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ORIGINAL ARTICLE

The Clinical Use of Allografts, Demineralized Bone Matrices, Synthetic Bone Graft Substitutes and Osteoinductive Growth Factors: A Survey Study

Mathias P. G. Bostrom, MD · Daniel A. Seigerman

Abstract The emergence of new bone grafting options and alternatives has led to significant uncertainty when determining the most appropriate product for surgical procedures requiring bone graft in orthopedics. Allografts, demineralized bone matrices, synthetic bone graft substitutes, and osteoinductive growth factors are all viable options, yet there is a lack of data reporting clinical usage of these products. This correspondence reports on the use of bone grafting products at the Hospital for Special Surgery for a 27-month period and makes recommendations based on surgical usage, safety, and cost. Approximately half (48.6%) of all bone graft substitutes were implanted during spinal surgery. Arthroplasty, trauma, and foot/hand cases all used considerable amounts of bone grafting products as well (20.1%, 19.0%, 12.1%, respectively). Considerable differences were noticed in usage of bone grafting products among each orthopedic discipline. Of all bone graft substitutes used in arthroplasty, 14.4% were demineralized bone matrices, whereas 56.8% were allografts. Demineralized bone matrix grafts were used in 82% of trauma surgery and 89% of foot/hand cases. An increase in synthetic bone graft alternatives was noticed near the end of our investigation period.

Key words Bone Graft · DBM · Allograft · Bonegraft substitutes

Introduction

The past decade has brought forth significant advances in bone grafting options for orthopedic surgeons. The overwhelming emergence of new bone graft materials and alternatives has led to uncertainty as to which product to use for specific procedures. It is estimated that more than 500,000 bone grafting procedures are completed each year in the United States [8]. Currently, there are no available data or consensus as to the specific type of graft to be used in particular surgical indications.

Autogenous bone still remains the "gold standard" of bone graft material in all facets of orthopedic surgery. The use of autografts diminishes the risk of infectious disease transmission, whereas osteoconductive, osteoinductive, and osteogenic properties of the graft are optimal. Moreover, there is no immune response after implantation, enhancing its ability to incorporate into its new site [23, 28]. As a graft, autogenous bone is ideal, but the harvest of autografts may be associated with severe donor site pain and morbidity even with new trapdoor harvesting techniques [3, 19]. In procedures requiring large amounts of graft, there may not be adequate quantities of autogenous bone available [19]. Because of the significant shortcomings of autogenous bone graft, a current understanding of available grafting alternatives is necessary.

An allograft, by definition, is any tissue harvested from one individual and implanted into another of the same species [3]. In a search for an adequate substitute for autogenous bone, cadaveric allograft has been a viable option. Structural and morselized forms are available and prepared as either fresh-frozen or freeze-dried [19] These grafts provide a structural framework or scaffold for host tissue to grow, hence making allograft osteoconductive. Conversely, its osteoinductive properties are mediocre at best. Upon implantation, the host is expected to experience an intricate immune response [19, 20]. Freezing or freeze-drying the allograft is crucial in minimizing this reaction; however, the fundamental properties of the material may be altered.

Although the risk of disease transmission through implantation of allograft is rare, its existence is not inconsequential. According to the American Association of Tissue Banks, no cases of HIV transmission have been reported in more than 2 million cases using allograft bone in the past

M.P.G. Bostrom, MD (✉) · D.A. Seigerman
Hospital for Special Surgery,
535 East 70th St,
New York, NY 10021, USA
e-mail: Bostromm@hss.edu

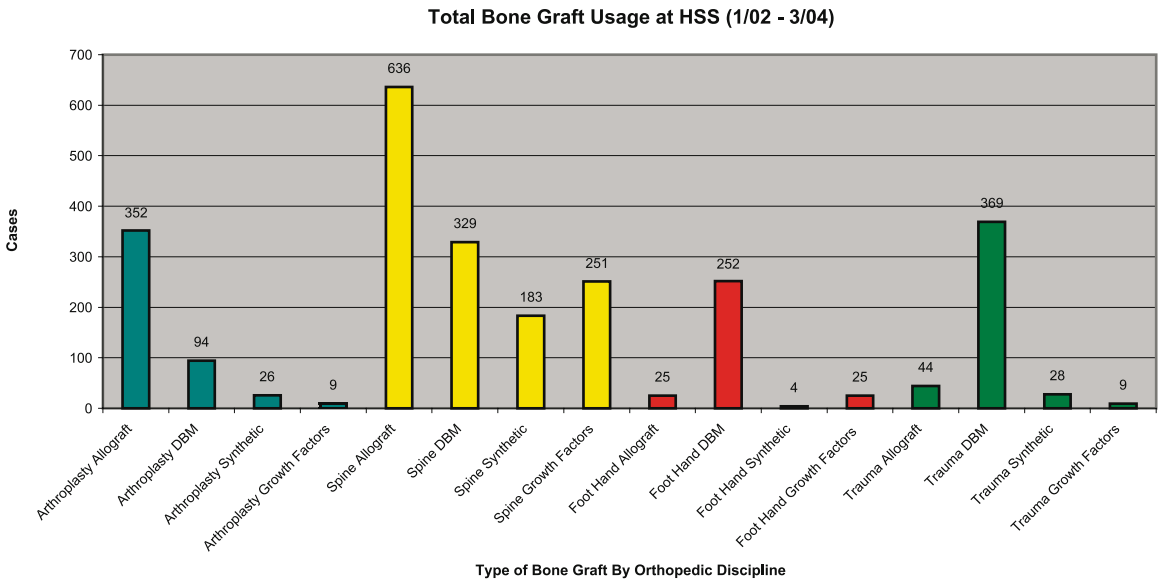

Fig. 1. Use of allograft, demineralized bone matrix, and synthetic bone graft material at the Hospital for Special Surgery from January 2002 through March 2004

5 years [1, 15]. Statistics indicate that current methodology used to screen bone for viral pathogens has been successful in eliminating such infections, yet these procedures are not fail-proof especially in regard to the transmission of bacterial infection.

