Allografts in Anterior Cruciate Ligament Reconstruction

69

Antonios Kouzelis, Christos S. Georgiou, Alkis Saridis, and Charalampos Matzaroglou

Contents

Introduction 851

Special Considerations with Allografts in ACL Reconstruction 852
Allograft Incorporation 852
Processing, Decontamination, and Their Effects on Allografts 853
Immunogenicity and Disease Transmission 854

What Is the Clinical Evidence? 855

Cross-References 857

References 858

Abstract

Allograft indications in anterior cruciate ligament reconstruction have recently expanded from revision cases and multiligament knee injuries to their routine use in some primary reconstructions. The surgeon making the decision will need to consider certain issues before employing an allograft: the potential for disease transmission, the possible immunogenic reactions, the procurement and sterilization protocols followed and their impact on graft strength and performance, and finally the cost implications. In this chapter the question of whether the advantages of the allograft use outweigh these risks and costs is being explored. This subject is of great importance as more anterior cruciate ligament reconstructions are performed and allograft sources become more readily available.

Introduction

Although the anterior cruciate ligament (ACL) is a common athletic injury and a large number of ACL reconstructions, with an estimated number of 175,000–200,000 in the USA (Hettrich et al. 2013), are performed annually, there still remains a considerable amount of controversy over whether an autograft or an allograft should be used. Allografts were in the past reserved for revision cases or for multiligament injuries, when the autologous tissue was not sufficiently

A. Kouzelis (✉) • C.S. Georgiou • A. Saridis • C. Matzaroglou
Department of Orthopaedic Surgery, University Hospital of Patras, Rio, Greece
e-mail: akouzelis@yahoo.gr; csgeorgiou@gmail.com; alkisaridis@hotmail.com; orthopatras@yahoo.gr

M.N. Doral, J. Karlsson (eds.), *Sports Injuries*,
DOI 10.1007/978-3-642-36569-0_95

available. Today, however, they are increasingly being used for some routine primary ACL reconstructions, especially in the USA (Granan et al. 2012). Various allograft tissue types exist, but the most commonly used are bone–patellar tendon–bone (BTB), hamstrings, quadriceps, Achilles tendon, and anterior tibialis tendon grafts.

Reconstruction with autografts has increased benefits of faster incorporation and no risk of immunologic rejection or disease transmission but leads to potential donor site morbidity, including anterior knee pain, patellar tendinitis or even late patellar tendon rupture, patella fracture, knee flexion weakness, altered quadriceps function, and saphenous nerve injury (Hu et al. 2013; Lamblin et al. 2013). Allografts have the main advantage of eliminating donor site morbidity but also the benefits of providing multiple grafts, shorter operative times, smaller incisions and improved cosmesis, less postoperative pain, and potentially faster rehabilitation (Siebold et al. 2003; Barrera et al. 2011; Hu et al. 2013). Unfortunately, however, allografts have the major disadvantages of potential disease transmission, possible immunogenicity, and slower maturation and increased costs (Barrera et al. 2011; Lamblin et al. 2013). To reduce the potential of disease transmission, gamma irradiation was extensively used in the past for allograft secondary sterilization (Hu et al. 2013). However, many published studies have indicated that gamma irradiation significantly decreases the biomechanical properties and structure of allografts in a dose-dependent pattern. Although the potential for disease transmission remains the main concern, the improved donor screening and modern processing and sterilization techniques have allowed a decrease in the use of high-dose gamma irradiation. According to the modern standards of the tissue banks, low-dose irradiation is limitedly used for the terminal tissue sterilization after graft procurement and before packaging.

In this chapter the incorporation process of the allografts in ACL reconstruction will be discussed and the effect of the various sterilization techniques in allograft stability. A review of the current evidence in the literature, which refers to the use of allografts, in terms of immunologic reactions and disease transmission, and their clinical performance, is also included.

