USE OF FRESH OSTEOCHONDRAL TRANSPLANTS FOR TREATING OSTEOCHONDRAL KNEE LESIONS

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ABSTRACT

Treatment of chondral and osteochondral knee lesions in young patients remains a challenge for orthopedic surgeons. The repair techniques currently available in Brazil, such as debridement, microfracture and autologous osteochondral transplantation are insufficient for treating large chondral and osteochondral lesions. Fresh homologous osteochondral transplants have been used in the knee joint in the United States with excellent results. In this article we are going to review the basic science, indications, surgical techniques and possible complications of fresh osteochondral allograft transplantation in the knee joint. We will also describe some surgeries performed in the Institute.

Keywords – Knee; Cartilage; Osteoarthritis; Transplantation, Homologous

INTRODUCTION

Lesion of the joint cartilage can compromise the quality of life of young, active patients, leading to incapacity to play sports, or to work. The aim of treatment of chondral and osteochondral lesions in

these patients is to reestablish the joint anatomy and to eliminate pain using a biological repair as the treatment option whenever it is possible. Most of these patients are not ideal candidates for knee arthroplasty surgeries. The results of treatment of large chondral lesions by surgical debridement or microfracture procedure are inadequate, and these techniques are not recommended for the treatment of large osteochondral lesions of the knee. Osteochondral autograft transplantation (OATS, mosaicplasty) is a good treatment option; however, it has the limitation of morbidity of the donor site , and is best-suited for small to medium lesions. The use of fresh osteochondral allograft transplantation (FOAT) for the treatment of large chondral and osteochondral lesions of the knee is a good biological option in young patients, with the main advantage that it is an organ with hyaline cartilage and live chondrocytes in a chondral matrix, with preserved collagen fiber architecture. FOAT has been used in other countries for decades[1-5]. This technique was initially introduced for the treatment of post-traumatic bone defects[6,7]; however, today, it is used for various pathologies of the knee, such as osteochondritis dissecans, secondary osteonecrosis, degenerative disease of the knee, and complications arising from fractures[8-11]. The current treatment options for large chondral and osteochondral lesions of the knee are autologous transplant of chondrocytes, and fresh osteochondral allograft transplantation, the principle of this technique being to reestablish the biological anatomy of the joint, and provide an osteochondral tissue capable of mechanical weight-bearing. Meanwhile, there have been no reports to date on the use of this technique in Brazil.

FOAT is a technique in which the osteocartilaginous organ taken from an organ donor is kept at a temperature of 4 to 10°C, but without being frozen at temperatures below zero, as in the case of preservation of bone and tendinous tissues, since freezing leads to cell death of the chondrocytes. After a period of storage in cellular preservation solutions, the cul-

tures are released from the donor and from the tissue, and the organ is then transplanted into the host[12,13].

Basic science

Storage of the osteochondral tissue leads to a decrease in chondrocyte cell viability, cellular metabolism, and cell density in the cartilaginous matrix, but without affecting the subchondral bone. Freezing the joint cartilage leads to chondrocyte cell death and decreases the histological and biomechanical properties of the matrix[14-16]. Possible causes of incapacity to survive freezing include the small penetration of cryopreservation solutions in the tissue, different freezing speeds of the various layers of the matrix, and the high water content in the extracellular matrix. During storage in a refrigerator, the viability and density of the chondrocytes can decrease over time. Due to the need to prepare cultures for viruses and bacteria in the donor and in the organs, the osteochondral tissue is generally stored for longer, and released at least 14 days after procurement[17]. McCulloch et al[18] and Williams et al[19] demonstrated good clinical results in the fresh transplant performed at up to 42 days of refrigeration. Frozen osteochondral tissues can be used in surgical procedures; however, there is a higher likelihood of delamination, fissures, and failure and collapse of the chondral surface[20,21].

After transplant, the cartilaginous matrix keeps the chondrocytes protected (immunoprivileged), as the matrix is avascular, and receives nutrients by diffusion. For this reason, the principal immunogenic tissue of the fresh transplant is the bone layer, which can lead to varying degrees of response depending on the amount of bone transplanted, but it does not require immunosuppression after the procedure[22]. The inflammatory response to the transplanted tissue generally decreases over time, and can continue for up to 18 to 24 months after the procedure[23].