The most apparent limitation of cadaveric allograft is its lack of osteoinductive capabilities. Demineralized bone matrix is a derivative of allograft bone. It is prepared by pulverization of allogenic bone to a consistent size, followed by mild acid extraction of the mineralized phase of bone [15, 20]. This process, developed by Urist et al in 1965, results in a composite of noncollagenous proteins, growth factors, and collagen [15, 35]. Manufacturers of demineralized bone matrices add different carriers to the composite. Glycerol, hyaluronic acid, gelatin, and calcium sulfate powder have been used for this function [6, 15]. Demineralized bone matrix is osteoconductive but does not provide structural support. Osteoinductive capabilities are increased because of the released growth factors during the demineralization process [20]. Sterilization techniques such as exposure to gamma irradiation and ethylene oxide significantly decrease the risk of transmitting infection but subsequently decrease the osteoinductive properties of the graft. When preparing demineralized bone matrix for implantation, it is usually mixed with bone marrow, increasing possible osteogenic factors and pluripotential cells. It can also be used as an autogenous bone graft expander [10].

Synthetic bone graft substitutes derived from nonbone substances are highly osteoconductive, yet have no intrinsic osteoinductive or osteogenic properties. The bond formed between these products and the host provides an adequate affinity for local growth factors that are crucial to the remodeling process. Synthetic graft materials do not contain cadaveric or autogenous bone; hence, there is minimal risk of disease transmission. The emergence of new synthetic bone graft products has been of great interest to the orthopedic community during the last decade.

These synthetic bone graft materials range from those with little or no osteoinductive capacity, such as calcium sulfate, to highly osteoinductive materials, such as BMP-2 and BMP-7. In addition, there are several composite materials also available.

Calcium sulfate (plaster of paris) has been used as a bone graft substitute since 1892 [19]. Current forms of highly processed calcium sulfates include Osteoset (Wright Medical, Arlington, TN, USA), and Bone Plast (Interpore Cross International, Irvine, CA, USA). Osteoset is available in 4.8- and 3.0-mm-diameter hard pellets and are indicated for filling small bone defects [8]. Its crystalline architecture is excessively random, providing no organized structure.

Coralline calcium phosphate is derived from *Gonipora*, a coral found in the South Pacific. Its highly organized microstructure, with longitudinal pores 500 to 600 μm in diameter and interconnections of 220 to 260 μm, simulates that of human cancellous bone [8]. Currently, Pro-Osteon, a manufactured coralline calcium phosphate converted by heat into hydroyapatite (Interpore Cross International, Irvine, CA, USA) is available for traumatic metaphyseal defects of long bones [8]. One of its initial disadvantages was its very long resorption time. A newer formulation with calcium carbonate may allow for faster resorption.

Table 1. Total bone graft usage by orthopedic discipline (January 1, 2002, to March 31, 2004)

Orthopedic discipline	No. of total cases	No. of cases using bone graft	Percent of cases requiring bone graft	Percent of total bone graft usage
Arthroplasty	9,592	472	4.9	20.1
Spine	3,142	1148	36	48.8
Foot/Hand	5,112	284	5.5	12.1
Trauma	2,927	449	15.3	19.0

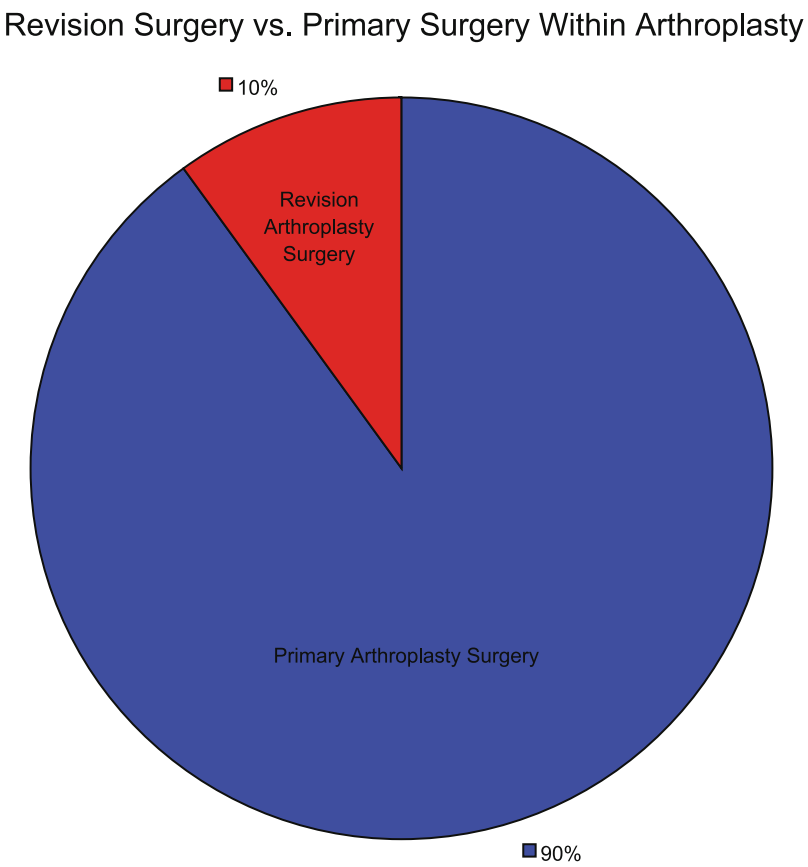

Fig. 2. Revision surgery vs primary surgery in arthroplasty cases between January 1, 2002, through March 31, 2004

Tricalcium phosphates are random porous ceramics that mimic the structure of native cancellous bone once incorporated and remodeled. Vitoss (Orthovita, Malvern, PA, USA) is a β-tricalcium phosphate currently indicated for bone defects of the spine, extremities, and pelvis [8]. Vitoss scaffold is approximately 90% empty space, with pore sizes ranging from 1 μm to 1 mm in diameter [36]. The extreme porosity and microstructure of this product enhances cell-mediated resorption and remodeling after implantation [8, 36]. However, to function properly it must be provided with bone marrow.

