Surgical implantation of structural allograft bone continues to increase despite advances in modern alternatives to allograft, including spine interbody fusion devices and endoprostheses. Although allograft bone historically has been prepared in bulk form with limited anatomic modifications, modern tissue processing includes preparations of amalgams of allograft bone tissue of specific shapes and sizes to suit specific surgical needs. Oversight of the allograft processing and delivery industry has been managed by the US FDA as well as through voluntary participation with the American Association of Tissue Banks (AATB). Guidelines for allograft bone products have primarily focused on avoiding the transmission of neoplastic and infectious disease. Few guidelines exist regarding donor eligibility and bone processing methods with an emphasis on the mechanical integrity of structural allograft bone. The lack of guidelines appears to have led to variation among allograft providers in terms of processing and donor screening regarding issues with recognized mechanical effects. Given the relative lack of data on which to base reasonable screening standards, a basic biomechanical evaluation was performed on one source of structural bone allograft, the femoral ring. Of the tested parameters, the minimum and maximum cortical wall thicknesses of femoral ring allograft were most strongly correlated with the axial compressive load to failure of the graft, suggesting that cortical wall thickness may be a useful screening tool for compressive resistance expected from fresh cortical bone allograft. Development of further biomechanical and clinical data to direct standard development appears warranted.
This chapter's authors discuss their clinical experience and review American tissue bank practices with regard to screening donors and processing structural bone allograft. These issues are further evaluated with biomechanical data evaluating factors important to the mechanical performance of cortical femoral shaft allograft. Further efforts to assess the importance of these parameters on clinical outcomes, as well as the development and adoption of biomechanical performance standards for structural allograft, may be warranted.

**Structural Bone Allograft in Orthopaedic Surgery**

The use of structural bone allograft is a long-established surgical technique used for interbody spinal fusion\(^1,2\) as well as for reconstruction of defects of the long bones.\(^3,4\) Despite recent advances in modern alternatives to structural bone allografts, including prosthetic interbody devices for spinal fusion and larger endoprostheses for limb and pelvic reconstruction, structural bone allograft implantation has continually increased in the United States since the late 1990s\(^5\) (Figure 1).

Compared with artificial interbody fusion devices and endoprostheses, structural bone allografts retain an advantage in biologic performance because of their osteoconductive properties. Also, they are cost effective and provide easier radiologic assessment of bony fusion than do metal or plastic implants.\(^6-8\)

However, the mechanical performance of structural bone allografts may be a disadvantage, made potentially worse by the negative effects of tissue processing and the less predictable effects of fatigue and postoperative remodeling on the strength of the graft. Although fracture of structural allografts following segmental grafting of various long bone defects has been well documented, with a reported incidence of 14% to 29% in recent literature,\(^9-11\) graft fracture after spinal fusion is a rare event.\(^2\) The incidence of graft fracture is reportedly zero to 2.7% following multilevel cervical corpectomy and fibular allograft fusion.\(^12-15\)

Bone resorption resulting from creeping substitution\(^16-18\) and immune response\(^17,19\) has been implicated in some cases.

Despite such low incidence of allograft bone fracture after spine surgery, this chapter's authors experienced two consecutive cases within 3 months of delayed fractures of anterior fibular strut allografts following combined three-level cervical corpectomy and posterior instrumented fusion\(^20\) (Figures 2 and 3). The allografts used for these patients had been harvested from the same donor, a 69-year-old woman. The occurrence of this rare complication in two patients who shared the same donor suggested that the grafts may have been structurally inadequate for the intended clinical use. At the time, the tissue bank involved did not use donor age or osteoporosis as exclusion criteria for structural allograft donation. The occurrence of these fractures led this chapter’s authors to question how allograft providers operate donor and tissue screening of structural allograft bone, especially with respect to variables that may influence mechanical strength of the graft.

**Current Regulation of Allograft Bone Screening**

The FDA began regulatory oversight of the recovery and processing of human cadaver tissues in 1993, after reports of serious disease transmission from allograft tissues.\(^21,23\) Since then, regulation of the human allograft supply with respect to infection control and disease transmission has continued to expand as additional pathogens have...
been identified and effective screening tests have been developed.

In addition to the FDA oversight, the allograft tissue industry is self-regulated through voluntary membership in the AATB. The AATB was established in 1976 and currently has 100 member organizations, accounting for 90% of human allograft tissue used clinically in the United States.

Current regulations have done much to address risks of disease transmission and tissue contamination. However, comparatively few guidelines exist regarding donor eligibility and bone processing issues with a potential effect on the mechanical integrity of structural allograft bone. Given this relative lack of guidelines from the FDA and the AATB, current practice with respect to these issues within the allograft industry has not been known.

**Current Practices of Allograft Providers**

To assess current practices among allograft providers with regard to screening and processing and the structural assessment of allograft bones, a questionnaire-based survey was developed by this chapter’s authors. At the time of the survey, 45 AATB member tissue banks were involved to some degree in procuring or processing structural allograft bone. Of these, 16 organizations participated in tissue...
processing and the sale of allograft bone. The questionnaire regarding tissue bank practices having a potential effect on mechanical integrity of allograft bone was circulated to all 16 AATB-accredited tissue banks involved in processing structural allograft bone.

Of the 16 AATB-accredited tissue banks, 14 responded to the questionnaire (Table 1). Forty-three percent of banks (6 of 14) reported no upper age restriction for structural allograft donors, or they accepted donors up to the age of 80 or 85 years, representing 15% of the total number of structural allograft bone donors (2,860 of 18,712) reported. The remaining eight banks reported upper age limits ranging from 55 to 75 years. Three banks reported differing age limits for male and female donors. The average upper age limits were 68.6 years for men and 66.8 for women.