Special Considerations with Allografts in ACL Reconstruction

Allograft Incorporation

Due to obvious technical difficulties in biopsies, the knowledge about graft healing process in human subjects is limited. It appears that after ACL reconstruction, the intra-articular region of the tendon graft first begins its incorporation process to the new environment (Scheffler et al. 2008). As reported the incorporation process (ligamentization) of an ACL graft consists of four phases: initial avascular necrosis, revascularization, cellular repopulation, and finally remodeling (Falconiero et al. 1998). During ligamentization, revascularization plays a key role by acting as a prerequisite for the other phases (Li et al. 2012). Graft revascularization is present as early as 3 weeks after operation and increases in prevalence over the next 5 weeks (Li et al. 2012). Simultaneously the intra-tunnel graft incorporation is taking place, which develops either by bone-to-bone or by tendon-to-bone healing (Scheffler et al. 2008). The whole process for autografts appears to last up to 12 months, although this is not a rule (Falconiero et al. 1998). In the case of allografts, however, the maturation process takes longer. Shino et al. (1988), after an arthroscopic and histological study of the remodeling process of human allogenic tendons, found that complete remodeling occurs by 18 months (Shino et al. 1988). Malinin et al. (2002), however, investigated entire retrieved ACL allografts and observed that the central portions of the grafts remained acellular even at 2 years postoperatively. They postulated that the complete remodeling and cellular replacement might require 3 years or longer (Malinin et al. 2002). The inferior allograft maturity at 2 years postoperatively in comparison to autograft tendons in ACL reconstruction was also confirmed by MRI cohort studies (Li et al. 2012). However, this delay in allograft maturation has not been

reflected to the clinical outcomes, as will be demonstrated in the relevance section.

Processing, Decontamination, and Their Effects on Allografts

Allografts are either used as non-sterilized fresh-frozen or cryopreserved tissue or are processed with different sterilization techniques prior to implantation. Every sterilization method contributes changes to the biomechanical features of grafts. Non-sterilized fresh-frozen allografts appear to be the strongest (Guo et al. 2012). They require meticulous serological screening of the donor and the donor's graft tissue to exclude the possibility of an infection. Even so the danger of a viral infection exists due to the time window in which the virus is undetectable (Scheffler et al. 2005). Reports from the Centers for Disease Control and Prevention on disease transmission after ACL fresh-frozen allograft reconstructions (Centers for Disease Control and Prevention 2001), the most unfortunate that of a 23-year-old man's death from Clostridium sordellii contamination (Kainer et al. 2004), have led to the implementation of graft sterilization methods (Yanke et al. 2013). Except from donor screening, the first step of the effort to stop disease transmission is aseptic recovery. Aseptic recovery minimizes the initial risk of contamination by infectious agents introduced when removing tissues from donors. Preventing the introduction of infectious agents during recovery and processing may obviate the requirement of sterilization. It does not however remove the existing bioburden in the tissue. Antibiotic soaks can effectively reduce bacterial concentration on the surface of grafts, but they are unable to penetrate and have no effect on viruses (Eastlund 2006).

Two types of sterilization have become most accepted for musculoskeletal tissue allografts: chemical sterilization, utilizing ethylene oxide gas, and ionizing radiation, gamma or electron beam. Ethylene oxide gas sterilization, although an effective method, is no longer used for allografts because the associated breakdown products, such as ethylene chlorhydrin, may cause chronic synovitis (Jackson et al. 1990) or even graft failure by dissolution (Roberts et al. 1991). On the contrary sterilization with peracetic acid–ethanol solution seems safe and not to affect biomechanical properties (Scheffler et al. 2005). Gamma irradiation is a secondary sterilization method preferred by many tissue banks. Non-spore-forming bacteria are susceptible to up to 0.5 Mrad of irradiation. Yeasts and molds require doses of approximately 0.8 Mrad, while bacterial spores may require up to 2.1 Mrad (Yanke et al. 2013). Viruses, and most importantly HIV, have been reported to require doses up to 4 Mrad. The latter is based on studies that assume that HIV is present in high levels (Fideler et al. 1994). However, after donor screening and tissue disinfection, the risk that HIV is present in an allograft is low (Hernigou 2000). It has been estimated theoretically to be between 1 in 600,000 (Buck et al. 1989) and 1 in 1,667,000 (Centers for Disease Control and Prevention 1995). Taking into account that the objective is to achieve a probability of 1 in 1,000,000, that virus is present before implantation, and that 0.4 Mrad of irradiation is required to reduce the population by 1 log cycle (Conway et al. 1991), a dose range of 1–2 Mrad is efficient in eradicating the virus after donor screening and tissue disinfection (Moore 2012). Low-dose (1.0–1.2 Mrad) gamma irradiation decreases BTB graft stiffness by 20 %, but it does not affect maximum load, maximum stress, elongation, strain at maximum stress, or other cyclic parameters (Yanke et al. 2013). This and other studies (Samsell and Moore 2012) indicate that treatment below 2–2.5 Mrad have minimal impact on biomechanical properties of the tendons. Parameters as irradiation temperature, dose range, and prior tissue treatment rather than the target dose alone seem to play a significant role (Samsell and Moore 2012). On the other hand, it is an old knowledge that using more than 3 Mrads for allograft sterilization to kill viral pathogens affects the biomechanical properties of the tissue (Fideler et al. 1994), by reducing crosslink density and by causing fragmentation of collagen (McGuire and Hendricks 2009). The use of such irradiation levels produces an estimated 25 % or 35 % reduction in strength for fresh-frozen or freeze-dried