As is clearly evident from this brief overview, there is an almost bewildering number of alternative choices for autogenous bone grafts available. The purpose of this study

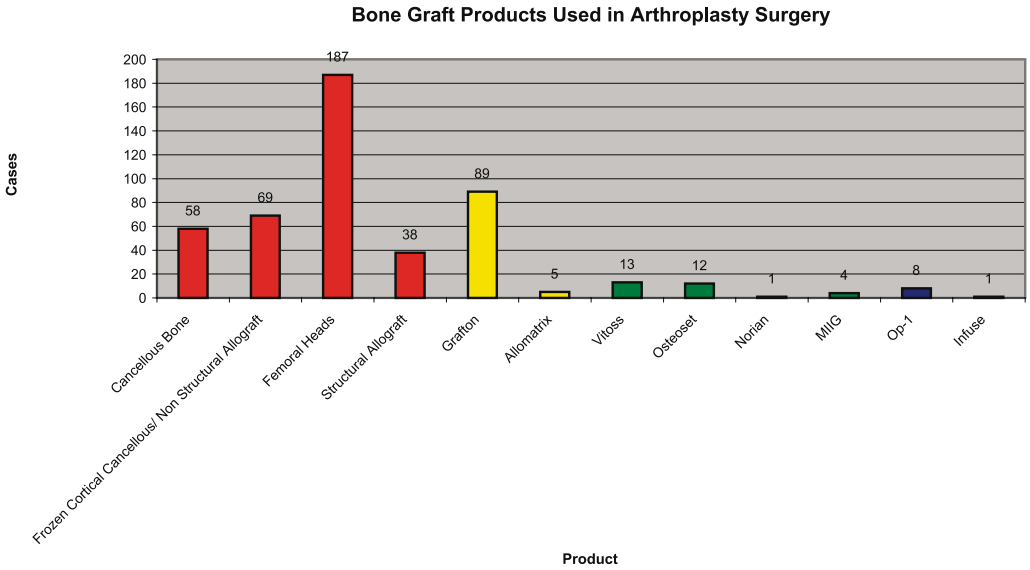

Fig. 3. Distribution of bone graft products used in arthroplasty surgery at The Hospital for Special Surgery from January 1, 2002, through March 31, 2004

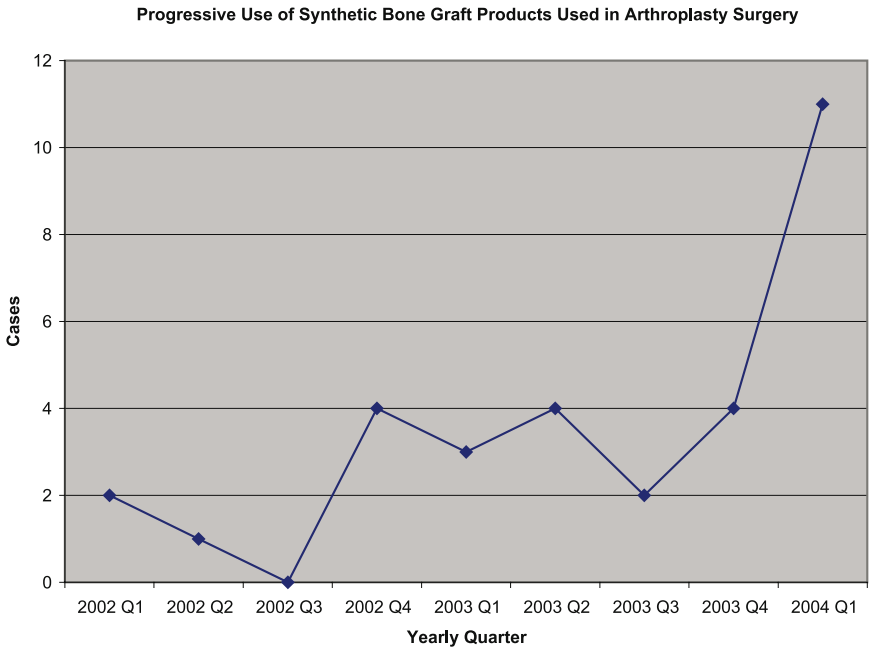

Fig. 4. Progressive use of synthetic bone graft alternatives in arthroplasty surgery displayed by yearly quarter from January 1, 2002, through March 31, 2004

was to provide a detailed analysis of all bone graft material used at a high-volume orthopedic institution and to make recommendations as to appropriateness of certain bone grafting products based on the surgical indications.

Materials and methods

Operating room and hospital records from January 1, 2002, through March 31, 2004, containing all bone graft products used in surgical cases were accessed and recorded as part of a master database. All cases included in this study were performed at The Hospital for Special Surgery (New York, NY). Demographic information, diagnosis, procedure, product used, quantity of product implanted, date of surgery, and the orthopedic surgeon were all included in the master database. Once complete, cases were separated into 4 databases based on orthopedic discipline (Arthroplasty, Spine, Foot/Hand, and Trauma).

Results

Nearly 50% of all bone graft synthetic material, including allograft, demineralized bone matrix and synthetic bone graft products, were used in spinal surgery (Fig. 1).

