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Nasal Dorsal Augmentation with Freeze-Dried Allograft Bone: 10-Year Comprehensive Review

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Background: The aim of this study was to evaluate freeze-dried cortical allograft bone for nasal dorsal augmentation. The 42-month report on 18 patients was published in 2009 in *Plastic and Reconstructive Surgery* with 89 percent success at level II evidence, and this article is the 10-year comprehensive review of 62 patients.
Methods: All grafts met standards recommended by the American Association of Tissue Banks, the U.S. Food and Drug Administration, and the Centers for Disease Control and Prevention. Objective evaluation of the persistence of graft volume was obtained by cephalometric radiography, cone beam volumetric computed tomography, and computed tomography at up to 10 years. Vascularization and incorporation of new bone elements within the grafts were demonstrated by fluorine-18 sodium fluoride positron emission tomography at up to 10 years. Subjective estimation of graft volume persisting up to 10 years was obtained by patient response to a query conducted by an independent surveyor.
Results: The authors report objective proof of persistence of volume alone or combined with proof of neovascularization in 16 of 19 allografts. The authors report the patient's subjective opinion of volume persistence in 37 of 43 grafts. The dorsal augmentation was assessed overall to be successful in 85 percent of 62 patients evaluated between 1 and 10 years, with a mean of 4.7 years.
Conclusions: Freeze-dried allograft bone is a safe and equal alternative for dorsal augmentation without donor-site morbidity. Further studies are needed to (1) confirm these findings for young patients needing long-term reconstruction, and (2) partially demineralize allograft bone to allow carving with a scalpel. (*Plast. Reconstr. Surg.* 143: 49e, 2019.)
CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, IV.

This article reports the long-term efficacy of freeze-dried allograft cortical bone to augment the dorsum of the nose. It expands on our initial report of 18 bone allografts that were evaluated with cephalometric radiographs, computed tomography, and fluorine-18 bone scans documenting persistence of augmentation for 42 months at level of evidence II.[1,2] This study of 62 bone allografts is prospective, and the objective and subjective assessment of results were delayed to at least 1.5 years postoperatively.[2] The dorsal augmentations were evaluated at up to 10 years, with a mean follow-up of 4.7 years, and there was an 85 percent success as defined by maintenance of volume and projection.

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The first choice for dorsal augmentation should be long pieces of septal cartilage followed by ear cartilage.[3] However, this flexible cartilage must be first triaged to the mobile lower third of the nose for use as struts, septal lengthening grafts, tip grafts, and battens. Residual small pieces can be diced and packaged into a pocket, but it does not have structural strength and, although one diced dorsum remained palpable out to 6 years,[4] there is no documentation of sustainability beyond 7 months.[5,6] If these septal and ear sources are inadequate, the surgeon is faced with a significant increase in morbidity and technical difficulty with harvesting autogenous cranial bone or rib cartilage.

Because there is no morbidity or technical complexity to opening a package and hydrating the contents, a prospective study of freeze-dried allograft bone was undertaken. Our data indicate that this safe, inexpensive, and morbidity-free cadaver bone has a degree of efficacy in the nose that is comparable to the success of autogenous skull and rib grafts.[7,8]

PATIENTS AND METHODS

All patients signed informed consent as to the experimental nature of this study and that the graft might not survive and that there was a remote chance of disease transmission. Institutional review board approval was obtained for the computed tomographic and fluorine-18 bone scan studies at the University of California Davis Medical Center. Maintenance of dorsal projection was evaluated by the following means,

Objective Evaluation

Cephalometric Radiography Protocol

Serial radiographs were taken 6 to 12 months apart measured from fixed skull points by means of the projection of barium paint on the skin overlying the allograft dorsal augmentation.[1]

Computed Tomographic/Bone Scan Imaging Protocol

The positron emission tomographic, computed tomographic, and fused positron emission tomographic/computed tomographic images were reviewed by a nuclear radiologist certified by both the American Board of Radiology and the American Board of Nuclear Medicine. Fluorine-18 positron emission tomographic/computed tomographic imaging was used to demonstrate volume preservation and vascularization of allografts.[1] Fluoride ion, injected intravenously, is delivered to osteoblasts and incorporated into new bone. In contradistinction to dead bone or scar tissue, only living vascularized bone "lights up," and therefore any allograft image seen is neovascularized bone.[9,10]

Cone Beam Volumetric Computed Tomographic Scan Protocol

The I-Cat Next Generation 13-17 (Imaging Sciences International, Hatfield, Pa.) cone beam computed tomography scanner was used to acquire a scan of the patient that generated RAW data that were imported into Dolphin Imaging Systems Version 11.95 software (Dolphin Imaging Systems, Chatsworth, Calif.), to build a true size cephalometric image format for analysis. The density and true size of each graft is accurately depicted, and sagittal views were assessed for change.