BTB grafts, respectively, and with accurate nonanatomic surgical technique or improper rehabilitation can lead to graft failures (Buck et al. 1990). Such high doses are, however, unnecessary with tissue banking standards that include donor screening, aseptic procurement and processing, antibiotic decontamination, and terminal sterilization with low-dose irradiation before packaging. Tissue banks that perform terminal sterilization do so at 1–2.5 Mrad; the addition of cross-linking and scavenging methods would have potentially even greater protective effect (Seto et al. 2008). Another option instead of gamma radiation is to use electron beam, which allows improved control of dose application and shorter irradiation times. High-energy electrons cause in this case chemical changes similar to gamma irradiation. However, significant decrease in structural properties remains a problem with high doses, although the potential of fractionation of radiation dosages is promising (Hoburg et al. 2011).

Commonly accepted allograft storage methods used include cryopreservation, fresh freezing, and lyophilization (McGuire and Hendricks 2009). Cryopreservation maintains viable tissues and cells by cryoprotected freezing but adds expenses (McGuire and Hendricks 2009). Lyophilization or freeze-drying includes freezing the tissue and then dehydrating it under high vacuum at a low temperature. Freeze-drying of allografts has been shown to reduce antigenicity of grafts and minimize the effect of free radicals because both antigens and radicals are less active at these conditions (Woo et al. 1986; Hoburg et al. 2011). As is shown also in the next chapter, there is growing evidence that the process of freeze-drying may decrease the risk of viral transmissions. Before freeze-drying, allografts go through multiple ethyl alcohol washes, which also may contribute to these properties. Freeze-drying cannot achieve terminal sterilization and thus eliminate the risk of disease transmission, but it may reduce risk of graft-to-host reactions without compromising graft structure (Hoburg et al. 2011).

The BioCleanse (Regeneration Technologies, Alachua, FL) is another sterilization process that is currently under discussion. It is considered safe since it has passed FDA approval for use on soft tissue grafts, but adds significant expense to the procedure (McGuire and Hendricks 2009). It uses a pressure chamber, where a repeated cycle of chemical sterilants and detergent washes followed by vacuum removal of the residues takes place. This method is reportedly effective against a broad range of viruses, including enveloped and nonenveloped RNA and DNA viruses. A study, comparing BioCleanse-treated BTB allografts with untreated controls identified no significant biomechanical differences between them (Jones et al. 2007).

It is obvious however that as the processing techniques vary among different tissue banks and until a uniform system would be established, surgeons should become familiar with them and ask their supplier how exactly the graft they intend to use was processed (McGuire and Hendricks 2009).

Immunogenicity and Disease Transmission

Cellular-mediated and humoral immune responses have been reported in the literature with allograft tissue (Harner and Fu 1993; McGuire and Hendricks 2009). In the past tunnel enlargement has been associated with the use of allograft tissue for ACL reconstruction (Wilson et al. 2004; Bach et al. 2005). A subclinical immune response was postulated responsible for this difference (Fahey and Indelicato 1994). However, allogenic tissue processing and decontamination with the removal and neutralization of antigens by washing and freezing processes significantly decrease immunogenicity (Bach et al. 2005; McGuire and Hendricks 2009). No significant local or systemic immune responses affecting graft healing or clinical outcome have been recorded in a number of studies comparing autografts and frozen allografts (Arnoczky et al. 1986; McGuire and Hendricks 2009). Wilson et al. (2004) reviewed the literature regarding tunnel enlargement after ACL surgery and stated, “Based on the current literature, it is difficult to conclude that there was an increased risk of tunnel lysis with allograft tissue as compared to autograft.” Sporadic cases of acute

synovitis after surgery with fresh-frozen allografts have been also recorded, without serious consequences or need for reoperation (Guo et al. 2012). There is no mention of these conditions in the meta-analyses (Prodromos et al. 2007; Krych et al. 2008; Carey et al. 2009; Foster et al. 2010; Tibor et al. 2010; Hu et al. 2013; Kraeutler et al. 2013; Lamblin et al. 2013) that evaluate the use of allografts in ACL reconstruction. Consequently, it seems that recipient immune reactions have limited or benign effects on clinical outcome. Tissue typing and host immunosuppression, both common processes with solid organ transplantation, seem unnecessary for tendon allografts (McGuire and Hendricks 2009).

