J Orthop Sci (2009) 14:259–265
DOI 10.1007/s00776-009-1322-2

JOURNAL OF
ORTHOPAEDIC SCIENCE

Original article

Femoral and acetabular revision using impacted nondemineralized freeze-dried bone allografts

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Abstract
Background. Favorable results have been obtained by the use of deep-frozen bone allografts in total hip arthroplasty. However, owing to the shortage of deep-frozen allografts and the risk of infectious disease, other materials have been studied, such as sterile nondemineralized freeze-dried allografts. The aim of this study was to describe midterm clinical outcomes and radiographic bone incorporation of human freeze-dried bone grafts in 42 revision total hip arthroplasty procedures using cancellous impacted bone grafting.
Methods. This report presented clinical and radiographic evidence of allograft incorporation in 42 hip reconstructions performed between 1996 and 2002. The patient group included 13 (31%) men and 29 (69%) women with mean ± SD age of 63 ± 14 years (range 28–80 years). Mean follow-up was 82 months (range 63–127) months. Clinical analysis was based on the D'Aubigné-Postel score. Radiographic incorporation was defined according to specific criteria.
Results. The D'Aubigné and Postel criteria showed adequate outcome in 38 (90%) of the patients. The radiographic evaluation revealed that allograft remodeling and incorporation were found in 39 (93.0%) and 36 (86.5%) of acetabular and femoral cases, respectively. The overall graft survival rate at an average follow-up of 8 years (range 5–10 years) was 90%.
Conclusions. Bone grafts obtained by the lyophilization process developed and carried out in our tissue bank provide suitable grafts for revision total hip arthroplasty. Clinical and radiographic midterm results were excellent, indicating that nondemineralized freeze-dried bone allografts are suitable for replacing deep-frozen grafts.

Introduction

Although there are several indications to perform revision total hip arthroplasty (THA), such as infection and instability, aseptic loosening is the most frequent. Most cases have been associated with some degree of bone loss.[1] The availability of autografts to replace these losses is limited, and the rate of complications at the donor site is significant. The demand for allograft tissue is far greater than the current supply.[2] Also, the use of deep-frozen allografts carries a certain risk, although rare, of spreading infectious disease.

Acetabular bone stock deficiencies in primary and revision THAs can be restored by bone impaction grafting with morselized bone chips and a cemented cup, as described by McCollum et al.[3] and Gates et al.[4] for primary protrusion acetabuli and later modified by Gie et al.[5]

Kershaw et al.[6] reported that cemented revision into poor bone stock has been associated with a failure rate sixfold higher than revision into average or reduced bone stock, and especially repeated revision procedures using cement carry a poor outcome. According to Gie et al.,[5] the use of allograft chips and cement might improve the results of femoral revision.

The shortage of deep-frozen allografts for revision THA at the Hip Surgery Service of Hospital de Clínicas de Porto Alegre (HCPA) University Hospital and the American CDC reports regarding infections associated with use of allografts[7] led us to search for an alternative tissue-processing technique to improve the availability and safety of allografts and the use of xenografts. Lyophilization and sterilization processes for bone grafts were developed at our Biomaterial Department, HCPA University Hospital. Grafts were initially tested in experimental animal studies and in a clinical study using bone grafts during other orthopedic procedures. As the results were excellent, we started to apply bone grafts for revision THA.

The purpose of this study was to present midterm clinical outcomes and radiographic bone incorporation of human freeze-dried bone grafts after 42 revision THA procedures with impacted cancellous bone grafting.

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Received: January 10, 2008 / Accepted: January 22, 2009

Materials and methods

Patients

A total of 42 revision THAs were performed between May 1996 and September 2002 using impacted freeze-dried cancellous bone allografts. All patients were followed up to December 2006, and during follow-up all patients were clinically and radiographically assessed at least once a year.

The group of patients included 13 (31%) men and 29 (69%) women with a mean age ± SD of 63 ± 14 years (range 28–80 years). The right or left side was affected in 28 and 14 cases, respectively. The underlying diseases and type of fixation when the primary THA was performed are shown in Table 1. Mean follow-up was 82 months (range 63–127 months). All patients received morselized and impacted freeze-dried bone grafts rehydrated in saline solution for 1 h before use. Postoperatively, patients were allowed to stand up within 2–3 days and to walk with low weight bearing on crutches within 3–4 months, followed by a gradual return to full weight bearing.[5] Patients were fully informed, and all of them gave informed consent. The study was approved by the Ethics Committee of HCPA University Hospital.