After transplant, there is no donor-host bone consolidation. Bone healing occurs by a process of gradual replacement (creeping substitution) in which the bone of the host grows to occupy the trabeculae and gaps in the transplanted bone, leading to remodeling by the osteoblasts and osteoclasts, and the creation of new Haversian systems. Long-term studies carried out with osteochondral tissue sample collections taken during revision surgery demonstrate high viability and cell density of the chondrocytes[19,24-26].

Clinical evidence

There is plenty of evidence in the literature to support the use of the FOAT for the treatment of osteochondral lesions of the knee.

Lexer[27,28], in 1908, described the first osteochondral transplant, but it was not until the second half of the last century that this procedure became widely accepted as a major reconstruction technique. Currently, it is used in various orthopedic procedures, including: arthrodesis of the spine, resection of bone tumors, arthroplasty revisions, and reconstruction of post-traumatic bone defects.

Gross et al.[3] demonstrated excellent results after 364 cases performed, and more than 25 years of follow-up, with 95% survival of the graft after 5 years, 80% after 10 years, 65% after 15 years and 46% after 20 years, providing a treatment option for patients who would be considered too young to undergo arthroplasty[3,25]. A 96% survival rate was shown by McCulloch et al[18] in a study of 25 consecutive patients treated for lesions of the femoral condyle, with minimum follow-up of two years. LaPrade et al[15] showed good clinical results for the FOAT stored for between 15 and 28 days after procurement, with a mean follow-up time of three years.

Davidson et al[29] performed a study describing biopsies from 10 knees (eight patientes) taken after mean follow-up of 40 months, from a 67-patients cohort. In this study, biopsies were taken from normal (untransplanted) tissue and from the graft. Histological analyses considering cell viability and cell density did not show statistical difference.

Gortz et al[9] reported good results in the treatment of secondary osteonecrosis of the knee caused by the use of corticosteroids, althoughinferior to those obtained after treatment of post-traumatic lesions. The authors reported the results long-term follow-up of FOAT surgeries for the treatment secondary osteonecrosis of 22 patients (28 knees) with a mean age of 24.3 years (range from 16 to 44 years). They described five clinical failures, but radiological failure was evident in only three knees after an average follow-up of 5.6 years.

Emmerson et al[30] observed a 15% failure rate in 65 knees at an average follow-up of 7.7 years (range from 2 to 22 years) after FOAT in patients with a mean age of 28.6 years (range from 15 to 54 years). The authors described as failures patients who underwent removal

of the graft, revision allograft, unicompartmental arthroplasties, and total arthroplasties surgeries.

We summarized osteochondral allograft reports in Table 1.

Table 1 – Fresh osteochondral transplant in the knee joint: number of cases, mean follow-up time, etiology of the lesions, failure rate and survival. ON – osteonecrosis, OCD – osteochondritis dissecans.

Study	Mean follow-up (years)	No. of cases	Causes of lesion	Failure rate	Survival
McCulloch et al[18]	2.9	25	Varied	4%	96%
LaPrade et al[15]	3	23	Varied	0%	100%
Williams et al[19]	4	19	Varied	21%	79%
Gortz et al[9]	5.6	28	Secondary ON	18%	89%
Emmerson et al[30]	7.7	66	OCD	15%	91%-5y 76%-15y
Gross et al[25]	10	60	Post-trauma, OCD	20%	95%-5y 85%-10y 74%-15y

Indications and selection of patients

The FOAT is indicated in the treatment of large chondral and osteochondral lesions of the knee (larger than 2 cm²), in which other types of cartilage repair procedure are are not indicated due to the size of the lesion. The most common disorders in which the FOAT is used are: osteochondritis dissecans, osteonecrosis, complications of knee trauma with osteochondral defects, and patellofemoral chondral lesion[12]. Another indication of the FOAT is to treat failures of other surgical techniques such as used for osteochondral lesions, such as microfractures, debridement, mosaicplasty, and autologous chondrocyte transplantation.