Although the risk is relatively low, allograft tissue-related viral transmission is an acknowledged subject of concern (McGuire and Hendricks 2009). With proper donor screening and serology testing, the estimated HIV risk is lower than 1:1,600,000 (Buck et al. 1989; McGuire and Hendricks 2009). There have been only three documented HIV cases in the literature as a consequence of frozen allograft tissue implantation from a HIV-positive donor (Simonds et al. 1992). Four patients received fresh-frozen allografts and three of these patients tested positive for HIV. Two patients received fresh-frozen femoral head allografts, and the third patient received a fresh-frozen BTB allograft for ACL reconstruction. None of the 42 recipients of freeze-dried grafts obtained from this donor became infected with HIV (Simonds et al. 1992). No freeze-dried allograft recipient was transformed to HCV positive in another case of a HCV-infected donor in the literature (Tugwell et al. 2005). In contrast, from the eight patients who received cryopreserved or fresh-frozen tendon–bone, four were tested positive for HCV. Freeze-drying and the washes used with it may have fundamental differences with the other graft storage options as cryopreservation and freezing. It seems that freeze-drying process has contributed to the prevention of viral disease transmission at least in these two cases (McGuire and Hendricks 2009).

The propensity for bacterial infections with fresh-frozen allografts has been emphasized by the Centers for Disease Control and Prevention (Centers for Disease Control and Prevention 2001; Kainer et al. 2004). This has led some to consider routine intraoperative cultures of allograft tissue before implantation. Positive routine cultures in ACL allografts have a reported incidence of 5.7–13.25 % (Fowler et al. 2011). In a retrospective study of 115 cases (Fowler et al. 2011), no patient with a culture-positive allograft developed a clinical infection postoperatively, whereas in another study of 247 patients (Guelich et al. 2007), 67 % grew organisms of high pathogenicity and 33 % of low pathogenicity, but the two cases of septic arthritis had negative intraoperative cultures. Routine preimplantation culture of soft tissue allografts thus cannot be recommended given the lack of correlation with clinical infection. Antibiotic treatment is not indicated only with the presence of a positive preimplantation allograft culture. In contrast, clinical signs of septic arthritis should be aggressively treated (Fowler et al. 2011). It is worth noticing that no difference in the infection rate between autografts and allografts (irrespective of the method of processing) has been recognized in the available meta-analyses. Furthermore, Maletis et al. (2013b) after a prospective cohort study of 10,626 cases from the Kaiser Permanente Anterior Cruciate Ligament Reconstruction Registry found no difference in the incidence of infection between allografts and BTB autografts (Maletis et al. 2013b).

What Is the Clinical Evidence?

Since the first description by Shino et al. in 1984 (Shino et al. 1984; Siebold et al. 2003) of the replacement of the ACL by an allogenic tendon graft, numerous case series were reported, and over 50 comparative studies have evaluated the clinical results of allografts and autografts in the past 30 years. Some studies have shown comparable success with both autograft and allograft tissues (Rihn et al. 2006) in ACL reconstruction, whereas other studies have found an unacceptable increased failure rate (Pallis et al. 2012). It appears that how irradiation affects clinical outcomes is dependent not only on the target dose but also on the specific use, the accuracy of surgical technique, and the

patient compliance to the rehabilitation instructions. Most of these publications, however, are low-quality, underpowered studies, or different graft sterilization techniques have been used in those studies. To our knowledge only eight systematic reviews of the clinical outcomes of allograft versus autograft for ACL reconstruction have been published so far; five of them were conducted over 3 years ago, between 2007 and 2010 (Prodromos et al. 2007; Krych et al. 2008; Carey et al. 2009; Foster et al. 2010; Tibor et al. 2010), and three (Prodromos et al. 2007; Krych et al. 2008; Tibor et al. 2010) identified differences in laxity in favor of autografts. Specifically, the study by Prodromos et al. (2007) is also the only meta-analysis in the literature that compares irradiated with nonirradiated allografts, showing worse outcome for the former. However, all these findings are either inconclusive (Krych et al. 2008) or compromised by methodological limitations (Prodromos et al. 2007; Samsell and Moore 2012) and by the limited availability of comparative clinical trials (Tibor et al. 2010).