Also, all patients completed the clinical and radiographic follow-up. Two patients died within 2 and 3 years after the procedure, respectively. Neither of these deaths was related to revision THA.

Only the femoral or the acetabular component was revised in 12 and 20 cases, respectively. In the remaining 10 cases, both components were replaced. However, these components were independently considered for bone incorporation analyses, thus resulting in a total of 52 components revised.

Allografts

All freeze-dried bone allografts were collected, processed, and sterilized at the HCPA University Hospital Tissue Bank (HCPATB; Biomaterials Department) following a modified protocol published by Kakiuchi et al.[8] Changes were made to decrease the fat and cell content in the final product, because their original protocol did not achieve this goal. The protocol was modified by increasing the time of graft exposure to chloroform and methanol using an ultrasonic washer and by exposing it to hydrogen peroxide to allow removal of organic residues and partial protein denaturation. With this process, the mechanical properties and the protein (27%) and mineral (65%) contents of bone tissue were preserved. The final product showed excellent handling properties after rehydration.

Operative technique

All patients were operated on by three surgeons from the same surgical team. A posterolateral approach was used after placing patients in the lateral position.

Acetabular component

Following exposure of the acetabulum, the cup was removed and the interface carefully cleaned. The acetabulum was then reamed to obtain the best possible bone bed. According to the literature, the size of allograft chips used in the acetabulum, for mechanical reasons, ranged from 5 to 8 mm.[9] Vigorous impaction on bone grafts was performed using special acetabular impactors and reverse reaming. Thirty acetabular revisions were performed, 16 with reinforcement rings (MDT, São Paulo, Brazil), 8 with metallic meshes, and 6 without any device. The use of reinforcement rings or metallic meshes was decided after considering the type and severity of each case. In patients with severe bone defects (i.e., those with great bone losses in which the acetabular cavities were thoroughly covered by impacted bone grafts), reinforcement rings were generally used to protect the graft from weight overload. The amount of bone graft used in both components ranged from 30 to 70 g.

Table 1. Patient characteristics

Features	No.	%
Sex (male:female)	13:29	31:69
Age (years), mean and range	63 (28–80)	
Follow-up (months), median and range	82 (63–167)	
Primary fixation (cemented:noncemented)	28:14	67:33
Underlying diseases	42	100
Primary osteoarthritis	16	38
Avascular necrosis	11	26
Posttraumatic osteoarthritis	6	14
Femoral neck fracture	4	10
Congenital hip dysplasia	3	7
Rheumatoid arthritis	2	5

Femoral component

After removing the primary stem, cement (when present), and fibrous tissues and then cleaning of the femoral canal, morselized allograft chips (3–5 mm)[9] were impacted using appropriate impactors. Severe femoral bone losses in some cases led us to use metallic meshes with cerclage wires to restore the canal and allow vigorous impaction of the bone graft until the prosthesis was rotationally stable. In all cases, regardless of the femoral bone defects, stability was assessed by applying a torsional force and noting any movement. A polished, tapered, collarless stem (Alfa/Baumer; Mogi Mirim, São Paulo, Brazil) was then cemented into the new graft canal using the bone cement Surgical Simplex P (Stryker Orthopaedics, Limerick, Ireland, UK). In all, 14 cemented stems without and 8 with metallic mesh were used in a total of 22 femoral reconstructions.

Clinical and radiographic analyses

The clinical evaluation followed the criteria established by D'Aubigné and Postel.[10] Standard anteroposterior and lateral radiographs of the pelvis were obtained in all patients preoperatively, immediately postoperatively, at 1, 3, and 6 months after operation, and once a year thereafter. All radiographs were analyzed by the assistant surgeons and two independent observers. Preoperative acetabular bone defects were assessed according to the D'Antonio classification[11]; 11 (37%) patients were type II, 11 (37%) were type III, and 8 (26%) were type IV. The femoral defects were classified according to the Endo-Klinic classification[12]; and six (28%) patients were type II, eight (36%) were type III, and eight (36%) were type IV (Table 2).