The FOAT should not be considered as an alternative to arthroplasty in individuals whose symptoms and age make them suitableto joint replacement procedures. Multicompartmental arthrosis, ligament instability, uncorrected lower limb axis deviations, inflammatory diseases, crystal arthropathy, and smoker patients are usually considered contraindications to FOAT. .

Preoperative planning should be detailed, and radiographs of both knees should be requested, as well as magnetic resonance imaging of the affected side. We routinely request radiographs in frontal view (AP) with weight-bearing, profile view at 30°, axial view of the patellas at 45° and posterioranterior (PA) view with the knees flexed at 40-45° (Rosemberg) of both knees,full-length standing AP radiography views. panoramic radiography of the lower limbs to measure the limb alignment, discounting the radiographic magnification. Based on this measurement, and on the weight and height of the donor and host, we determine the compatibility of the size of the grafts.

Magnetic resonance imaging should be used to evaluate the osteochondral lesion, subchondral bone lesion, and associate meniscal-ligament lesions. Ligament lesions should be corrected before, or during the FOAT, and the limb aligned (Figure 1). In cases of treatment of lesions in the extensor apparatus, proximal and distal corrections should be carried out, to obtain good alignment of the patellar dislocation.

In lesions of the lateral plateau, magnetic resonance imaging assists in the evaluation of the lateral meniscus, which should be transplanted together with the plateau, if it is damaged[31-33].

Figure 1 – (A) Secondary osteonecrosis of the lateral femoral condyle (LFC). (B) Varus osteotomy of the distal femur to correct limb alignment prior to transplant. (C) Fresh osteochondral transplant of the LFC (fresh osteochondral transplant carried out at the Institute of Orthopedics and Traumatology of the Hospital das Clínicas of the FMUSP).

Procurement and processing

In the United States, the main source for obtaining tissues for FOAT is procurement provided by death verification services equipped with surgical rooms, in which the tissues can be harvested safely. Another source is organ donation. In Brazil, we do not yet have the procurement option in the death verification services, although the *Serviço de Verificação de* Óbitos *da Capital* (Death Verification Service) – SVOC in São Paulo has a dedicated room for tissue collection. At present, tissues for FOAT are obtained from organ donor patients who have opted to donate bones, from which tendons, bones and cartilage are harvested.

For the use of osteochondral tissue in FOAT, the joint capsule must be kept intact, without the intra-

articular structures - including the cartilage - coming into contact with the outside environment. The knee is harvested by en bloc resection, dissecting only the skin and subcutaneous layers, performing an osteotomy in the distal femur 10 cm above the joint line, and an osteotomy in the proximal tibia and fibula, two centimeters below the most distal part of the tibial tuberosity (TT).

The en bloc piece is placed in a lactated ringer solution, and hermetically packaged in three layers, for transport at a temperature of 4° Celsius. After procurement, the tissues are taken to the Tissue Bank of IOT-HC-FMUSP for immediate processing.

The processing stage is carried out in a dedicated, classified surgical room (class 100 or ISO 5) equipped with laminar flow module. The room also has a pass-through chamber, and all the environments are rigorously controlled for air particles number and uses positive pressure air particles and positive pressure, to guarantee the quality of the tissues processed there. Access to the room is allowed only after proper sterile gown technique using synthetic fabric (SMS), to prevent dispersion of the particles.

The joint capsule is open via the medial parapatellar, and the structures are measured with a caliper, for paring with the hosts of the FOAT list. The joint cartilage is analyzed, and only the parts in which this structure is intact will be used. Any chondral lesion is rejected, and this tissue is sent for freezing, to be used in other procedures.

If there is a pairing of donor and receptor, the tissue is prepared by isolating the necessary compartment: condyles, plateaus, trochlea and patella; in this stage, the cultures are harvested for analysis.

The tissues are wrapped in a triple layer, vacuum sealed, containing the preservation medium that helps maintain the viability of the chondrocytes.