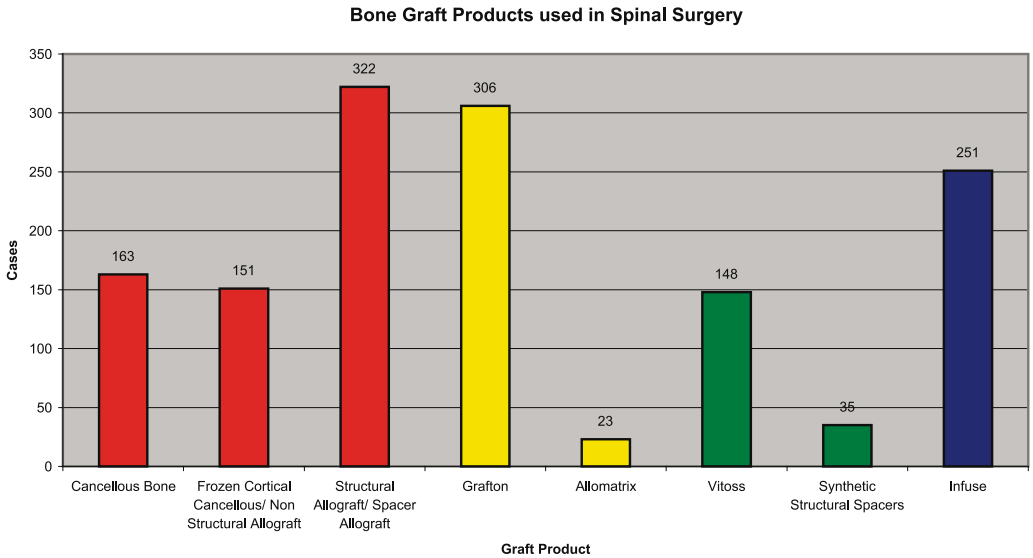

Fig. 5. Distribution of bone graft products used in spinal surgery from January 1, 2002, through March 31, 2004

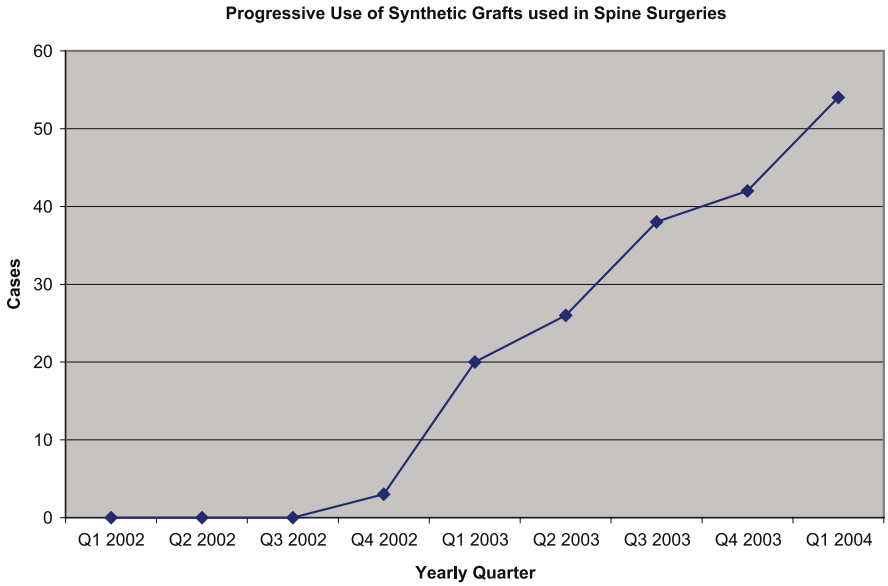

Fig. 6. Progressive use of synthetic bone graft alternatives used in spinal surgery displayed by yearly quarter from January 1, 2002, through March 31, 2004

Arthroplasty and trauma cases each make up approximately 20%, whereas foot and hand surgeries compose 12% of all bone graft products used (Table 1). Interestingly, approximately 5% of both arthroplasty and foot and hand cases require bone graft, whereas bone grafting is observed in more than 7 times that amount in spine cases (36.5%). 15% of all orthopedic trauma cases used bone graft (Table 1). Although these results were certainly expected, analysis of the different types of graft used in each orthopedic discipline showed marked differences in types of grafts used.

Arthroplasty

Of the 9,592 arthroplasty cases performed at our institution, 955 were revision arthroplasty surgeries. Nearly all bone graft synthetic usage in this orthopedic discipline was used in revision procedures (Fig. 2). Although femoral head allograft is used most frequently, it only comprises 30.2% of all grafts used in arthroplasty cases. Use of cancellous allograft bone, frozen cortical cancellous nonstructural allograft, and structural allografts is significant in such surgical procedures. Overall, allografts are used in 56.8% of all arthroplasty cases requiring bone graft. Demineralized bone matrix, specifically Grafton (Osteotech/MTF), was used in 14.4% of all arthroplasty cases using bone graft products (Fig. 3). Quarterly data show a continued increase in synthetic bone graft products used in this orthopedic discipline. Vitoss (Orthovita) and Osteoset (Wright Medical) are most frequently used as synthetic bone graft alternatives for arthroplasty surgery at this institution. Figure 4 shows the increase in use of synthetic bone graft products over the duration of this 27-month survey.

Spine

Over the duration of this study, structural allograft was the most frequently used bone graft product for spinal surgery. Twenty-eight percent of all spine surgeries requiring bone graft used allograft spacers, whereas in the latter part of this

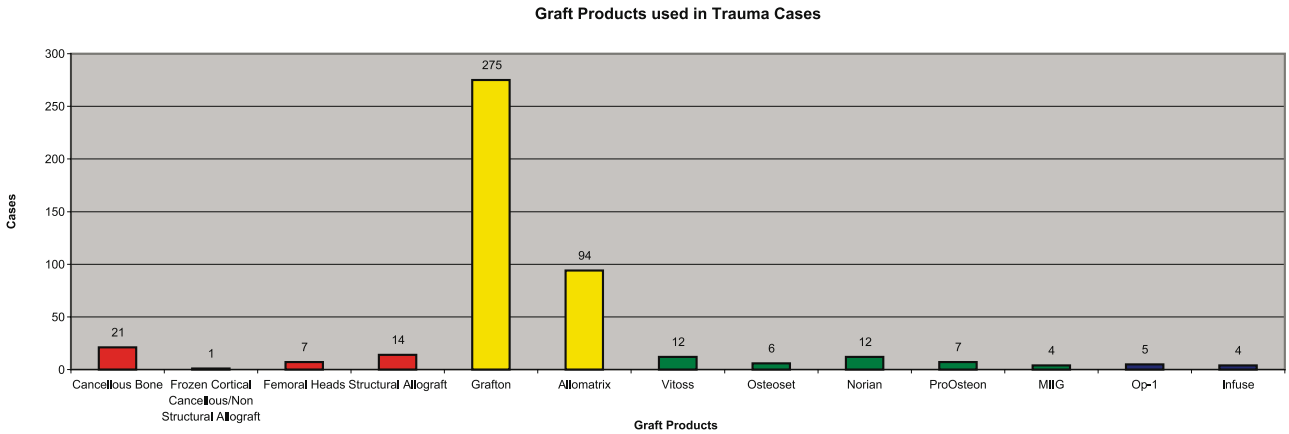

Fig. 7. Distribution of bone graft products used in trauma surgery from January 1, 2002, through March 31, 2004