Subjective Evaluation

Subjective Survey Protocol

Patients were contacted by means of e-mail, phone call, and letter by a third-party physician volunteer who asked whether the dorsal augmentation had decreased in size to a noticeable degree or by a loss of greater than 20 percent.

Preparation of Allografts

The description of the bone bank cortical allograft preparation protocol can be found in the original article.[1] We primarily used nonirradiated bone to avoid potential radiation damage to the growth factors, but 21 percent of allografts were irradiated for reasons of choice and availability (Table 1). Evidently, the amount of radiation (15 kGy) that is required to eliminate any human immunodeficiency virus or hepatitis C virus does not damage growth factors.[11,12] Processing removes periosteum that perhaps should be left intact because it contains osteogenic cells and osteoinductive signals.[13] Freezing the bone allows for storage, and there is evidence that it preserves osteoinductive ability.[14]

Matchstick bone precut to 6 × 6 × 50 mm was initially used but proved to be rather narrow. We now prefer whole tibia or fibula from which a thicker and wider graft can be cut, and one can choose the ideal dorsal contour from six edges.

Insertion and Fixation

All allografts were cortical bone and were contoured with a high-speed saw and burr, and appropriate holes were drilled before insertion by means of a closed approach. The grafts were

Table 1. Summary

Patient	Age (yr)	Donor Age (yr)	Recipient Site	Decreased Size	LOE A (yr)	LOE B (yr)	Irradiated
A.T. 35§	35	71	2°	No*	10.5	10.5	No
C.B. 22	22	31	1°	No	2.0	8.5	No
S.D. 52	52	38	6°	No	2.1	5.0	No
S.S. 46	46	71	1°	No	1.8	9.0	No
J.Y.K. 48	48	68	1°	No	1.8	8.5	No
J.R. 38¶	38	67	4°	No*	2.0	9.0	No
K.S. 43¶	43	60	2°	No*	2.0	8.0	Yes
N.B. 50‡	50	67	1°				
L.P. 45	45	51	2°	No	1.0	8.6	No
B.H. 52	52	51	2°	No	1.6	8.5	Yes
R.V. 51	51	62	1°	No		8.3	No
R.B. 21	21	59	1°	No	1.1	8.0	No
W.W. 54‡	54	52	1°	No			
A.S. 42	42	59	1°	No	10.5	10.5	No
C.T. 26	26	17	2°	No	10.0	10.0	No
M.C. 21	21	59	1°	No	1.0	7.7	No
K.S. 45	45	59	3°	No	1.1	7.0	No
N.G.†§	41	59	1°	>50%	2.5	2.5	No
N.G.†	44	40	2°	No		5.0	Yes
E.H. 47	47	63	1°	No		6.0	No
M.K. 48	48	63	2°	No		6.5	No
D.K. 31	31	63	1°	No, <20%	1.0	6.5	No
N.M. 39‡	39	52	1°				
B.V. 37‡	37	63	2°				
T.M. 22‖	22	49	2°	>50%		6.0	No
N.M. 23	23	38	1°	No		6.2	No
L.J. 35	35	52	3°	No		1.0 yr	No
G.B. 35	35	57	2°	No		5.8	No
S.F. 42	42	76	4°	No		5.5	No
D.T. 55	55	50	3°	No		5.5	No
B.R. 41	41	51	2°	No		4.8	No
S.B. 62	62	51	2°	No		5.5	No
M.B. 27	27	43	1°	No		1.3	Yes
J.C. 34	34	49	1°	No		5.8	No
K.B. 29†§	29	59	2°	>50%	1.0	1.0	No
K.B. 30†	30	59	3°	No		4.8	No
A.B. 27	27	65	1°	No	9.0	9.0	No
K.M. 29	29	53	1°	No		1.0	No
L.M. 55	55	71	3°	No		6.3	No
S.A. 30‡	30	51	2°				
J.P. 27	27	65	4°	No		5.0	No
K.C. 37	37	27	1°	No		1.0	No
A.C. 27	27	65	3°	No		1.0	Yes
A.B. 38	38	65	3°	No		4.0	Yes
S.N. 22§	22	53	1°	>50%		1.0	No
M.B. 39	39	43	1°	No	7.0	7.0	No
C.N. 48	48	43	1°	No		4.5	No
V.M. 27§	27	51	1°	>50%		4.0	No
M.B. 29	29	51	2°	No		3.5	No
M.A. 45	45	29	2°	No		3.5	No
M.O. 38	38	27	1°	No		4.0	No
R.J. 55‡	55	57	2°				
J.R. 41	41	57	3°	No		4.0	No
K.L. 26	26	45	2°	No		3.5	No
P.M. 56	56	35	1°	No		3.5	No
S.S. 42	42	21	3°	No		3.5	No
J.B. 32‡	32	21	2°				
L.S. 30§	30	35	1°	>50%		3.0	No
S.S. 50	50	21	1°	No		3.8	No
D.T. 25	25	50	2°	No		2.0	No
S.P. 26	26	19	1°	No		1.0	No
K.B. 41	41	51	3°	No		2.5	No
M.M. 34	34	61	1°	No		2.5	Yes
S.R. 35	35	74	1°	No		1.5	Yes
C.T. 25	25	67	1°	No		2.0	Yes
S.L. 36	36	55	1°	No		1.8	Yes
K.A. 51	51	39	1°	No		1.5	Yes
T.R. 51	51	42	1°	No		1.8	Yes
S.D. 38	38	22	3°	No		1.8	Yes