Generally the cultures take around 14 days to be released, during which time the host is prepared and the surgical procedure is scheduled.

Surgical technique

There are basically two types of surgical technique used to perform fresh osteochondral knee transplant: the surface technique, and the use of osteochondral cylinders.

The knee is approached by medial or lateral parapatellar arthrotomy, depending on the site to be targeted. For cases of multiple lesions, an ample arthro-

tomy should be performed, as in cases of total knee arthroplasty, facilitating access to all the structures, taking care not to damage the meniscal insertions during access.

In the osteochondral cylinder technique, the site of the lesion is identified, placing a measuring cylinder of the same diameter as the lesion, after inserting a 2.5 mm Kirschner wire in the center of the lesion. Debridement of the lesion is carried out with trilaminate bone cutter, until good quality subchondral bone is reached (Figure 2). A depth of 3 to 5 mm is sufficient when there is no disease of the subchondral bone. In cases of osteochondritis dissecans or secondary osteonecrosis, the preparation of a deeper host bed may be necessary.

After preparation of the host bed, we carried out the measurement of its depth in four corners, in order to obtain a graft with dimensions and depth identical to the host bed.

Ideally, the donor graft should be removed from the corresponding host site. For this purpose, we request, from the tissue bank, an entire medial femoral condyle, if the treatment is for a lesion of the medial femoral condyle. The hemicondyle of the donor is fixed to a metal device or on two reduction forceps, and a cylindrical cutter of specific size is used to remove the graft (Figure 3 – A-D). After preparing the graft, it undergoes pulsatile or pressure cleaning, to eliminate residue and cells from the bone marrow of the donor, which could contribute to increasing the host's immune response.

The final stage of the transplant is the placement of the graft in the host bed. It is very important not to hit the graft when placing it in the host bed, as this could lead to early cell death and failure of the procedure[34] (Figure 3E). If it is not possible to achieve adequate stability of the graft in the host bed, Kirschner wires, or pins and absorbable darts, can be used for its fixation.

Another technique used in the FOAT is the surface technique. In this procedure, the lesion and the graft are prepared by the free-hand method, attempting to adjust the sizes for the transplant. For this procedure, chisels, curettes, and delicate drills are used, using a piece of paper or gauze to measure and plan the size of the tissue to be transplanted (Figure 4).