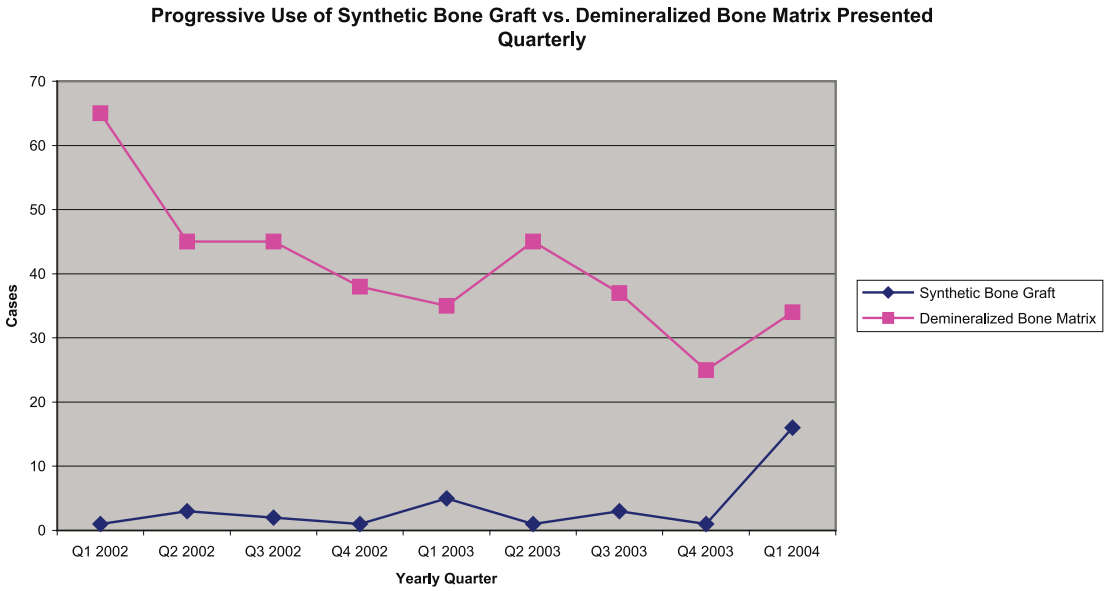

Fig. 8. Quarterly usage of synthetic bone graft material vs demineralized bone matrix over a 27-month period

survey, more synthetic spacers were used primarily for interbody fusions. Virtually equal amounts of both cancellous bone and nonstructural allografts were used compared with Grafton demineralized bone matrix (27.35% vs 28.65%, respectively) (Fig. 5).

Infuse (Sofamor Danek Surg Nav Tech) was the only osteoinductive growth factor used for spinal surgery. Interestingly, more Infuse was implanted in spinal operations than synthetic bone graft substitutes. This use was different from other orthopedic disciplines. Figure 10 shows the overall distribution for osteoinductive growth factors over the duration of this study.

The use of allografts and demineralized bone matrices was quite consistent during the 27-month period of investigation, yet the same could not be reported for synthetic graft products. Synthetic bone graft substitutes were used in only 3 cases in 2002, whereas these graft alternatives were used in 180 cases throughout the remainder of the study (Fig. 6).

Trauma

Analysis of bone graft usage for trauma surgery is certainly surprising. Eighty-two percent of all trauma cases requiring bone graft used demineralized bone matrix. This finding is certainly quite different from what was reported for other orthopedic disciplines. Only 9% of all traumatic bone grafting procedures implanted allograft when bone grafting was necessary because of their non-osteoinductive nature and concerns with their use in open fractures (Fig. 7).

Despite an overall elevated use of demineralized bone matrix in orthopedic trauma cases, a marked decrease in demineralized bone matrix is coupled with an increase in synthetic grafting products for the duration of this 27-month

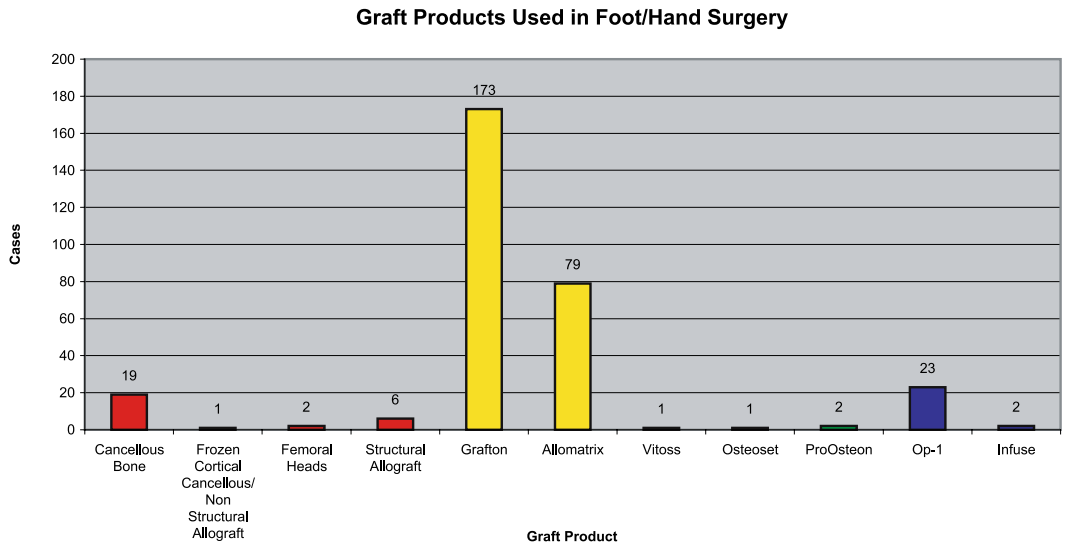

Fig. 9. Distribution of bone graft products used in foot/hand surgery from January 1, 2002, through March 31, 2004