Since 2010 several studies have been published adding data and making the previous systematic reviews obsolete. This new knowledge has been presented in meta-analysis from three recent studies (Hu et al. 2013; Kraeutler et al. 2013; Lamblin et al. 2013). In the best designed study, Hu et al. (2013) systematically reviewed all the level I and II prospective studies that evaluated the clinical outcomes of BTB autograft versus BTB allograft and soft tissue autograft versus soft tissue allografts for primary ACL reconstruction. The analysis excluded studies that included gamma-irradiated allografts. Nine studies, with 410 patients in the autograft and 408 patients in the allograft group, were determined to be appropriate. Hu et al. (2013) found no significant differences between allograft and autograft on the outcomes of instrumented laxity measurements, Lachman test, pivot shift test, objective International Knee Documentation Committee (IKDC) Scores, Lysholm scores, and clinical failures. However, a subgroup analysis of Tegner scores involving only BTB grafts reported a statistical difference in favor of autografts. The authors concluded that there was insufficient evidence to identify which of the two types of grafts was significantly better for ACL reconstruction, though the subgroup analysis indicated that reconstruction with BTB autograft might allow patients to return to higher levels of activity in comparison with BTB allograft (Hu et al. 2013). In another recent meta-analysis, this time reviewing studies with level of evidence from I to III, Lamblin et al. (2013) compared autografts again with nonirradiated but also nonchemically treated allografts. The authors excluded also those studies that compared BTB with soft tissue grafts. With a similar pool size as the analysis by Hu et al. (2013), they found no significant differences between autografts and allografts in Lysholm scores, IKDC scores, Lachman examinations, pivot shift testing, KT-1000 measurements, or failure rates. Lamblin et al. (2013) concluded that the results after autograft ACL reconstruction are comparable to those using nonchemically processed nonirradiated allograft tissue. Still none of these newer studies have stratified outcomes according to age or other confounding variables such as activity level. Furthermore the minimum follow-up set at the eligibility criteria was 2 years in both of them.

The third and the most recent of the 2013 meta-analysis compared BTB autografts and allografts and has the largest pool of 5,182 patients (Kraeutler et al. 2013). In order to increase the power of the analysis, the authors have included heterogenous data that are both comparative and non-comparative studies with different surgical techniques and both irradiated and nonirradiated allografts. Outcomes on subjective IKDC, Lysholm, Tegner, single-legged hop, and KT-1000 arthrometer were statistically significant in favor of autografts. Reflecting the methodological limitations, the return to preinjury activity level (in contrast to the Hu et al. (2013) study), overall IKDC, pivot shift, and anterior knee pain were significant in favor of allografts, although allograft BTB demonstrated a threefold increase in rerupture rates. There was no significant difference between the two groups for Cincinnati Knee scores. The authors advocated the use of BTB

autografts based on graft rupture, knee laxity, and overall patient satisfaction, but they have also stressed the need of more high-quality randomized controlled trials with specified age and activity level to draw reliable conclusions (Kraeutler et al. 2013).

The Scandinavian national ACL registries, that is, the Danish, the Swedish, and the oldest Norwegian, generate also useful data about ACL reconstructions. No association between graft failure and use of allografts has been revealed after a prospective cohort study of 12,193 primary ACL reconstructions performed between 2005 and 2010 of the Danish knee ligament reconstruction registry. On the contrary, the use of allograft tissue for the revision procedure resulted in a higher risk of re-revision (Lind et al. 2012). A 2012 cross-sectional ACL reconstruction registry comparison between the Norwegian Knee Ligament Registry (NKLR) with 11,217 patients registered and the US Kaiser Permanente Anterior Cruciate Ligament Reconstruction Registry (KP ACLRR) with 11,050 patients has shown that between 2005 and 2010 in the NKLR, allograft was used less (0.2 % vs. 41 %) for primary ACL reconstructions than in the KP ACLRR. A similar distribution of graft usage was found in the revision cohorts (Granan et al. 2012). In contrast with the USA where allografts are widely used in ACL reconstruction, a similar approach of the Scandinavian surgeons to patients seems to exist as shown also by the Swedish registry. The 2010 annual report depicts a scarce use of allografts in primary reconstructions with figures up to 30 per year and a relatively larger scale use in revision surgery and multiple ligament reconstructions (Swedish ACL Register 2011). With so small numbers any statistical correlation is not possible. In the USA, however, the Multicenter Orthopaedic Outcomes Network (MOON) after a prospective study of 980 patients has found that the use of allografts compared with autografts in ACL reconstruction is a risk factor for subsequent surgery (Hettrich et al. 2013). Kaeding et al. (2011) from the same consortium have found that both graft type and patient age are significant predictors of graft failure. The odds of graft rupture with an allograft reconstruction were four times higher than those of autograft reconstructions. For each 10-year decrease in age, the odds of graft rupture increased 2.3 times. Patients in the age group of 10–19 years had the highest percentage of graft failures (Kaeding et al. 2011). These associations were also confirmed by a recent retrospective cohort study of 9,817 primary ACL reconstructions from the KP ACLRR (Maletis et al. 2013). In terms of clinical performance based on IKDC and Knee Injury and Osteoarthritis Outcome Score (KOOS) results at two and six postoperatively, a MOON cohort study of 448 patients has also found that the use of allografts is a predictor of worse outcome (Spindler et al. 2011). As far as the question which allograft is best, to the best of our knowledge, the only study to date is that of Siebold et al., who have compared fresh-frozen patellar versus Achilles tendon allografts for primary ACL reconstruction. The Achilles tendon-bone allograft seemed to be advantageous as its failure rate was 4.8 % compared to the 10.4 % rerupture rate of the patellar tendon allografts. On the contrary, no significant difference between the two groups was found in subjective (as assessed by Cincinnati Knee Score and Lachman, pivot shift, and varus/valgus stress tests) and objective (assessed by KT-1000 arthrometer testing, IKDC, and Cincinnati Sports Activity Score) clinical outcomes (Siebold et al. 2003).

