ASPECTS OF CURRENT MANAGEMENT

Current trends in the use of tendon allografts in orthopaedic surgery

Tendon allografts play an important role in tendon and ligament reconstruction, particularly where there is a shortage of suitable available local tissue. Although currently used predominantly for ligament reconstruction around the knee, they have occasional indications in the upper limb and elsewhere. The advantages of using allograft tissue include a lack of donor site morbidity, high tensile strength, decreased surgical time, smaller surgical incisions and a low risk of arthrofibrosis. The disadvantages include their limited availability, high cost, susceptibility to rejection due to immuno-incompatibility between the donor and recipient and potential risk for bacterial, viral and prion disease transmission. This review addresses the current status of the use of tendon allografts in the United Kingdom, including issues surrounding their procurement, processing, biological integration and use.

Biology and biomechanics of integration

All tendon grafts, whether autogenous or allogenic, undergo a similar process of integration with graft necrosis, revascularisation, cell repopulation and remodelling. Following the implantation of autogenous tissue there is fibroblastic in-growth during the first two months, followed by ten months of remodelling of the graft and two years of steady maturation. In comparison, incorporation of allograft in the knee has been demonstrated to occur more slowly and less completely in both animal and human studies. Despite eventual macroscopic similarities between implanted tissue and the native ligaments, both allografts and autografts exhibit differences in their histological morphology and biomechanical properties. All types of grafts lose strength after implantation and allografts have lost a significant proportion by both six and nine months following implantation. Despite this, clinical studies have demonstrated no significant change in knee laxity or in the knee scores after long-term follow-up of three and seven years.

The process of integration of allograft is significantly affected by the method of processing the tissue. Fresh allograft tissue is unsuitable for implantation because it is highly immunogenic and tissue typing is impractical. The processes of fresh-freezing, freeze-drying or cryopreserving allograft tissue significantly reduce the immunogenicity of the tissue by killing fibroblasts within it. This removes the loci for the major histocompatibility antigens, allowing allografts to be used in immunologically-incompatible hosts without provoking a significant immune response. Both gamma irradiation and ethylene oxide are used to reduce the risk of disease transmission during processing. These techniques may also have a detrimental effect on both the biomechanical and biological properties of the graft.

Tendon procurement and donor screening

The procurement of allograft tissue for use in orthopaedic surgery varies between countries and healthcare systems. In North America, commercial tissue banks accredited by the American Association of Tissue Banks predominate. In the United Kingdom, allograft harvesting, processing and supply is predominantly coordinated by tissue banks run by bodies such as the National Blood Service and Scottish National Blood Transfusion Service, who are regulated by the Medicines and Healthcare Products Regulatory Agency.

Tendon allografts may be obtained by harvesting tissue either from multi-organ donors or from cadavers. There are significant advantages in using allografts obtained through multi-organ donation, as tissue transplant coordinators are able to ensure that donors are appropriately identified and screened, and that the allografts are collected aseptically using standard protocols under standard operating theatre conditions. There are disadvantages of multi-organ donations, including the relative
Table I. Summary of the key issues in donor screening for tissue donation that require discussion with transplant co-ordinators (adapted from Scottish National Blood Transfusion Service guidelines) with contraindications in bold