Acetabular radiographic incorporation parameters were defined as an even radiodensity of graft and host bone and a continuous trabecular pattern throughout. Allograft failure was defined as a socket migration of >5 mm. Radiolucent lines (>2 mm and progressive) and signs of graft resorption were analyzed using the method suggested by DeLee and Charnley.[13]

Table 2. D'Antonio and Endo-Klinik acetabular and femoral defect classifications

Type	D'Antonio[11] (no.)	Endo-Klinik[12] (no.)
I	0	0
II	11 (37%)	6 (28%)
III	11 (37%)	8 (36%)
IV	8 (26%)	8 (36%)
V	0	0
Total	30 (100%)	22 (100%)

Femoral radiographic incorporation analyses were classified by comparing the most recent radiograph with those obtained immediately after operation and all other radiographs. Signs of loosening, change of the stem position, and excessive subsidence (>6 mm) were evaluated. Subsidence was measured from a position on the prosthesis to a reproducible landmark on the bone or the tip of the greater trochanter. Radiolucent lines (>2 mm and progressive) and signs of graft resorption in the seven Gruen zones were also analyzed. Allografts were classified as incorporated when remodeling or trabeculation occurred in at least two Gruen zones.[14]

Results

All patients completed the follow-up, and no severe complications occurred postoperatively. Only two patients died within 2 and 3 years after the procedure, respectively, but the deaths were unrelated to the revision THA.

Overall, no minor events were observed clinically. However, a case of superficial skin infection (cellulitis) occurred 6 months after the procedure and was successfully treated with intravenous antibiotics. Only a patient who had the acetabular component revised needed to be re-revised 3 years postoperatively due to traumatic displacement of the hip. In this case, a graft sample taken from the acetabular cavity was obtained intraoperatively. The patient recovered uneventfully and was in good clinical condition at the last follow-up visit. The histopathological result is shown in Fig. 1.

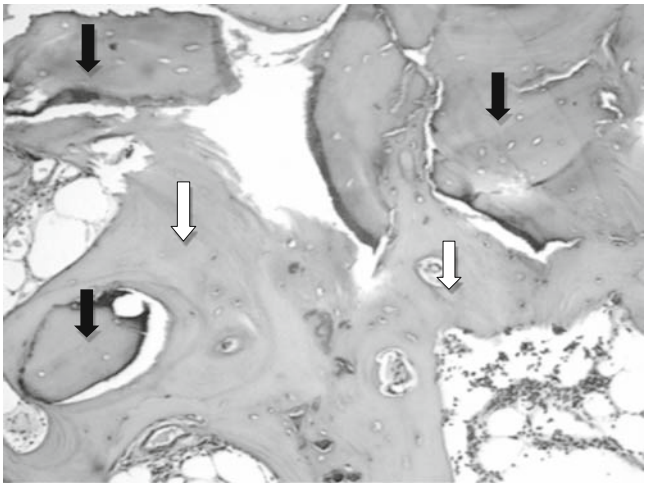

Fig. 1. Histological microphotography of the acetabular grafted cavity showing new bone formation (*white arrow*) and residual bone matrix of the grafted bone (*black arrow*). H&E × 250

Table 3. D'Aubigné and Postel hip rating score according to the revised component

D'Aubigné and Postel[10] score	No. of revision components			
	Acetabular	Femoral	Both	Total
12[a]	10	9	6	25
11[a]	7	1	1	9
10[a]	2	1	2	5
9[b]	0	1	0	1
8[b]	1	0	0	1
≤7[b]	0	0	1	1
Total	20	12	10	42