Cross-References

- ▶ Anterior Cruciate Ligament Graft Selection and Fixation
- ▶ Anterior Cruciate Ligament Injuries and Surgery: Current Evidence and Modern Development
- ▶ Combined Anterior and Posterior Cruciate Ligament Injuries
- ▶ Costs and Safety of Allografts
- ▶ Graft Remodeling and Bony Ingrowth After Anterior Cruciate Ligament Reconstruction
- ▶ Perioperative and Postoperative Anterior Cruciate Ligament Rehabilitation Focused on Soft Tissue Grafts
- ▶ Revision Anterior Cruciate Ligament Reconstruction

References

Arnoczky SP, Warren RF, Ashlock MA (1986) Replacement of the anterior cruciate ligament using a patellar tendon allograft. An experimental study. J Bone Joint Surg Am 68(3):376–385

Bach BR Jr, Aadalen KJ, Dennis MG et al (2005) Primary anterior cruciate ligament reconstruction using fresh-frozen, nonirradiated patellar tendon allograft: minimum 2-year follow-up. Am J Sports Med 33(2):284–292

Barrera Oro F, Sikka RS, Wolters B et al (2011) Autograft versus allograft: an economic cost comparison of anterior cruciate ligament reconstruction. Arthroscopy 27(9):1219–1225

Buck BE, Malinin TI, Brown MD (1989) Bone transplantation and human immunodeficiency virus: an estimate of risk of acquired immunodeficiency syndrome (AIDS). Clin Orthop 240:129–136

Buck BE, Resnick L, Shah SM et al (1990) Human immunodeficiency virus cultured from bone. Implications for transplantation. Clin Orthop 251:249–253

Carey JL, Dunn WR, Dahm DL et al (2009) A systematic review of anterior cruciate ligament reconstruction with autograft compared with allograft. J Bone Joint Surg Am 91(9):2242–2250

Centers for Disease Control and Prevention (CDC) (1995) Case-control study of HIV seroconversion in health-care workers after percutaneous exposure to HIV-infected blood – France, United Kingdom, and United States, January 1988–August 1994. MMWR Morb Mortal Wkly Rep 44(50):929–933

Centers for Disease Control and Prevention (CDC) (2001) Unexplained deaths following knee surgery–Minnesota, 2001. MMWR Morb Mortal Wkly Rep 50(48):1080

Conway B, Tomford W, Mankin HJ et al (1991) Radiosensitivity of HIV-1–potential application to sterilization of bone allografts. AIDS 5(5):608–609

Eastlund T (2006) Bacterial infection transmitted by human tissue allograft transplantation. Cell Tissue Bank 7(3):147–166

Fahey M, Indelicato PA (1994) Bone tunnel enlargement after anterior cruciate ligament replacement. Am J Sports Med 22(3):410–414

Falconiero RP, DiStefano VJ, Cook TM (1998) Revascularization and ligamentization of autogenous anterior cruciate ligament grafts in humans. Arthroscopy 14(2):197–205

Fideler BM, Vangsness CT Jr, Moore T et al (1994) Effects of gamma irradiation on the human immunodeficiency virus. A study in frozen human bone-patellar ligament-bone grafts obtained from infected cadavera. J Bone Joint Surg Am 76(7):1032–1035