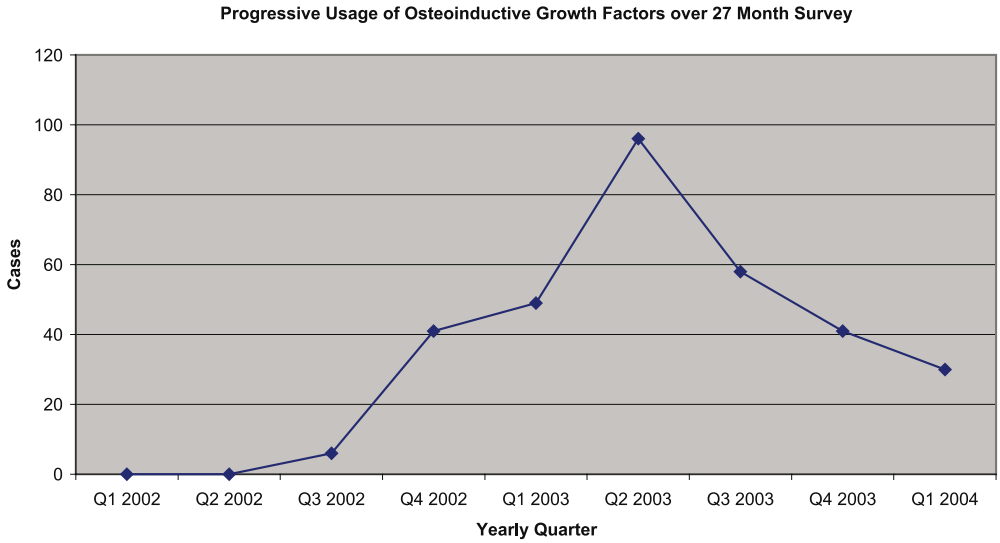

Fig. 10. Quarterly usage of osteoinductive growth factors during the 27-month survey

survey (Fig. 8). The emergence of other reliable synthetic products with more specific indications is beginning to replace demineralized bone matrix in this orthopedic discipline.

Foot/Hand

Foot and hand surgery is associated with tremendous use of demineralized bone matrices when compared with both allografts and synthetic bone graft products. Of all bone grafts used in foot and hand cases, 89% were demineralized bone matrices (Fig. 9). In addition, unlike other orthopedic disciplines, there is no increase in use of synthetic products, and similarly, there is no decline of demineralized bone matrix use over the duration of this survey. Allografts, demineralized bone matrices, and synthetic products were used quite consistently throughout the 27-month period.

Growth factors

The use of bone morphogenic proteins as bone graft alternatives were significant at this institution. Products used were OP-1 (Stryker) and Infuse (Sofamor Danek Surg Nav Tech). An interesting distribution of these products was noticed during the 27-month study. A spike in usage was observed during the second quarter of 2003, whereas a linear decrease in these products was observed thereafter (Fig. 10).

Discussion

A survey of allografts, demineralized bone matrices, synthetic bone graft substitutes, and osteoinductive growth factors used at a high-volume orthopedic institution may be quite valuable with respect to determining the appropriateness of each of these products based on surgical indication. Determining usage totals for each bone graft material at a time when new products are frequently introduced to the market may help clear ambiguity as to what products have been used in certain surgical situations.

During the past decade, we have noticed revolutionary changes in the array of bone grafting products available [3, 18–20]. Allografts were the first alternatives for autografts, which were subsequently interchanged and/or replaced by demineralized bone matrix in certain

Table 2. Price chart for all synthetic bone graft products used at the Hospital for Special Surgery

Product	Quantity	Price (US$)	Manufacturer/Source
Osteoset calcium phosphate	4.8 mm/10 mL	625.00	Wright Medical
Osteoset Resorbable Kit	25 mL	985.00	Wright Medical
Minimally Invasive Injectable Putty (MIIG)	5 mL	935.00	Wright Medical
Minimally Invasive Injectable Putty (MIIG)	15 mL	1,490.00	Wright Medical
Vitoss Micro Morsels	10 mL	690.00	Orthovita
Vitoss Standard Morsels	10 mL	575.00	Orthovita
Vitoss Macro Morsels	10 mL/15 mL	1,410.00	Orthovita
Vitoss Scaffold Foam	25×100×4	1,380.00	Orthovita
Norian Bone Void Filler	10 mL	2,315.00	Synthes
Peek PR	7–17 mm	2,420.00	Synthes
Peek TR	7–17 mm	3,585.00	Synthes
Peek Cervical		1,035.00	Synthes

circumstances [2, 4, 17, 29, 37]. Present trends indicate dramatic increases in the use of synthetic bone graft alternatives [18]. Virtually equal amounts of allografts and demineralized bone matrices (40.1% vs 39.6%), respectively, were used in all surgical cases requiring bone graft at this institution over the duration of this study. The comparative use of synthetic bone graft alternatives and osteoinductive growth factors are similar as well (9.14% vs 11.2%, respectively).

Overall, allografts and demineralized bone matrix use was level, whereas synthetic usage increased dramatically toward the end of this survey, and continues to increase past the investigation period. The reason for this is multifactorial. The introduction of available, cost effective, and biologically improved synthetic bone graft products has allowed this increase in usage [14, 18, 19]. More importantly, our understanding of the proper clinical indications for the use of these grafts has also improved, making their use appropriate.

The risk of disease transmission, not only by viral pathogens but also by bacterial organisms, is the greatest limitation to the use of cadaveric allograft. In addition, its lack of osteoinductive properties limits its clinical usefulness. Certain of its structural properties have not been replicated by any of the synthetic materials, and thus considerable usage of allograft was noticed during this investigation [18, 22].