[a] Good or very good scores
[b] Poor scores

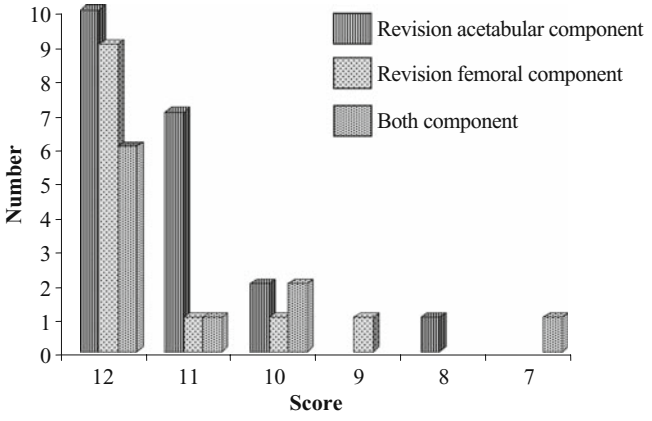

Fig. 2. D'Aubigné and Postel hip scores

The D'Aubigné and Postel criteria[10] were used for clinical evaluation, and a mean ± SD score of 11 ± 5 – 12 was found, which showed that the outcome was satisfactory in 90% of the patients (Table 3, Fig. 2).

All patients were examined at a radiographic review. The results of the two patients who died during this study were also included in the analysis because the deaths were unrelated and occurred 2 and 3 years after the revision.

The acetabular radiographic evaluation at 24 months postoperatively revealed that there was allograft remodeling and incorporation in 93% of the patients. Two patients had a progressive radiolucent line in zones 1 and 2, and another one had a more irregular radiodensity pattern, different from the usual aspect. In all remaining cases, signs of radiographic incorporation of the graft were very good; an example is shown in Fig. 3. None of the patients showed cup migration of >5 mm.

The femoral radiographic evaluation at 24 months postoperatively revealed that there was allograft remodeling and incorporation in 86.5% of the cases, which was considered a good result (Fig. 4). A radiolucent line was observed in all Gruen zones on the immediately postoperative radiograph of one patient, and the line was seen throughout the first year. However, the patient was clinically well, and the radiolucent line progressively disappeared during subsequent follow-up visits. In no case was there excessive subsidence (>6 mm) or change in the femoral stem position. Three patients showed progressive radiolucent lines and unchanged graft appearances without trabeculation.

Discussion

The most adequate grafts for hip surgery are those undergoing minimal changes due to any processing procedure. Physical and chemical analyses showed that freeze-dried bone produced by the Kakiuchi et al. modified protocol kept the mineral and protein contents as well as having satisfactory handling properties, although freeze-dried grafts did not have same texture and malleability as deep-frozen bones. The Kakiuchi et al. protocol was modified by increasing the time of exposure to chloroform and methanol, by additionally using an ultrasonic washer, and by exposing it to hydrogen peroxide. The amount of fat content significantly decreased from about 1.0% (prior to those changes) to <0.06%. Technical and mechanical analyses of the use of freeze-dried bones showed that, after rehydration, they could be adequately handled.[15,16]

Some studies of nondemineralized freeze-dried bone grafts found no mechanical differences from the deep-frozen ones. When differences were found, they favored the freeze-dried bones because fat, blood, and medullary cells are totally removed during the processing procedure.[17,18]

According to the D'Aubigné and Postel criteria, the mean results were considered good and very good in 90% of the cases. Follow-up data showed that the use of human freeze-dried grafts did not cause any damage to patients during the follow-up period. Comparison of these results with those of studies with a similar follow-