Foster TE, Wolfe BL, Ryan S et al (2010) Does the graft source really matter in the outcome of patients undergoing anterior cruciate ligament reconstruction? An evaluation of autograft versus allograft reconstruction results: a systematic review. Am J Sports Med 38(1):189–199

Fowler JR, Truant AL, Sewards JM (2011) The incidence of and clinical approach to positive allograft cultures in anterior cruciate ligament reconstruction. Clin J Sport Med 21(5):402–404

Granan LP, Inacio MC, Maletis GB et al (2012) Intraoperative findings and procedures in culturally and geographically different patient and surgeon populations: an anterior cruciate ligament reconstruction registry comparison between Norway and the USA. Acta Orthop 83(6):577–582

Guelich DR, Lowe WR, Wilson B (2007) The routine culture of allograft tissue in anterior cruciate ligament reconstruction. Am J Sports Med 35(9):1495–1499

Guo L, Yang L, Duan XJ et al (2012) Anterior cruciate ligament reconstruction with bone-patellar tendon-bone graft: comparison of autograft, fresh-frozen allograft, and γ-irradiated allograft. Arthroscopy 28(2):211–217

Harner CD, Fu FH (1993) The immune response to allograft ACL reconstruction. Am J Knee Surg 6:45–46

Hernigou P (2000) Allograft sterility as exemplified by human immunodeficiency virus and sterilization by irradiation. J Arthroplasty 15(8):1051–1058

Hettrich CM, Dunn WR, Reinke EK et al (2013) The rate of subsequent surgery and predictors after anterior cruciate ligament reconstruction: two- and 6-year follow-up results from a multicenter cohort. Am J Sports Med 41(7):1534–40

Hoburg A, Keshlaf S, Schmidt T et al (2011) Fractionation of high-dose electron beam irradiation of BPTB grafts provides significantly improved viscoelastic and structural properties compared to standard gamma irradiation. Knee Surg Sports Traumatol Arthrosc 19(11):1955–1961

Hu J, Qu J, Xu D et al (2013) Allograft versus autograft for anterior cruciate ligament reconstruction: an up-to-date meta-analysis of prospective studies. Int Orthop 37(2):311–320

Jackson DW, Windler GE, Simon TM (1990) Intraarticular reaction associated with the use of freeze-dried, ethylene oxide-sterilized bone-patella tendon-bone allografts in the reconstruction of the anterior cruciate ligament. Am J Sports Med 18(1):1–10 (discussion 10–11)

Jones DB, Huddleston PM, Zobitz ME et al (2007) Mechanical properties of patellar tendon allografts subjected to chemical sterilization. Arthroscopy 23(4): 400–404

Kaeding CC, Aros B, Pedroza A et al (2011) Allograft versus autograft anterior cruciate ligament reconstruction: predictors of failure from a MOON prospective longitudinal cohort. Sports Health 3(1):73–81

Kainer MA, Linden JV, Whaley DN et al (2004) Clostridium infections associated with musculoskeletal-tissue allografts. N Engl J Med 350(25):2564–2571

Kraeutler MJ, Bravman JT, McCarty EC (2013) Bone-patellar tendon-bone autograft versus allograft in

outcomes of anterior cruciate ligament reconstruction: a meta-analysis of 5182 patients. Am J Sports Med 41(10):2439–48

Krych AJ, Jackson JD, Hoskin TL et al (2008) A meta-analysis of patellar tendon autograft versus patellar tendon allograft in anterior cruciate ligament reconstruction. Arthroscopy 24(3):292–298

Lamblin CJ, Waterman BR, Lubowitz JH (2013) Anterior cruciate ligament reconstruction with autografts compared with non-irradiated, non-chemically treated allografts. Arthroscopy 29(6):1113–1122

Li H, Tao H, Cho S et al (2012) Difference in graft maturity of the reconstructed anterior cruciate ligament 2 years postoperatively: a comparison between autografts and allografts in young men using clinical and 3.0-T magnetic resonance imaging evaluation. Am J Sports Med 40(7):1519–1526

Lind M, Menhert F, Pedersen AB (2012) Incidence and outcome after revision anterior cruciate ligament reconstruction: results from the Danish registry for knee ligament reconstructions. Am J Sports Med 40(7):1551–1557

Maletis GB, Inacio MC, Desmond JL et al (2013a) Reconstruction of the anterior cruciate ligament: association of graft choice with increased risk of early revision. Bone Joint J 95-B(5):623–628

