BPTB. The majority of patients had −1 to 2 mm of anterior laxity compared to the non-involved knee and had less than a 3 mm side-to-side difference in anterior translation for the 30 lb. and maximal manual KT-1000 tests. The irradiated allograft group had less side-to-side difference in anterior translation during the maximal manual KT-1000 test; however, this difference was not significant when age, time from injury to surgery, and medial or lateral compartment chondrosis at the time of surgery were included in the statistical model. There were no graft failures in the allograft group and only one graft rupture in the autograft group that occurred during a twisting injury.

At the time of follow-up, we found that 75% or more of patients in both groups had normal or nearly normal radiographic findings according to IKDC guidelines of the medial, lateral, and patellofemoral compartments. The development of radiographic degenerative changes was related to patient age, time from initial injury to surgery, and the status of the cartilage and menisci at the time of reconstruction. These findings are similar to those of Shelbourne and Gray [23], who reported that patients who have increased articular cartilage and meniscus damage at the time of ACL reconstruction have increased arthritic changes on follow-up. In our study, fewer patients undergoing irradiated allograft BPTB ACL reconstruction had normal radiographs of the medial compartment. This can be explained by the increased age (44 ± 8.4 years vs. 25.3 ± 9.3 years), median time from injury to surgery (17.1 weeks vs. 9.7 weeks), medial meniscus surgery (43.6% allograft vs. 3.2% autograft), and the degree of medial compartment chondrosis [51.3% allograft (grades 1–4) vs. 1.6% autograft (grades 1–4)] at the time of surgery in the irradiated allograft group. When corrected for these variables, the difference in radiographic findings of the medial compartment was no longer significant.

An equal proportion of individuals in each group had normal patellofemoral radiographic findings. However, radiographic findings of the patellofemoral joint were related to age and degree of patellofemoral chondrosis at the time of surgery. When we adjusted for these variables, individuals undergoing autograft BPTB ACL reconstruction were 7.5 times more likely than individuals undergoing allograft BPTB reconstruction to have radiographic changes of the patellofemoral joint at follow-up. These radiographic findings support the recommendation of allograft rather than autograft BPTB in patients who have patellofemoral symptoms preoperatively.

Several studies comparing allograft and autograft BPTB ACL reconstruction have reported an increased incidence of anterior knee pain and difficulty kneeling as well as loss of extension following autograft BPTB ACL reconstruction [10, 21, 24]. We found that individuals who had an autograft reconstruction had significant numbness and dysesthesia in the area of the incision than individuals who underwent irradiated allograft reconstruction, but there was no difference in patient-reported problems with kneeling. Furthermore, there was no difference in patellofemoral crepitus or pain between the two groups on follow-up examination. None of the allograft patients in our study developed loss of motion postoperatively that required manipulation or debridement, but three autograft patients had postoperative loss of motion that required arthroscopic debridement and application of a drop-out cast to restore motion. At follow-up, we did not find a statistically significant difference in loss of extension or flexion between the two groups; however, there was a trend toward greater loss of extension in the autograft group ($p = 0.07$).

This study has several limitations. The study was a retrospective case control design. Because we did not randomly assign graft type, differences between the groups other than graft type may have contributed to the results. To account for this, we explored differences between groups that may have affected clinical outcome. The variables that we explored as potential confounding variables included height, weight, race, age, time from injury to surgery, mechanism of injury (sports vs non-sports), more than one episode of giving way prior to surgery, meniscal surgery, and chondrosis of the medial, lateral, and patellofemoral compartments at the time of surgery. To be considered a confounding variable, there had to be a significant difference in the variable between groups and the variable had to be related to the clinical outcome variable being examined [18]. Of the potential confounding variables, only age, time from injury to

surgery, meniscal surgery, and chondrosis of the medial, lateral, or patellofemoral compartment at the time of surgery were significantly different between the two groups. Thus, we explored the relationship of these variables to each of the clinical outcome variables in the data analysis procedures. If the confounding variable was liberally related to the clinical outcome variable ($p < 0.10$), we included the confounding variable in a general linear model to statistically adjust for the effect of the confounding variable before examining the effect of graft type on the clinical outcome variable. This in essence allowed us to ''statistically equate'' the groups before we tested for the effect of graft type. We acknowledge that there may be other potential confounding variables that we did not measure or examine that may have influenced the results of this study. Future efforts to compare the clinical outcome of irradiated allograft BPTB versus autograft BPTB grafts in ACL reconstruction should make use of a prospective randomized design. Finally, as this was a retrospective study, we did not have preoperative outcomes data and therefore, we are not able to report a change in the clinical outcome of these patients as a result of ACL reconstruction.

The results of this study demonstrate that irradiation can be used as a means of sterilization of allograft BPTB without compromising the clinical outcome of ACL surgery. Both the patient-reported and objective outcomes of irradiated BPTB allograft ACL reconstruction are statistically and clinically similar to those obtained using autograft BPTB. The allograft BPTB grafts used in this study were irradiated with a dose of 2.5 Mrad prior to distribution from the tissue bank, which is a dose commonly used by tissue banks for sterilization. Although this dose is bacteriocidal, there is evidence that larger doses may be needed to eliminate viruses such as HIV. Fideler et al. [9] studied the effects of gamma irradiation on allograft BPTB and found that doses of 2–2.5 Mrad were ineffective in destroying HIV. Doses of 3–4 Mrad were necessary to inactivate the virus [9]. Although additional research is needed to determine the optimal virucidal dose of irradiation and its clinical implications, it is evident that low dose irradiation (2.5 Mrad) is effective against bacteria and can prevent allograft-associated bacterial infection without adversely affecting the clinical outcome of ACL reconstruction.

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