LOE, level of evidence; A, high level of evidence; B, lower level of evidence/patient's opinion.
*Surgeon opinion that allograft resorption was >20%.
†Replacement allograft was successful in same patient.
‡Lost to follow-up.
§Graft absorption was >20% by objective or subjective evaluation protocols.
‖Infection.
¶Surgeon thinks more resorption (>20%) than patient has reported.

positioned under nasal bone periosteum, and they most often were intended as an onlay and were secured with 4-0 polydioxanone percutaneously at the nasion and internal at the anterior septal angle. When used as a cantilever, more aggressive fixation required a transcutaneous threaded Kirschner wire or, rarely, a 1.5-mm titanium screw.

Assessment of Persistence of Allograft

To evaluate the degree of persistence of a potentially resorbable graft, objective evidence is preferred and was achieved in 19 patients. Our most attainable and least expensive objective tool for assessing the persistence of graft size was serial cephalometric radiographs. Unfortunately, these radiographs became obsolete in favor of cone beam scans, and we were unable to compare the new volumetric (cone beam) scans to the prior radiographs. Thus, the continuity of follow-up by radiography ceased at 3.5 years. Changing the method of objective evaluation to expensive cone beam computed tomographic scans limited the number of cases with objective follow-up. Nonetheless, we do have comparative cone beam studies taken 6 and 7 years apart in two patients.

We also had fluorine-18 positron emission tomographic/computed tomographic imaging in five patients ranging from 15 to 42 months postoperatively.[1] Three of these original five patients returned for comparison bone scans at 10 years postoperatively.

Therefore, because of the aforementioned untimely demise of cephalometric radiographs, the restrictive expense of serial cone beam scans, and the prohibitive cost of fluorine-18 positron emission tomographic/computed tomographic imaging, we had to resort to subjective evidence in 44 patients. We thought self-reporting from the patient might be a higher level of subjective evidence than the surgeon's opinion. Actually, despite inherent bias, the surgeon's observation may be more accurate; however, the patient's opinion is paramount in cosmetic surgery. We were able to demonstrate two levels of evidence (level A and level B) (Table 1). Level A is the highest level of evidence. It is objective evidence that consists of serial cephalometric radiographs with or without fluorine-18 positron emission tomographic/computed tomographic imaging or cone beam scans. Level B is the next best level of evidence achievable and is subjective evidence, consisting of patient opinion of loss in graft size greater than 20 percent.

Table 2. Primary and Secondary Rhinoplasty

	No. of Patients (%)
Total	62
Primary rhinoplasty	31 (50)
Secondary rhinoplasty	16 (26)
3–5 previous rhinoplasties	15 (24)

RESULTS

This study started with 69 patients and was culled to 62, with seven lost to follow-up. The mean follow-up was 4.7 years. The average age of patients was 38 years and the average age of donors was 52 years. Only 50 percent of the patients were primary rhinoplasty patients, with 26 percent secondary and 24 percent at least tertiary (Table 2). If objective data showed—and/or the patient reported—that the dorsal augmentation had not noticeably decreased, or any change was less than 20 percent, they were counted as a success.

Objective Results (Group A)

Group A consisted of 19 patients who were followed using the objective studies described. Three patients were followed at least 10 years, and the mean objective follow-up was 3.6 years. There was no significant absorption in 16 of these 19 patients (84 percent). Two patients (N.G. and K.B.) had greater than 50 percent absorption requiring successful replacement grafts. One patient (A.T., case 2) had fluorine-18 uptake and no change in midsection computed tomography over 7 years, yet he is considered a failure because he demonstrated partial resorption in the cephalic 30 percent where it was overlying a prior graft, which may have limited osteoconduction. In contrast, another patient (D.K.) had early less than 20 percent loss on radiography at 1 year; however, because it remained unchanged over the next 7 years, he is listed as a success (Table 1).