<table>
<thead>
<tr>
<th>General health information*</th>
<th>Travel risk assessment</th>
<th>Behavioural risk assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-term steroid therapy</td>
<td>Travel outside UK (previous 12 months)</td>
<td>Male/male sexual activity</td>
</tr>
<tr>
<td>Blood transfusion (since 1980)</td>
<td>Feverish illness while abroad (or up to four weeks of return to the UK)</td>
<td>Snorting/injection of non-prescription drugs</td>
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<tr>
<td>Significant weight loss, diagnosis or investigation of cancer</td>
<td>Birth or maternal origin or work/residence in rural Central or South America (for more than four weeks)</td>
<td>HIV/Hepatitis B/Hepatitis C infection or injury in the last 12 months putting donor at risk (i.e. needle-stick injury)</td>
</tr>
<tr>
<td>Recent infection, recent contact with infectious disease or immunisations (in the last eight weeks)</td>
<td>Blood transfusion in Central or South America Continuous period (more than six months) in Sub-Saharan Africa (except South Africa) or Papua New Guinea</td>
<td>Received payment with money or drugs for sex</td>
</tr>
<tr>
<td>Hepatitis, jaundice or liver disease</td>
<td></td>
<td>Prison (more than three days in previous 12 months)</td>
</tr>
<tr>
<td>Serious infection e.g. active tuberculosis, active malaria, West Nile virus, SARS, typhoid fever, toxoplasmosis, rabies, encephalitis, Lyme disease or brucellosis</td>
<td></td>
<td>Sex (up to 12 months) with partner who has been sexually active in countries with widespread AIDS/HIV (includes most countries in Africa)</td>
</tr>
<tr>
<td>Operations or illnesses, including organ/tissue transplant, neurosurgical operations for a tumour or cyst of the spine/brain or implantation of dura mater (before August 1992)</td>
<td></td>
<td>Sex in the last 12 months with anyone included above</td>
</tr>
<tr>
<td>Brain disease (i.e. Parkinson’s, Alzheimer’s), recent memory loss, confusion, unsteady gait or family history of CJD, vCJD, or Gerstmann-Strassler-Schnienker disease</td>
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<tr>
<td>Acupuncture, tattooing, body piercing, botox injections in the last 12 months</td>
<td></td>
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<tr>
<td>Received human pituitary extracts e.g. growth hormones, fertility treatment or test injections for hormone imbalance</td>
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</tr>
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* SARS, severe acute respiratory syndrome; CJD, Creutzfeld-Jakob disease; vCJD, variant Creutzfeld-Jakob disease

Adequate screening of donors is a vital component of allograft procurement. All biological tissue carries some risk of bacterial, viral or prion disease transmission. Although cases of transmission of HIV and Hepatitis C have been reported in patients receiving musculoskeletal allografts, most reported cases have involved bone rather than tendon. The estimated risk of transmission of viral disease from an adequately-screened donor is approximately one in 1 500 000, which compares favourably with the estimated risk from blood transfusion of between one in 400 000 and one in 600 000.26 Multi-organ donor screening includes a thorough review of the donors’ medical records for factors that may influence their risk of transmitting potentially infectious or malignant disease. Blood samples are obtained for serological testing against a number of prevalent organisms. Polymerase chain reaction (PCR) assays are used to amplify and detect viral nucleic acid, allowing detection of viruses such as HIV during the window between infection and the donor mounting an immune response by antibody production. At present there is no routine testing for variant Creutzfeld-Jakob disease so that patients at risk by contact or those with atypical dementia are excluded from donation. The very low risk of transmission of prions, or as yet unidentified pathogenic viruses, must be discussed with the patient during the process of consent. To date, there have been no reported cases of transmission of Creutzfeld-Jakob disease as a result of the use of tendon allografts.

Graft harvest

Although a variety of tendon allografts are currently available in the United Kingdom, tendo Achillis and patellar tendon allografts predominate. Fascia lata, rotator cuff, tibialis posterior, tibialis anterior, gracilis and semitendinosus grafts are also available commercially. The tendo Achillis grafts are retrieved through a paratendinous incision of approximately 20 cm. The musculotendinous junction is identified and the tendon dissected free from the attached muscle fibres, ensuring that the maximum length of graft possible is obtained. At least two-thirds of the tendo Achillis should be included in this single tendon-bone
unit (Figs 1 and 2). Patellar tendon allografts (bone-tendon-bone) are retrieved through a longitudinal midline incision of approximately 25 cm over the front of the knee exposing the patella, patellar tendon and tibial tuberosity. The graft is harvested as a bone-tendon-bone unit with a generous block of tibial tuberosity (approximately 3.5 cm long and at least 2 cm wide) to avoid fracturing the distal bone block. Tendons 2 cm wide or more are suitable for splitting to provide two patellar tendon allografts (Fig. 3).24 Following harvest the graft is packaged in a rigid double container and bar-coded. Samples of both soft tissue and bone are obtained for aerobic and anaerobic testing and the graft is frozen, without preservatives, at -80°C in freezers while the results of bacterial and viral screening are awaited.