An example of this type of technique is surgery for complete lesions of the femoral condyle, lesions of
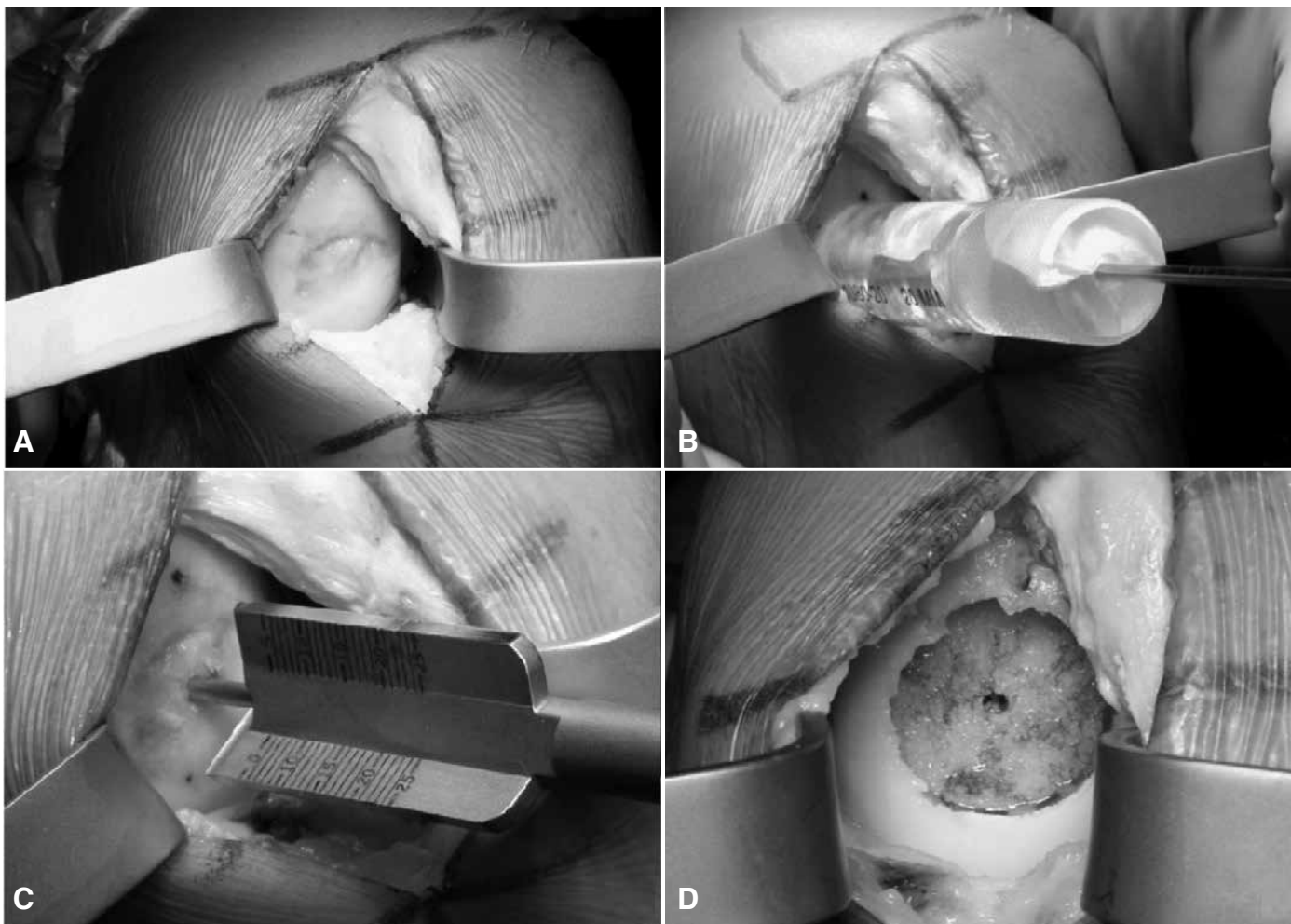
Figure 2 – (A) Osteochondral lesion in the medial femoral condyle. (B) Positioning of the measuring cylinder to determine the diameter of the lesion. (C) Debridement of the lesion with a trilaminate bone cutter. (D) Host bed after debridement. Note the quality of the subchondral bone and the depth of the lesion (Authorized by Dr. William Bugbee, Scripps Clinic, San Diego).

the tibial plateau, or lesions of the entire patella. In these cases, it is not usually possible to achieve sufficient stability of the transplanted tissue, therefore the use of additional fixation is necessary, with Kirschner wires, and screws or absorbable darts.

In the case of lesion of the tibial plateau, the integrity of the meniscus in the affected compartment should be evaluated. If it is damaged, the donor meniscus should be transplanted together with the tibial plateau.

Postoperative period

Numerous postoperative protocols have been described in the literature. In general, we should prevent weight-bearing on the transplanted graft until it has healed, and satisfactory strength of the quadriceps has been obtained. For lesions of the femorotibial joint, in which grafts not contained were used with secondary fixation, we implemented a period of restricted weight-bearing for six weeks, with full weight-bearing being

allowed after 12 weeks. These patients spend six weeks with a postoperative immobilizer, and are instructed to perform movements on a continuous passive motion (CPM) machine, where available, or daily physiotherapy sessions.

Grafts performed on the patellofemoral joint can be treated with immediate partial weight-bearing, with a locked immobilizer and in full extension. The degree of range of passive movement is gradually progressed over the weeks, seeking to achieve 90° of flexion at around six weeks. Active movement and total weight-bearing of the knee are allowed at eight weeks. Depending on the stability of the graft, we can change the period of weight-bearing and range of movement of the knee.