Subjective Results (Group B)

All 62 patients reported to the surveyor their opinion about the perseverance of dorsal projection, and we had to rely on this subjective evidence alone in 43 of the cases. This group (group B) of 43 patients was followed for 1 to 8.3 years, with a mean follow-up of 3.7 years. Only six patients reported significant resorption (>20 percent), and each stated that it was over 50 percent, suggesting that resorption tends to be an "all-or-nothing" phenomenon. The success rate was 86 percent in group B (Table 1).

Table 3. Absorption

	No. of Patients (%)
Total	62
No absorption	53 (85)
>20% absorption	9 (15)

Overall Results

Five of the absorptions were not associated with any trauma or infection and may be attributable to some donor processing or recipient-site problem. There was one reported loss caused by methicillin-resistant *Staphylococcus aureus* occurring well after initial healing. Infection can occur with any implant or autograft and is not an indictment of allograft, and an isolated case suggests no propensity of allograft to become infected. Nonetheless, this patient remains in the study as an allograft failure.

Two patients demonstrated either "willing-to-please" confirmation bias or did not notice gradual loss of graft over 5 to 10 years. The trained investigator can trump the patient's opinion under the circumstances when it does not favor the study. Therefore, the final failure rate must increase from seven to nine.

Thus, 53 of 62 patients had successful augmentation based on the described objective and/or subjective criteria. The mean long-term follow-up of all patients was 4.7 years. The success rate for nasal dorsal augmentation with freeze-dried allograft bone is 85 percent and the failure rate is 15 percent (Table 3). The infection rate was one of 62 (2 percent).

CASE REPORTS

Case 1

A 27-year-old Hispanic woman (C.T.) underwent allograft bone dorsal and premaxillary augmentation (Fig. 1). Serial cephalometric radiographic, computed tomographic, and fluorine-18 bone scanning images 7 years apart show no significant change in volume, and the fluorine-18 uptake was equal to the maxillary bone (Fig. 2) (see case 1 in Table 4). [**See Figure, Supplemental Digital Content 1**, which shows (*left*) a computed tomographic scan (lateral view) of the patient in case 1 obtained in 2007, 1 year after augmentation of the premaxilla and nasal dorsum with allograft bone. (*Right*) Computed tomographic scan (lateral view) obtained in 2014, 8 years after augmentation of the premaxilla and nasal dorsum with allograft bone, demonstrating no significant change, ***http://links.lww.com/PRS/D156***.]

Case 2

A 35-year-old Filipino man (A.T.) underwent secondary allograft dorsal augmentation. [**See Figure, Supplemental Digital Content 2**, which shows the patient in case 2 (*left*) preoperatively, with a wide and underprojected nose; (*center*) 5 years postoperatively after dorsal augmentation with allograft bone; and (*right*) 10 years postoperatively, showing partial allograft resorption at the nasion, ***http://links.lww.com/PRS/D157***.] Computed tomographic scans obtained at 3 and 10 years show persistence of volume in the midportion of the graft, and fluorine-18 uptake shows vascularization between soft tissue and cranium (see case 2 in Table 4). [**See Figure, Supplemental Digital Content 3**, which shows (*above, left*) a computed tomographic scan, midsection, of the patient in case 2 obtained in 2014, 10 years after dorsal augmentation with allograft bone showing no significant change in

Fig. 1. Case 1. (*Left*) Preoperative nasal dorsal and premaxillary deficiency. (*Right*) Five years after nasal dorsal and premaxillary augmentation with allograft bone.