Graft processing

Graft processing requires sterile laboratory conditions and aims to ensure that maximum use is made of donor tissue by trimming, sizing and splitting if required. It also seeks to minimise antigenicity within the tissue and to ensure that the graft material is free from bacterial and viral contamination, while minimising damage to its structural integrity.

Bacterial decontamination of the surface of the graft with minimal tissue damage may be achieved by immersion in an antibiotic solution. The problem of deep bacterial, viral or prion infection should be addressed by a combination of harvesting under aseptic conditions, donor screening, bacterial testing and controlled processing. In grafts which are obtained by processes not fulfilling these criteria, sterilisation by gamma irradiation or ethylene oxide may be used. For composite tendon allografts the effects of the sterilisation processes on all elements of the graft must be considered.

Gamma irradiation has a viricidal and bacteriocidal effect both by direct alteration of nucleic acids leading to genome destruction and by the production of free radicals. Freeze-dried grafts require higher doses of irradiation because of the relative absence of water from which the free radicals are generated. The dose of radiation chosen should destroy infective agents including bacteria, bacterial spores, viruses and prions without producing structural damage to the allograft. Gamma irradiation produces dose-dependent damage to collagen. A minimum dose of 35 kGy is required to eliminate HIV in tissue. However, many tissue banks, particularly in the United States, use gamma irradiation in doses ranging from 10 to 25 kGy in order to obtain a compromise between sterilisation and damaging the structural integrity of the graft.27 Cyclical loading experiments have demonstrated that even low dose irradiation (20 kGy) can lead to increased elongation of the graft and a decreased load to failure compared with non-irradiated controls.23

Ethylene oxide, applied in a gaseous state with inert diluents such as carbon dioxide, has been widely used in the sterilisation of biological tissue.27 The principle concerns regarding its use in tendon allografts include the degree of bone penetration that may be achieved by the gas, and reports of graft dissolution, persistent synovial effusion and a poor clinical outcome.22,28 Persistent effusions in the knee have been reported in patients receiving allograft treated with ethylene-oxide for up to 14 months following graft implantation due to the presence of toxic reaction products within allograft and synovium.28 The difficulty in obtaining adequate viral clearance using sterilisation methods serves to emphasise the importance of having a thorough pro-
gramme of donor screening. Processed graft material may be stored at -80˚C for three to five years prior to use. The importance of strict adherence to protocols is illustrated by reports of Clostridium Septicum infection following anterior cruciate ligament (ACL) reconstruction, thought to have occurred because of graft contamination during processing in the tissue bank.25

Allograft implantation

The risks and benefits of using allograft tissue must be discussed with the patient as part of the process of consent. The surgeon should remain aware of the moral and ethical issues surrounding the use of allograft tissue, as well as the risks of disease transmission. Allograft tendon is transported to the hospital on dry ice under temperature-controlled conditions, and the packaging and expiry date is checked. The donor tendon may then be transferred to a sterile container and cut and shaped immediately prior to grafting. The thawing process from -20˚C should take at least one hour. Alternatively, the graft may be immersed in sterile saline warmed to 37˚C for 30 minutes. The graft should be used within four hours if stored at room temperature or within 24 hours if stored at 1˚C to 6˚C. It may be stored for up to six months at -20˚C.36 Prior to a decision to use allograft during reconstruction, a check should be made as to whether the recipient is allergic to the antibiotics used during processing, as trace amounts may remain within the tissue. Further microbiology samples may be taken at the time of implantation at the discretion of the surgeon.