Eighty-six percent of banks (12 of 14) considered chronic steroid exposure to be an exclusion criterion, representing 86% of the total structural allograft bone donors (18,712 of 18,712) reported. Seventy percent of banks (10 of 14) reported a history of osteoporosis to be an exclusion criterion, representing 70% of the total structural allograft bone donors (13,022 of 18,712) reported. Fifty percent of banks (7 of 14) reported using dual-energy x-ray absorptiometry (DEXA) scans as screening for potential donors or tissue.

These findings indicate wide variation in tissue banks’ approaches to issues potentially affecting mechanical integrity of structural allograft bone. This contrasts with presumably consistent compliance with screening and processing requirements designed to avoid disease transmission and tissue contamination. Although those considerations must remain primary in ensuring safety of the allograft bone supply, issues of mechanical bone integrity would also seem to be important from the standpoint of quality control, given the increasing use of structural allograft in load-bearing applications.

Biomechanical and clinical studies to determine which factors are most relevant to structural allograft mechanical properties and clinical success seem warranted to determine whether further standards for donor and tissue acceptance are appropriate. Given the relative lack of data on which to base reasonable screening standards, a basic biomechanical evaluation of one source of structural bone allograft was undertaken.

Biomechanical Performance of Femoral Ring Allograft

To determine which factors most strongly affect the mechanical strength of structural allograft bone, multiple

<p>| Table 1 |</p>
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<th>Tissue Banks’ Response to Survey Questions Regarding Donor Exclusion Criteria for Structural Bone Allograft</th>
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<tr>
<td><strong>Criterion</strong></td>
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<tr>
<td>Age limit</td>
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<tr>
<td>Chronic steroid exposure</td>
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<tr>
<td>Rheumatoid arthritis/ankylosing spondylitis</td>
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<td>Tobacco use</td>
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<td>Hysterectomy/oophorectomy</td>
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<td>Diagnosis of osteoporosis</td>
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donor and graft variables were assessed for their effect on compressive load resistance of femoral ring allograft. Fresh-frozen human femurs from 34 cadaver donors were each sectioned into ten 20-mm thick specimens. Bone mineral density (BMD), as measured by DEXA scans of the proximal femur; donor age; and graft dimensions were recorded for each specimen. A total of 327 specimens was ultimately tested under quasi-static axial compression. Linear regression models assessed load to failure as a function of BMD, sex-specific donor age, minimum/

Figure 4  Scatterplots indicating the compressive load to failure as function of bone mineral density (A), sex-specific age (B), minimum (C) and maximum (D) cortical wall thicknesses, and minimum (E) and maximum (F) outer ring diameters. (Adapted with permission from Hart RA, Daniels AH, Bahney T, Tesar J, Sales JR, Bay B: Relationship of donor variables and graft dimension on biomechanical performance of femoral ring allograft. J Orthop Res 2011;29[12]:1840-1845.)
maximum cortical wall thickness, and minimum/maximum outer ring diameter.

As shown in Figure 4, correlations between minimum and maximum cortical wall thickness and load to failure were statistically significant ($r = 0.73$, $P < 0.001$, and $r = 0.74$, $P < 0.001$, respectively). BMD showed a weaker negative correlation with load to failure ($r = -0.11$, $P = 0.05$). Correlations between load to failure and minimum and maximum outer ring diameter and age ($r = 0.06$, $P = 0.31$) were not significant. Of the tested parameters, the minimum and maximum cortical wall thicknesses of femoral ring allograft were the most strongly correlated with the axial compressive load to failure of the graft. These findings suggest that cortical wall thickness may be a useful screening tool for compressive resistance expected from fresh cortical bone allograft. It is important to note that remodeling and fatigue during healing may further reduce the strength of an allograft spacer. Thus, an ideal interbody device should withstand a substantially higher force level than the anticipated clinical load at the time of implantation. Knowing the appropriate maximum load to failure potentially affects suitability of the implant. For example, although 70% of the specimens supported up to five times estimated clinical loading, only 13% of the specimens supported 10 times these expected loads (Table 2).

These results were extended with a further nonlinear analysis of the predictive strength of the various parameters. This analysis showed that BMD and age are so weakly correlated with strength that they may be safely excluded from consideration as a screening parameter for allograft bone strength.

It is critical to acknowledge that optimizing load to failure of femoral ring allografts may not optimize their clinical performance. For example, thicker-walled grafts might limit space available for osteogenic material within the ring with a concomitant negative effect on fusion rates. Alternatively, a thicker wall may limit slight subsidence of the graft into vertebral end plates, again with a potential negative effect on fusion rates. Further efforts to determine the importance of various parameters on clinical outcomes would represent the benchmark for data. In the meantime, however, the basic biomechanical data described in this chapter are useful to consider as an initial basis for rational screening approaches to potential allograft bone donation.

### Summary

Use of structural allograft bone in spine fusion and other orthopaedic surgical applications continues to increase. Unlike artificial implants, no biomechanical performance standards for structural allograft bone are currently in place. As a result of this lack of standardization, practices among tissue processors and suppliers remain variable within the United States. Development of further biomechanical and clinical data to direct standard development appears warranted. In the meantime, surgeons should discuss with their allograft providers their individual approach to these issues.

### References