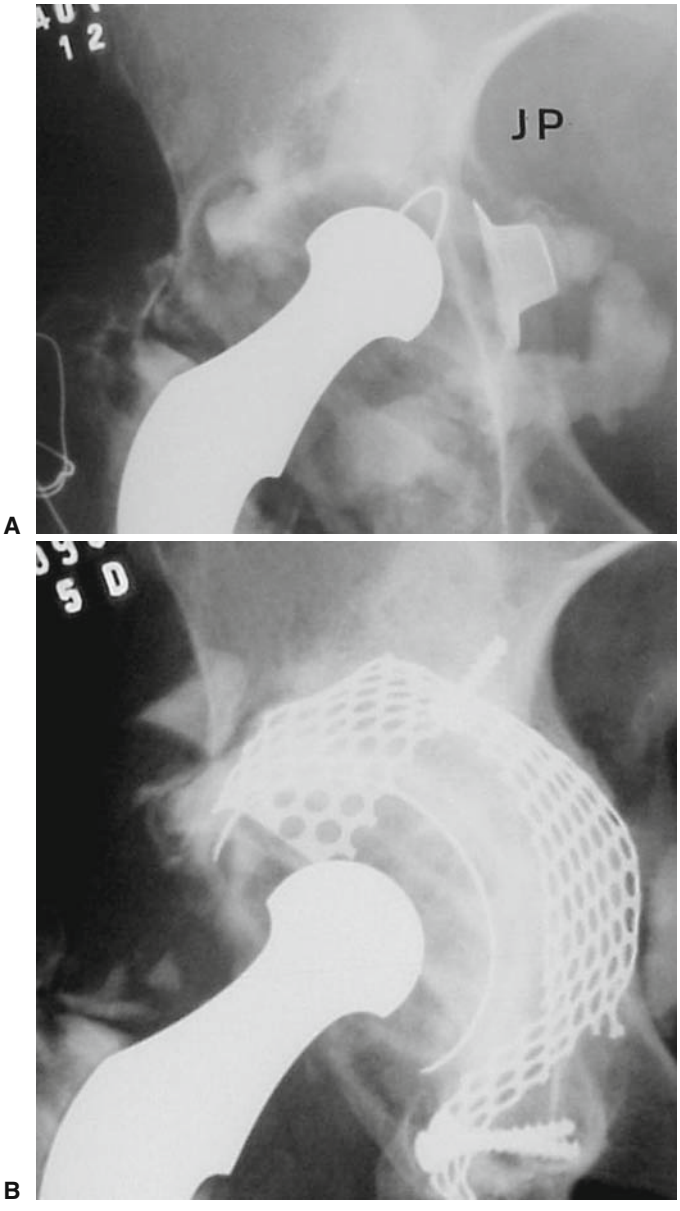

Fig. 3. Anteroposterior (AP) radiographic view of the right hip with a freeze-dried allograft. **A** Postoperative view. **B** At the 72-month follow-up