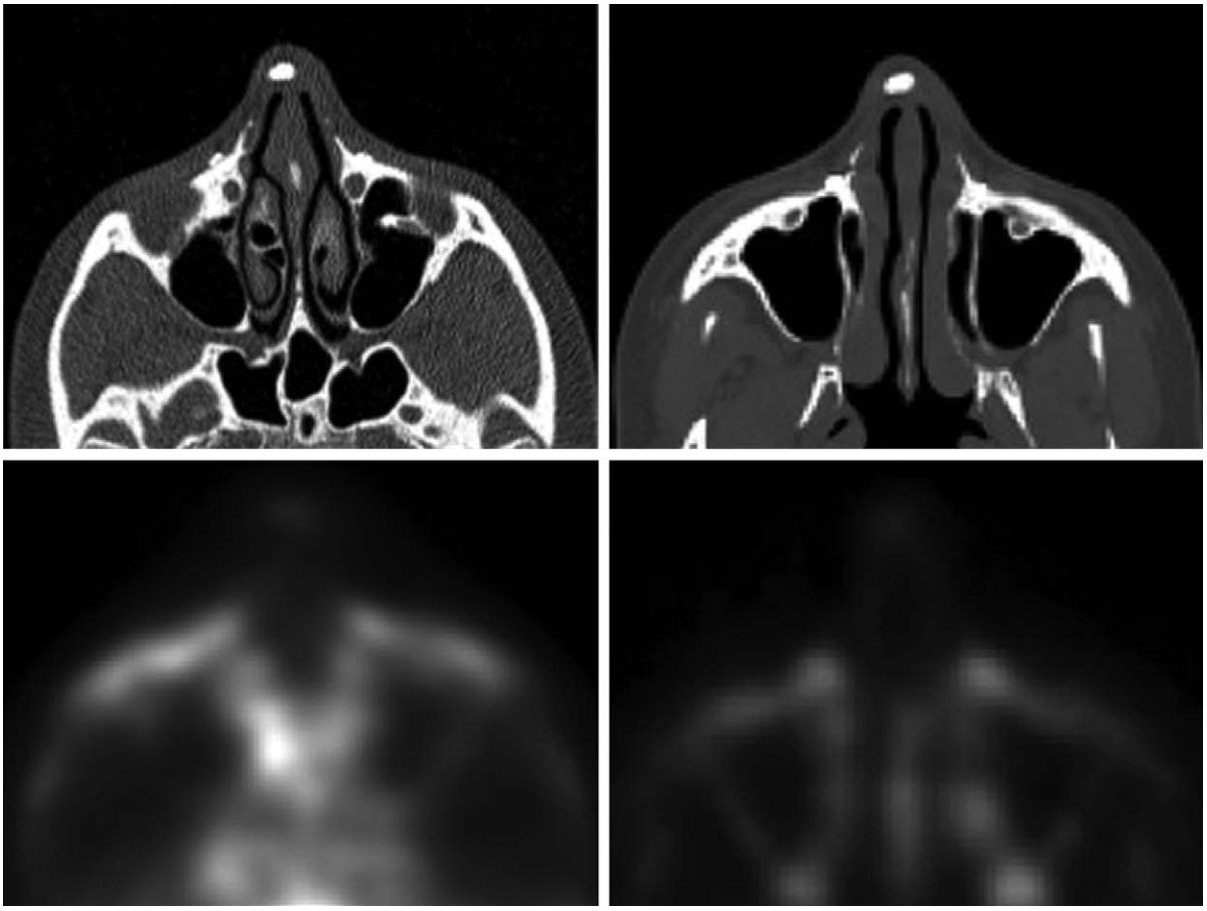

Fig. 2. Case 1. (*Above*, *left*) Computed tomographic scan obtained in 2014, 8 years after augmentation of the premaxilla and nasal dorsum with allograft bone. (*Below*, *left*) Computed tomographic scan obtained in 2007, 1 year after augmentation of the premaxilla and nasal dorsum with allograft bone. (*Above*, *right*) Fluorine-18 positron emission tomographic scan obtained in 2014, 8 years after augmentation of the premaxilla and nasal dorsum with allograft bone. (*Below*, *right*) Fluorine-18 positron emission tomographic scan obtained in 2007, 1 year after augmentation of the premaxilla and nasal dorsum with allograft bone.

caudal two-thirds of the allograft. (*Below, left*) Computed tomographic scan, midsection, obtained in 2007, 3 years after dorsal augmentation with allograft bone. (*Above, right*) Fluorine-18 positron emission tomographic scan, midsection, obtained in 2014, 10 years postoperatively, demonstrating continued vascularization of the midportion of the allograft. (*Below, right*) Fluorine-18 positron emission tomographic scan, midsection, obtained in 2007, 3 years postoperatively, demonstrating revascularization of the midportion of the allograft, ***http://links.lww.com/PRS/D158***.] The patient was satisfied, but on 10-year examination and on scans, late 30 percent resorption in the nasion was evident, and he is considered a failure.

Table 4. Fluorine-18 Uptake in Allograft

Case	Midsection of Graft*
1	3
2	2
3	4

*Grading key: 0, less than soft tissue; 1, equal to soft tissue; 2, between soft tissue and maxillary bone; 3, equal to maxillary bone; 4, greater than maxillary bone.

Case 3

A 35-year-old black woman (A.S.) underwent allograft bone augmentation of her nasal dorsum and premaxilla (Figs. 3 and 4). Computed tomographic bone scans at 18 months compared to 9 years show maintenance of projection. Fluorine-18 uptake was greater than that within the surrounding maxillary bone, consistent with ingrowth of vascular and osseous elements (Figs. 5 and 6) (see case 3 in Table 4).

Case 4

A 25-year-old Eurasian woman (A.B.) desired more narrowing of her dorsum and had dorsal allograft augmentation. Her photographs represent a 9-year result. [**See Figure, Supplemental Digital Content 4**, which shows the patient in case 4. (*Left*) Preoperatively, a wide relatively flat nose; (*right*) 9 years after dorsal augmentation with allograft bone; her primary desire was to narrow the anteroposterior appearance of her nose, ***http://links.lww.com/PRS/D159***.] Volumetric cone beam scan in 2010 and comparison follow-up scan in 2017 demonstrate no change in dorsal allograft. This view of the volumetric scan illustrates the measurement indices. [**See Figure, Supplemental Digital Content 5**, which shows the patient in case 4. (*Left*) Cone beam

Fig. 3. Case 3. (*Left*) Preoperative image, showing wide and amorphous nose. (*Right*) Nine years after nasal dorsal and premaxillary augmentation with allograft bone.