Risks and complications

Infection in a fresh osteochondral allograft transplant is very rare, but can be devastating. The risk of infection by *Clostridium* increases proportionally to
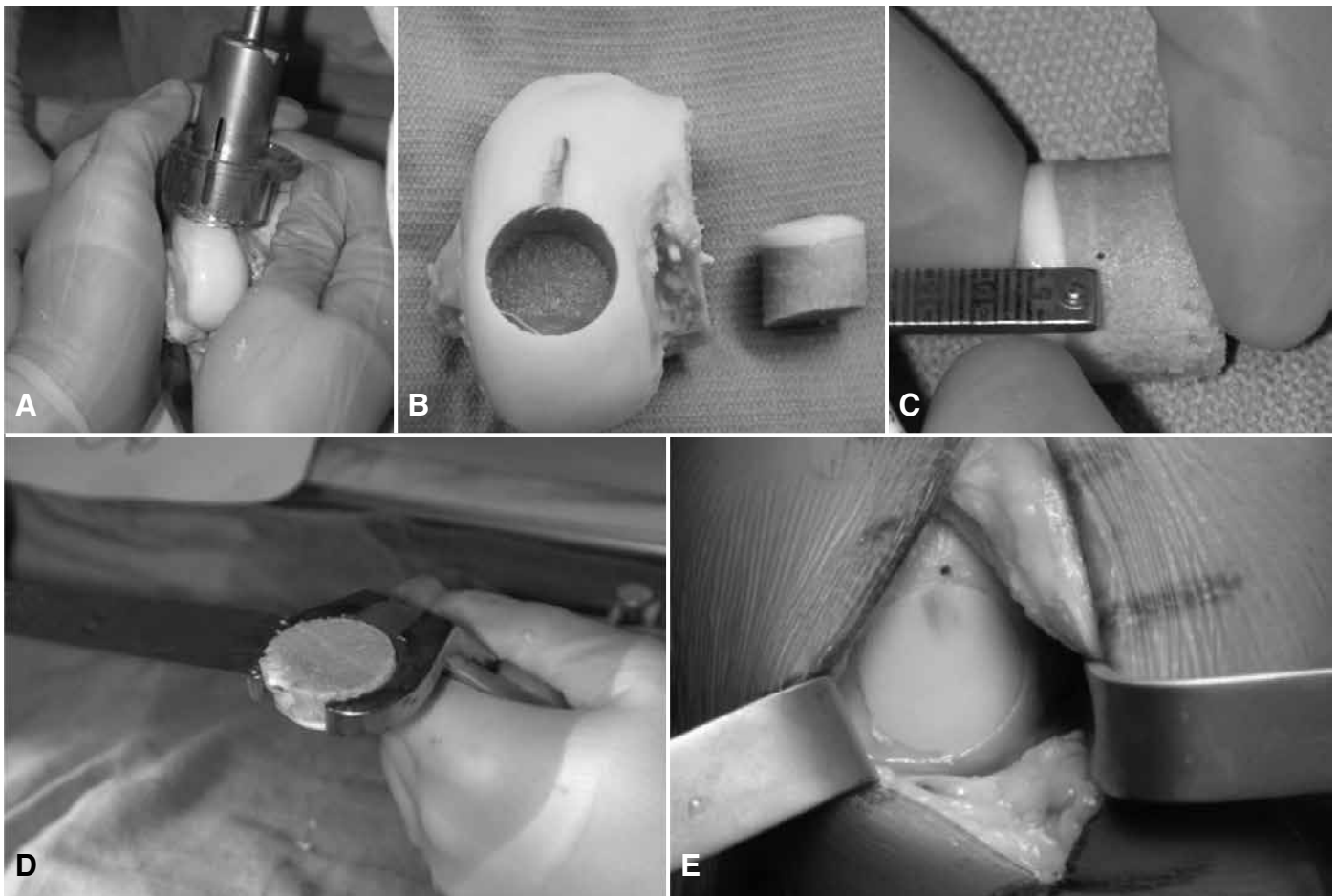
Figure 3 – (A) Removal of the donor graft of the medial femoral condyle. (B) Graft removed from the medial femoral condyle, marking the north position of the graft. Note that the depth of the graft is greater than that of the host bed. (C) Measuring the depth of the graft identical to the depth of the four quadrants of the host bed. (D) Positioning of the graft in reduction forceps, so that it can be prepared using a saw. (E) Transplanted graft, perfectly positioned in relation to the host bed, without presenting any uneven areas, or bulges (Authorized by Dr. William Bugbee, Scripps Clinic, San Diego).
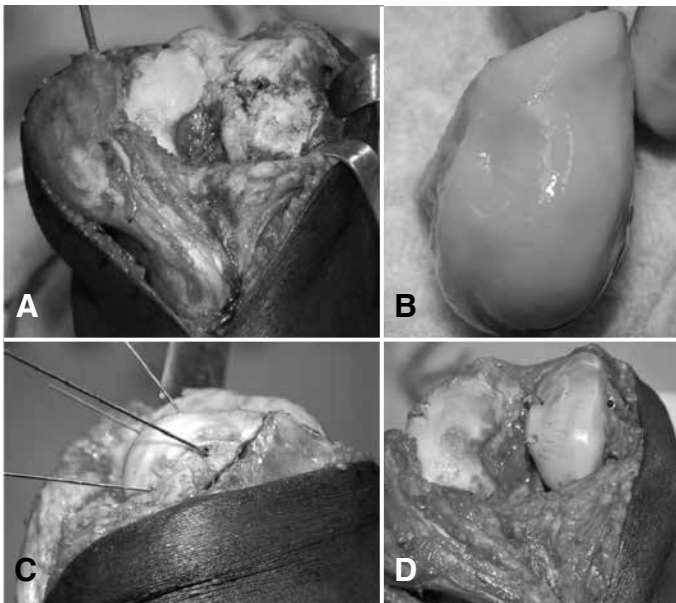
Figure 4 – (A) Necrosis with bone loss of the lateral femoral condyle (LFC). (B) Fresh osteochondral graft of the LFC. (C) Fresh graft fixation restoring the anatomy of the LFC. (D) Final appearance of the graft fixation (fresh osteochondral transplant carried out at the Institute of Orthopedics and Traumatology of the Hospital das Clínicas of the FMUSP).