Indications for allografts

Reconstruction of the anterior cruciate ligament. Tendon allografts are rarely indicated in primary reconstruction of the ACL unless there are particular concerns regarding the morbidity associated with graft harvest. Despite this, a number of recent studies have demonstrated comparable clinical and radiological results when using allograft tissue in primary reconstruction of the ACL, whether cryopreserved or fresh-frozen, when compared to autografts.31-35 Although a number of allograft tissues have been used for primary reconstruction of the ACL including tendo Achillis, bone-patellar tendon-bone and fascia lata, there is little clinical evidence to support the choice of one type of allograft over another. A recent direct comparison between tendo Achillis and bone-patellar tendon-bone allograft demonstrated comparable outcomes at a mean follow-up of 37.7 months, although the authors noted a lower rate of failure in the patients receiving a tendo Achillis graft.36 A key factor restricting the use of allograft for primary reconstruction of the ACL is the perception of its higher cost. This belief has been recently questioned by Cole et al37 who demonstrated a cost advantage in using freeze-dried tendo Achillis allografts when compared to patellar tendon autograft when all of the costs involved in the procedure were considered. For revision reconstruction of the ACL, autograft (patellar tendon or hamstring) may be obtained from the injured or non-injured knee. If suitable tissue is not available from the injured knee and there are overriding concerns regarding the morbidity associated with harvest from the non-injured knee, allograft tissue may be used, with results comparable to autograft using non-irradiated fresh-frozen patellar tendon.38

Reconstruction of the posterior cruciate ligament (PCL). Autogenous hamstrings, patellar tendon and quadriceps tendon have all produced favourable outcomes in reconstruction of the PCL. Allograft has a role particularly where there is an associated collateral ligament injury requiring reconstruction. Studies comparing autograft (double-bundle hamstrings/patellar tendon) with allograft (tendo Achillis, tibialis anterior) in isolated reconstruction of the PCL have shown comparable results using a variety of outcome measures including functional and clinical assessments, instrumented testing (KT-1000) and knee scores (Lysholm, International Knee Documentation Committee).39,40 It is interesting to note that there is no overall consensus in the choice of graft for reconstruction of the PCL. A recent survey of surgeons in the United States performing reconstruction of the PCL noted a marked preference for tendo Achillis allograft with both early and late reconstruction. This is possibly a result of the greater ease of passage of the tendinous portion of the graft along the femoral and tibial tunnels.41

Multiple ligament reconstruction. In more complex ligament injuries of the knee, tendon allograft provides a distinct advantage over autograft because of the limited availability of uninjured host tissue.42 In addressing postero-lateral instability of the knee patellar tendon, tendo Achillis and tibialis posterior allograft have all been used to successfully augment the injured structures.43 Reconstruction of the medial collateral ligament has also been carried out either in isolation or in conjunction with auto- or allograft reconstruction of the ACL using tendo Achillis.44

Other uses. Tendon allografts have been used in surgery on the extensor mechanism of the knee for the treatment of patellofemoral instability and in the treatment of chronic patellar tendon rupture using tendo Achillis allograft.46,47 In addition, both tendo Achillis and patellar tendon allografts have been used successfully in reconstruction of the extensor mechanism in patients with chronic loss of extension following total knee replacement, restoring active extension, improving functional capacity and ambulatory function.48,49 Other uses of tendon allograft in the lower limb include the use of patellar tendon and fascia lata allograft in reconstruction of the lateral ligament of the ankle.13,14

Although less commonly used in the upper limb, tendon allografts are now being considered for use in reconstructive surgery. Applications include the management of elbow instability, rupture of the pectoralis major tendon,15 rupture of the biceps tendon,10 chronic triceps insufficiency and triceps deficiency in patients following total elbow arthroplasty.12 In addition, tendo Achillis allografts have
been used for the reconstruction of the tendon of biceps brachii following the excision of tumoural calcinosis.\textsuperscript{11}

Tendon allografts have an important role to play in reconstruction of the tendon and ligament in a number of anatomical sites. Surgeons using tendon allografts must be aware of the major issues surrounding their procurement, processing and use. Adequate screening and processing can reduce, but will not eliminate, the risk of disease transmission. This must be discussed with the patient during the process of consent. An understanding of the comparative remodelling between auto- and allograft and the likely effects of processing may be used to help the choice of graft used and to direct rehabilitation to minimise the risk of rupture.

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References


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