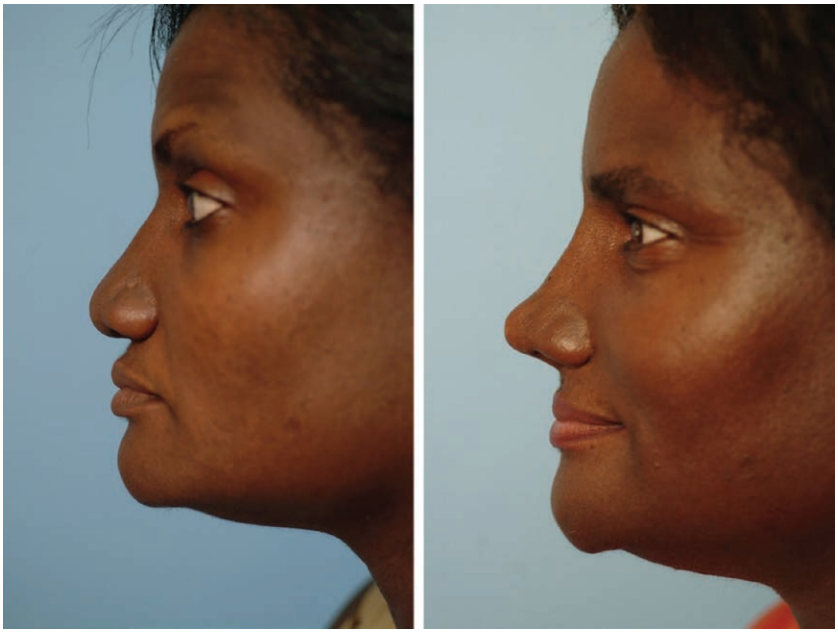

Fig. 4. Case 3. (*Left*) Preoperative image, showing wide and amorphous nose. (*Right*) Nine years after nasal dorsal and premaxillary augmentation with allograft bone.

computed tomographic scan obtained in 2010, 2 years after dorsal and premaxilla augmentation with allograft bone. (*Right*) Cone beam computed tomographic scan obtained in 2017, 9 years after dorsal and premaxilla augmentation with allograft bone showing no change, ***http://links.lww.com/PRS/D160***.]

Case 5

A 39-year-old Caucasian/Puerto Rican woman (M.B.) underwent dorsal and pyriform aperture augmentation with allograft bone (Fig. 7). Volumetric cone beam scans were obtained 1 year postoperatively, and comparison scans 6 years later show no significant loss of volume of allografts (Fig. 8).

PROS AND CONS COMPARED TO ALTERNATIVES

The factors favoring the use of allograft over autogenous bone or rib include no donor-site morbidity and the unlimited amount of material

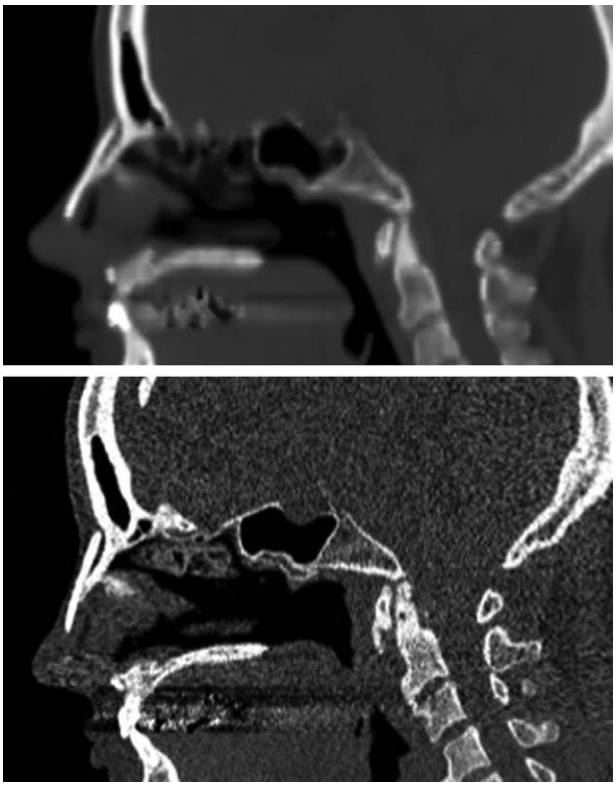

Fig. 5. Case 3. (*Left*) Computed tomographic scan obtained in 2007, 2 years after nasal dorsal and premaxillary augmentation with allograft bone. (*Right*) Computed tomographic scan obtained in 2014, 9 years after nasal dorsal and premaxillary augmentation with allograft bone.