When selecting an alternative for allograft, it is necessary to use a product that diminishes the risk of infection and subsequently provides an osteoconductive framework for healthy host bone to incorporate. Demineralized bone matrix is a viable alternative [9, 24, 28]. Removing the mineralized phase of bone through a rigorous sterilization process certainly decreases the risk of viral and bacterial infection [12, 18, 26]. Nevertheless, demineralized bone matrix is not a sterile product; thus, this risk of disease transmission is not eradicated. Substantial use of demineralized bone matrix including Grafton and Allomatrix products was reported during the investigation. These materials are available in many formulations, some of which are advantageous for certain surgical indications. A possible explanation for the high volume (89%) of these products used in foot and hand surgeries may be the availability of injectable putties and gel formulations of these products. These variations allow surgeons to implant such material accurately in small surgical sites [26].

Synthetic bone graft materials offer an effective alternative for autografts, allografts, and demineralized bone matrix. β-Tricalcium phosphate products are sterilely prepared, osteoconductive, and are highly effective in filling bone void defects of the spine, extremities, and pelvis [8, 16, 25, 30, 32]. There is no risk of disease transmission associated with these synthetic bone grafts. Synthetic bone graft contains no inherent osteoinductive properties and thus requires the host bone environment to be well vascularized to have the appropriate cellular and osteogenic factors available. In the case of a contained defect, tricalcium phosphate products used alone are acceptable. In situations where the bone defect is large, a combination of allograft and a synthetic bone graft alternative is generally recommended.

Although composite synthetic structural grafts (metal cages with osteoinductive growth factors) were introduced as alternatives to allograft spacers in spine surgery, synthetic structural grafts are not available to replace femoral struts, or other long-bone allografts. Cases involving periprosthetic fractures of the femur still require structural allografts. At present, there are no alternatives for such grafts; thus, structural allograft products are needed.

With respect to bone defects in arthroplasty surgery, specifically revision of total joint replacements, cancellous allografts, femoral head allografts, Grafton demineralized bone matrix, and β-tricalcium phosphate (Vitoss) are all viable options to fill a surgical bone void [11, 21, 27, 34]. The selection of these materials is based on many factors. One is the surgeon's personal preference and comfort level. Other factors include cost, availability of the product, and an accurate understanding of the present choices surgeons

Table 3. Price chart for all osteoinductive growth factors used at the Hospital for Special Surgery

Product	Quantity	Price (US$)	Manufacturer/ Source
OP-1	One usage	5,000.00	Stryker
Infuse	Small, medium, large	3,500.00/4,400.00/ 4,900.00	Metronics

Table 4. Price chart for all demineralized bone matrix products used at the Hospital for Special Surgery

Product	Quantity	Price (US$)	Manufacturer/ Source
Allomatrix Injectable Putty	10 mL	1,225.00	Wright Medical
Grafton Gel	10 mL	992.00	MTF/Osteotech
Grafton Flex	2.5×5 cm	726.00	MTF/Osteotech
Grafton Putty	10 mL	1,021.00	MTF/Osteotech
Grafton Crunch	5 mL/15 mL	813.00/ 1,375.00	MTF/Osteotech

Table 5. Price chart for all allografts used at the Hospital for Special Surgery

Product	Quantity	Price (US$)	Manufacturer/ Source
Cancellous Chips/ Freeze Dried	30 mL	376.00	MTF
Cancellous Chips/Frozen	30 mL	396.00	MTF
ACF Allograft Spacers	6–15 mm	910.00	MTF
PLIF Allograft Spacers	7–17 mm	2,230.00	MTF
FRA Allograft Spacer	9–11 mm	3,105.00	MTF
Femoral Shaft	3–20 cm	530.00– 1,681.00	MTF
Femoral Head Allograft	N/A	979.00– 990.00	MTF

have when choosing a bone graft product. Vitoss, when prepared with bone marrow, provides an excellent osteoconductive structure, with osteogenic capabilities from the marrow. It is a sterile product, diminishing potential disease transmission, and it incorporates successfully into host tissue.

Osteoinductive growth factors were used most frequently in spinal surgery during the period of investigation [13, 31]. When this survey was being conducted, a study was being conducted at this institution to test the effects of Infuse on spinal fusion surgery. This caused a significant increase in the use of this product in spinal surgery. Moreover, along with the standard consent forms that patients must sign before surgery, they also received a booklet detailing possible adverse effects OP-1 or Infuse may have on women within childbearing age, pediatric patients, and patients with a history of cancer [33]. Beyond our study, it became hospital policy that all patients receiving either OP-1 or Infuse graft must sign an additional consent form explaining the possible adverse effects these products may have. A combination of these factors may explain the sudden decline in use of these products after the second quarter of 2003 (Fig. 10).

Despite their potential limitations such as cost, possible adverse effects, and lack of osteoconductive properties, these growth factors are highly osteogenic [5, 6]. Therefore, it is recommended to use such products when host bone is biologically compromised to aid in the incorporation of additional bone graft material.

It is important to consider cost when selecting a bone graft product. The prices for bone grafts examined in this study are presented in Tables 2, 3, 4, and 5. Most allografts are less expensive than demineralized bone matrices or synthetic substitutes. Surprisingly, demineralized bone matrices are oftentimes more expensive than similar synthetic products. Osteoinductive growth factors are significantly more expensive than any other product, yet their use in patients with compromised biological environments may be critical and the cost may be justified in these specific cases.

Safety, efficacy, and cost are all crucial factors when selecting the proper bone graft or bone graft substitute in all areas of orthopedic surgery. With respect to patient safety, use of noncadaveric bone is ideal, yet adequate products have not been available until recently. Synthetic alternatives have become reasonably priced and may be functionally superior to other grafting options. It is certainly advantageous to use a synthetic product when possible, yet demineralized bone matrices and allografts remain reasonably safe and effective products.