Maletis GB, Inacio MC, Reynolds S et al (2013b) Incidence of postoperative anterior cruciate ligament reconstruction infections: graft choice makes a difference. Am J Sports Med 41(8):1780–5

Malinin TI, Levitt RL, Bashore C et al (2002) A study of retrieved allografts used to replace anterior cruciate ligaments. Arthroscopy 18(2):163–170

McGuire DA, Hendricks SD (2009) Allograft tissue in ACL reconstruction. Sports Med Arthrosc 17(4):224–233

Moore MA (2012) Inactivation of enveloped and non-enveloped viruses on seeded human tissues by gamma irradiation. Cell Tissue Bank 13(3):401–407

Pallis M, Svoboda SJ, Cameron KL et al (2012) Survival comparison of allograft and autograft anterior cruciate ligament reconstruction at the United States Military Academy. Am J Sports Med 40(6):1242–1246

Prodromos C, Joyce B, Shi K (2007) A meta-analysis of stability of autografts compared to allografts after anterior cruciate ligament reconstruction. Knee Surg Sports Traumatol Arthrosc 15(7):851–856

Rihn JA, Irrgang JJ, Chhabra A et al (2006) Does irradiation affect the clinical outcome of patellar tendon allograft ACL reconstruction? Knee Surg Sports Traumatol Arthrosc 14(9):885–896

Roberts TS, Drez D Jr, McCarthy W et al (1991) Anterior cruciate ligament reconstruction using freeze-dried, ethylene oxide-sterilized, bone-patellar tendon-bone allografts. Two year results in thirty-six patients. Am J Sports Med 19(1):35–41

Samsell BJ, Moore MA (2012) Use of controlled low dose gamma irradiation to sterilize allograft tendons for ACL reconstruction: biomechanical and clinical perspective. Cell Tissue Bank 13(2):217–223

Scheffler SU, Scherler J, Pruss A et al (2005) Biomechanical comparison of human bone-patellar tendon-bone grafts after sterilization with peracetic acid ethanol. Cell Tissue Bank 6(2):109–115

Scheffler SU, Unterhauser FN, Weiler A (2008) Graft remodeling and ligamentization after cruciate ligament reconstruction. Knee Surg Sports Traumatol Arthrosc 16(9):834–842

Seto A, Gatt CJ Jr, Dunn MG (2008) Radioprotection of tendon tissue via crosslinking and free radical scavenging. Clin Orthop Relat Res 466(8):1788–1795

Shino K, Kawasaki T, Hirose H et al (1984) Replacement of the anterior cruciate ligament by an allogeneic tendon graft. J Bone Joint Surg (Br) 66(5):672–681

Shino K, Inoue M, Horibe S et al (1988) Maturation of allograft tendons transplanted into the knee. An arthroscopic and histological study. J Bone Joint Surg (Br) 70(4):556–560

Siebold R, Buelow JU, Bös L et al (2003) Primary ACL reconstruction with fresh-frozen patellar versus Achilles tendon allografts. Arch Orthop Trauma Surg 123(4):180–185

Simonds RJ, Holmberg SD, Hurwitz RL et al (1992) Transmission of human immunodeficiency virus type 1 from a seronegative organ and tissue donor. N Engl J Med 326(11):726–732

Spindler KP, Huston LJ, Wright RW et al (2011) The prognosis and predictors of sports function and activity at minimum 6 years after anterior cruciate ligament reconstruction: a population cohort study. Am J Sports Med 39(2):348–359

Swedish ACL Register (2011). Annual report 2011. https://www.artroclinic.se/info/rapport2011en.pdf. Accessed 17 Jun 2013

Tibor LM, Long JL, Schilling PL et al (2010) Clinical outcomes after anterior cruciate ligament reconstruction: a meta-analysis of autograft versus allograft tissue. Sports Health 2(1):56–72

Tugwell BD, Patel PR, Williams IT et al (2005) Transmission of hepatitis C virus to several organ and tissue recipients from and antibody-negative donor. Ann Intern Med 143(9):648–654

Wilson TC, Kantaras A, Atay A et al (2004) Tunnel enlargement after anterior cruciate ligament surgery. Am J Sports Med 32(2):543–549

Woo SL, Orlando CA, Camp JF et al (1986) Effects of postmortem storage by freezing on ligament tensile behavior. J Biomech 19(5):399–404

Yanke AB, Bell R, Lee A, Kang RW et al (2013) The biomechanical effects of 1.0 to 1.2 Mrad of gamma irradiation on human bone-patellar tendon-bone allografts. Am J Sports Med 41(4):835–840