with which to work.[15,16] There is morbidity associated with the harvesting of both cranial bone and rib cartilage, and the incidence of complications varies with surgeon training and experience.[17–19] A study of 30 fresh human cadaver heads found that the skull is significantly weakened (36 percent) by harvesting cranial bone grafts. This finding should give pause when safer alternatives are available.[20] The harvesting of rib results in a scar, possible persistent pain, and pneumothorax, and ossification of the rib cartilage may make it unworkable.[21]

There is a lack of objective evidence in dorsal augmentation, but there are retrospective subjective reports of minimal absorption and satisfactory results in the vast majority of cranial bone grafts.[17,22,23] A respected surgeon's opinion is valuable yet vulnerable to recall bias. Perhaps "satisfactory" means less than 25 percent resorption and perhaps "vast majority" means at least 80 percent. Posnick et al. lamented on his inability to objectively measure, yet he estimated a resorption rate of 15 to 20 percent with autogenous cranial bone grafts to the nose.[24] One patient questionnaire reflected a decrease in size in 19 percent of rib grafts used for dorsal augmentation.[25] Another "patient reporting" study showed 17 percent absorption of rib cartilage as a dorsal onlay.[26] Our 15 percent compares reasonably with these estimated 15 to 20 percent resorption rates of rib and cranial autografts.

Allografts do not have the potential to curl like a cranial bone graft or warp like a rib graft.[26–29] Despite attempts to reduce rib cartilage warping with intraoperative carving, warping has been shown to occur after 1 month and is likely to continue over time and thus remains an unpredictable problem.[21,30–33] Cortical allografts share with autograft rib and bone traits desirable (i.e., linear lines, strength, and ability to overcome resistance of skin envelope) and undesirable (i.e., rotation, malposition, and shelving that is noticeable through thin skin).

An advantage of rib cartilage is the ease of carving to size in the operating room. In contrast, cortical mineralized bone, whether autograft or allograft, needs to be cut and shaped with expensive high-speed saws, burrs, and drills. Working with high-speed tools probably creates heat damage to growth factors.[27,34]

A concern that is more specific to allograft is the variation of donor bone quality. Deterioration of bone morphogenetic protein/growth factors may be related to a potential 24-hour window of delay in postmortem processing and to the age of the donor.

DISCUSSION

This study provides long-term evidence supporting freeze-dried allograft bone for nasal dorsal augmentation. It is important to understand that this processed bone is extremely safe and does not stimulate an immune system rejection response. The bone bank preparation is approved by the American Association of Tissue Banks, eliminates antigenic protein and lipid cells, and includes irradiation, which kills viruses and bacteria. Theoretical human immunodeficiency virus transmission is one per 1,600,000.[35,36] The Centers for Disease Control and Prevention reports no cases of human immunodeficiency virus or hepatitis C with these processed freeze-dried bones.[37,38]

Freeze-dried mineralized allograft has been proven successful in maxillofacial surgery[39] and has been used in up to one-third of orthopedic cases, especially cervical spine fusions.[40–48] The periodontal literature supports the use of demineralized allograft bone in powder form, which has more available bone growth factors,[49–51] but powder does not hold its shape well.[52] The established