References

1. American Association of Tissue Banks. http://www.aatb.org. August 6, 2004
2. Balabhadra RSV, Kim DH, Zhang H (2004) Anterior cervical fusion using dense cancellous allografts and dynamic plating. Neurosurgery 54:1405–1412
3. Bauer TW, Muschler GF (2000) Bone graft materials: An overview of the basic science. Clin Orthop 371:10–27
4. Bono CM, Lee CK (2004) Critical analysis of trends in fusion for degenerative disc disease over the past 20 years. Spine 29: 455–463
5. Boden SD, Grob D, Damien C (2004) Ne-Osteo bone growth factor for posterolateral lumbar spine fusion: results from a nonhuman primate study and a prospective human clinical pilot study. Spine 29:504–514
6. Bostrom MPG, Camacho NP (1998) Potential role of bone morphogenetic proteins in fracture healing. Clin Orthop 355S: S274–S282
7. Bostrom MPG, Yang X, Kennan M, Sandhu H, Dicarlo E, Lane JM (2001) An unexpected outcome during testing of commercially available demineralized bone graft materials. Spine 26: 1425–1428
8. Bucholz RW (2002) Nonallograft osteoconductive bone graft Substitutes. Clin Orthop 395:44–52
9. Cammisa FP Jr, Lowery G, Garfin SR, Geisler FH, Klara PM, McGuire RA, Sassard WR, Stubbs H, Block JE (2004) Two-year fusion rate equivalency between Grafton® DBM gel and autograft in posterolateral spine fusion. Spine 29:660–666
10. Khan SN, Fraser JF, Sandhu HS, Cammisa FP Jr, Girardi FP, Lane JM (2005) Use of osteopromotive growth factors, demineralized bone matrix, and ceramics to enhance spinal fusion. J Am Acad Orthop Surg 13:129–137
11. Cook SD, Salkeld SL, Patron LP, Barrack RL (2002) The effect of demineralized bone matrix gel on bone ingrowth and fixation of porous implants. J Arthroplasty 17:402–408
12. Edwards JT, Diegmann MH, Scarborough NL (1998) Osteoinduction of human demineralized bone: characterization in a rat model. Clin Orthop 357:219–228
13. Einhorn TA (2003) Clinical applications of recombinant human BMPs: early experience and future development. J Bone Joint Surg Am 85:82–88
14. Finkemeier CG (2002) Bone-grafting and bone-graft substitutes. J Bone Joint Surg 84:454–464
15. Gamradt SC, Lieberman JR (2003) Bone graft for revision hip arthroplasty biology and future applications. Clin Orthop 413: 183–194
16. Gazdag AR, Lane JM, Glaser D, Forster RA (1995) Alternatives to autogenous bone graft: efficacy and indications. J Am Acad Orthop Surg 3:1–8
17. Gibson S, McLeod I, Wardlaw D, Urbaniak S (2002) Allograft vs. autograft in instrumented posterolateral lumbar spinal fusion. Spine 27:1599–1603
18. Hollinger JO, Brekke J, Gruskin E, Lee D (1996) Role of bone substitutes. Clin Orthop 324:55–65
19. Keating JF, McQueen MM (2001) Substitutes for autologous bone graft in orthopaedic trauma. J Bone Joint Surg 83-B:3–8
20. Kim DH, Jenis L, Berta SC, Vaccaro AR (2003) Bone graft alternatives in spinal fusion surgery. Cur Opin in Orthop 14: 127–137
21. Kligman M, Padgett DE, Vered R, Roffman M (2003) Cortical and cancellous morselized allograft in acetabular revision total hip replacement minimum 5-year follow-up. J Arthroplasty 18: 907–913
22. Lavernia CJ, Malinin TI, Temple HT, Moreyra CE (2004) Bone and tissue allograft used by orthopaedic surgeons. J Arthroplasty 19:430–435
23. Lohmann CH, Andreacchio D, Koster G, Carnes DL, Dean BD, Schwartz Z (2001) Tissue response and osteoinduction of human bone grafts in vivo. Arch Orthop Trauma Surg 121: 583–590
24. Louis-Ugbow J, Murakami H, Kim H, Minamide A, Boden SD (2004) Evidence of osteoinduction by Grafton demineralized bone matrix in nonhuman primate spinal fusion. Spine 29: 360–366
25. Lu L, Currier BL, Yaszemski MJ (2000) Synthetic bone substitutes. Curr Opin Orthop 11:383–390
26. Martin GJ Jr, Boden SD, Titus L, Scarborough NL (1999) New formulations of demineralized bone matrix as a more effective

graft alternative in experimental posterolateral lumbar spine arthrodesis. Spine 24:637–645
27. Morgan HD, McCallister W, Cho MS, Casnellie MT, Leopold SS (2004) Impaction allografting for femoral component revision. Clin Orthop 420:160–169
28. Pokorny JJ, Davids H, Moneim M (2003) Vascularized bone graft for scaphoid nonunion. Tech Hand Up Extrem Surg 7:32–36
29. Price CT, Connolly JF, Carantzas AC, Ilyas I (2003) Comparison of bone grafts for posterior spinal fusion in adolescent idiopathic scoliosis. Spine 28:793–798
30. Resnick DK (2002) Vitoss™ bone substitute. Neurosurgery 50: 1162–1164
31. Riley EH, Lane JM, Marshall UR, Karen LM, Lieberman JR (1996) Bone morphogenic protein-2. Biol Appl 324:39–46
32. Sauer ST, Marymont JV, Mizel MS (2004) Specialty update: What's new in foot and ankle surgery. J Bone Joint Surg 86: 878–886
33. Stryker® Biotech (2003) Hopkinton, MA
34. Thien TM, Welten MLM, Verdonschot N, Buma P, Yong P, Schreurs W (2001) Acetabular revision with impacted freeze-dried cancellous bone chips and a cemented cup a report of 7 cases at 5 to 9 years' follow-up. J. Arthroplasty 16:666–670
35. Urist MR, Dawson E (1981) Intertransverse process fusion with the aid of chemosterilized autolyzed antigen-extracted allogeneic (AAA) bone. Clin Orthop 154:97–113
36 Vitoss™ (2000) Synthetic cancellous bone void filler—an overview, Orthovita, Malvern, Pa
37. Yazici M, Asher MA (1997) Freeze-dried allograft for posterior spinal fusion in patients with neuromuscular spinal deformities. Spine 22:1467–1471
38. Yee AJM, Bae HW, Friess D, Robbin M, Johnstone B, Yoo JU (2003) Augmentation of rabbit posterolateral spondylodesis using a novel demineralized bone matrix-hyaluronan putty. Spine 28: 2435–2440