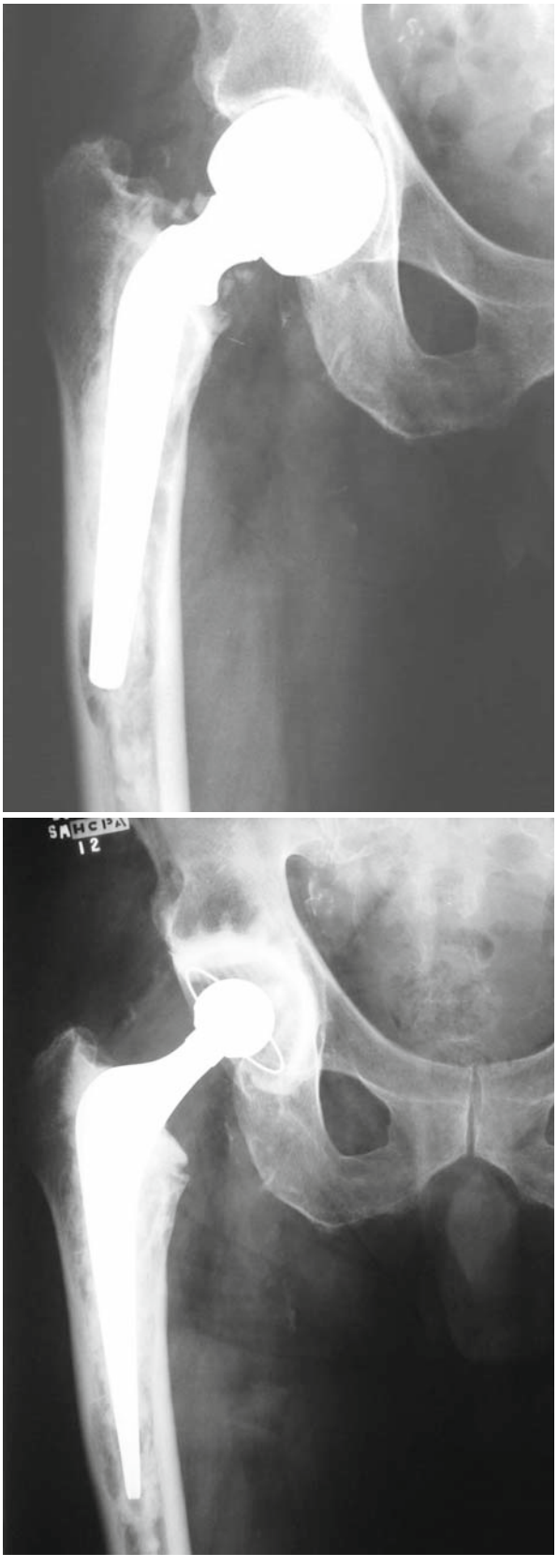

Fig. 4. Preoperative (*top*) and postoperative (*bottom*) AP radiographic views of the right hip with a freeze-dried allograft (49-month follow-up)

up period but using deep-frozen allografts revealed no differences that might be associated with the use of freeze-dried bone grafts.[15] A thorough comparison, however, is not possible because of the lack of reference parameters in the literature about the use of freeze-dried grafts in revision THA and the learning curve associated with the use of these grafts.

Some studies that clinically and radiographically evaluated the use of human freeze-dried grafts in several bone diseases found very good results. However, few indexed studies about the use of freeze-dried grafts in

revision THA were found.[19–21] A range of freeze-dried bone grafts are currently available to surgeons, such as demineralized, partially demineralized, and deproteinized grafts or grafts that are minimally changed after processing, such as the one produced at the HCPATB. Therefore, different mechanical and biological responses to graft procedures have been obtained, which leads to some degree of confusion when choosing the most adequate graft for each procedure.

Except for the criteria for femoral assessments described by Gie et al.,[5] Lind et al.,[22] and a few others, radiographic evaluations found in the literature are subjective. Radiolucency, density, and trabecular formation may not, in many instances, be properly demonstrated owing to the background appearance of metallic materials (e.g., meshes, plates, acetabular reinforcement rings) and cement, which hampers radiographic analyses.

Despite subjectivity and according to the radiographic criteria used, the HCPATB results with freeze-dried bone grafts are comparable to those of other studies and to those of studies using deep-frozen allografts. Gie et al.,[5] using impacted freeze-dried allografts, analyzed radiographic bone integration in 56 femoral revisions 30 months postoperatively and found 89% with bone integration. These results are similar to those found in the present study with lyophilized grafts. Moreover, Lind et al.,[22] using a similar technique of impacting deep-frozen grafts and cement during a similar follow-up, found a similar rate of 88% of graft incorporation.

When subsidence, frequently mentioned in many studies, is little, it shows accuracy limitations on radiographic analysis. According to Gie et al.,[5] the relation between subsidence and the quality of graft packing and cementing is still unclear. For these reasons, we considered only a subsidence of >6 mm, which we believed was significant and did indeed predict failure. Proper grafts and surgeon skills or the severity of the cases and the inherent limitations of the impaction technique are the factors that positively or negatively affected the outcomes reported herein.

Many available lyophilized grafts are partially or completely demineralized, resulting in a significant decrease in mechanical resistance, thereby making it difficult to accept these grafts for use in revision THA. Although some authors recommend caution in the use of lyophilized grafts in hostile acetabuli,[20] we have used the same type of graft in all cases with satisfactory results. This may be due to the fact that only nondemineralized allografts were used in the present study.

According to the literature, the use of freeze-dried bone grafts reduces the risk of infectious or tumor diseases, as chemical reagents are used to inactivate bacteria and viruses and to remove all cell components.[23,24] Additionally, an effective validated sterilization cycle was added to our protocol.

Conclusion

The results of this study demonstrated that bone grafts obtained by the lyophilization process developed and followed at our tissue bank are suitable to be used in revision THA. The use of freeze-dried allografts clearly showed excellent clinical and radiographic midterm results, similar to those obtained by deep-frozen allografts. However, these good results should be later confirmed by a longer postoperative follow-up.

No part of the investigation has been carried out or supported in grant by any related company or entity. None of the authors own stock, acted as a consultant, established contract work, served as an officer or member of the board, or received more than (US)$2000 a year from any related company or entity within the past 2 years.

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