the elapsed time the time betweendonor death and tissue removal[35,36]. These risks are higher in the United States, as the majority of tissues are obtained from the death verification services, equipped with a tissue procurement room.

In Brazil, all tissues are presently obtained directly from organ donors, which vastly decreases the risk of bacterial infection. There is also a systematic protocol in place for the selection of donors, based on the legislation of the Brazilian Association of Organ Transplantation (ABTO), where tests are carried out for bacteria, viruses, fungi, syphilis, hepatitis, HIV and HTLV. The harvested tissues are kept in quarantine until the results of the virus and bacteria cultures have been released, and only then are the tissues cleared for transplant. At the IOT-HC-FMUSP, this quarantine period lasts around 14 days, until the cultures are released, remembering that the tissues will only be used if the cultures are negative. If the results are positive, the tissues are disposed of.

Failure of the FOAT generally occurs in the bone layer. Delayed bone consolidation, or failure to consolidate, are rare, but can occur. Usually the failure occurs with fragmentation of the graft and collapse of the subchondral bone, eliminating the support for the cartilage. Clinical symptoms of graft failure include new on-set of pain, joint effusion, and mechanical symptoms associated with movement. If the patient does not present any clinical symptoms, the radiographic image should be used to identify any presence of graft failure. The ideal graft after a FOAT surgery on a magnetic resonance image evaluation shows isosignal in the bone layer, wihout any displacement or uneven areas in the joint surface, and also demonstrating good bone integration[19].

FINAL CONSIDERATIONS

The use of the FOAT is an excellent treatment option for young patients with large osteochondral lesions of the knee, and allowing good results in long-term follow-up. The best results are obtained in the treatment of young patients, with unipolar lesions, less than 12 month after the onset of the symptoms. Lesions resulting from the use of corticosteroids, bipolar lesions, and degenerative disease, such as osteoarthritis, have poorer long-term results. The fresh grafts should be used within 30 days of procurement the tissue, according to a Ministry of Health guidelines.

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