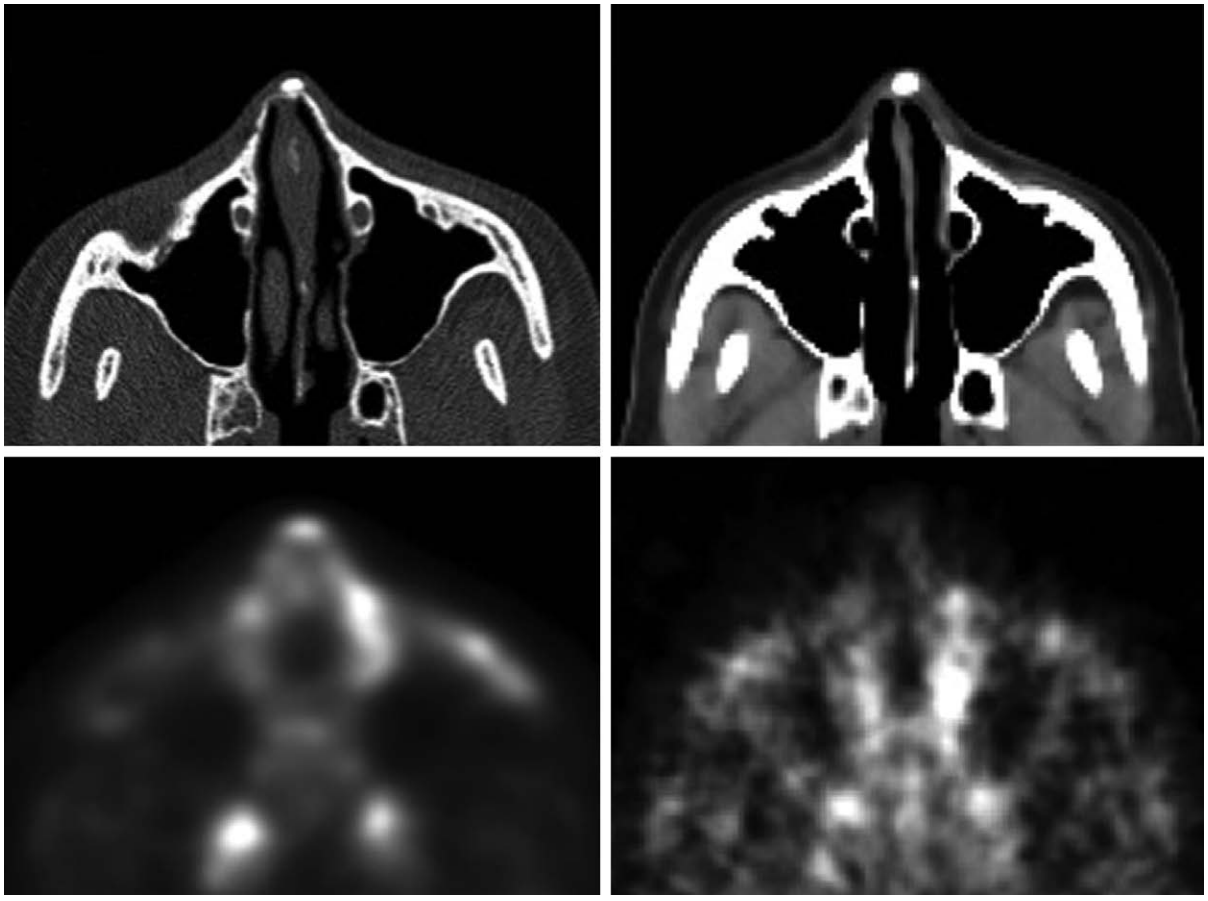

Fig. 6. Case 3. (*Above*, *left*) Computed tomographic scan obtained in 2014, 9 years after nasal dorsal and premaxillary augmentation with allograft bone. (*Below*, *left*) Computed tomographic scans obtained in 2007, 2 years after nasal dorsal and premaxillary augmentation with allograft bone. (*Above*, *right*) Fluorine-19 positron emission tomographic scan obtained in 2014, 9 years after nasal dorsal and premaxillary augmentation with allograft bone. (*Below*, *right*) Fluorine-19 positron emission tomographic scan obtained in 2007, F2 years after nasal dorsal and premaxillary augmentation with allograft bone.

amount of bone morphogenetic protein and growth factors assayed for demineralized bone has to also be present, albeit less readily available, in the mineralized form of the bone.[51,53] Mineralized cortical bone was chosen for this study because it is strong enough to give structural support and to overcome soft-tissue resistance.

This study suggests that allograft bone may remodel through a combination of osteoconduction and osteoinduction. Osteoconduction involves providing a scaffold on which recipient-site mesenchymal stem cells, capillaries, and tissue can migrate to produce bone. Allografts are highly osteoconductive and are the prototype for an osteoconductive matrix.[54,56] Osteoinduction is the process of stimulating mesenchymal stem cells at the recipient site to differentiate into osteoblasts.[35,57] The growth factors embedded in the cortical allograft bone matrix include insulin-like growth factor type II, transforming growth factor, platelet-derived growth factor, and bone morphogenic proteins, all of which make allograft bone potentially osteoinductive.[54] Bone morphogenetic protein (BMP)-4 has been shown to induce osteogenic differentiation of osteoblasts from osteoprogenitor cells.[55] Interaction of BMP-2, BMP-4, and BMP-7 may contribute to osteoinduction.[51]

In the dorsum of the nose, there is only partial host bone–to-allograft bone contact, in which the cephalic portion of the allograft sits on nasal bones and the caudal portion sits on midvault cartilage. Because we did not see significantly more allograft resorption in the distal half, osteoconduction may prove to be no more important than osteoinduction.

Bone graft incorporation involves a clot that serves to nourish the graft until distinct capillaries develop. Granulation tissue ingrowth will revascularize the graft.[57] Neovascularization depends on cytokines and growth factors to stimulate sprouting of local endothelial cells (angiogenesis) and

Fig. 7. Case 5. (*Left*) Preoperative image, with a low radix and acute nasolabial angle. (*Right*) Four years after nasal dorsal and premaxillary augmentation with allograft bone.

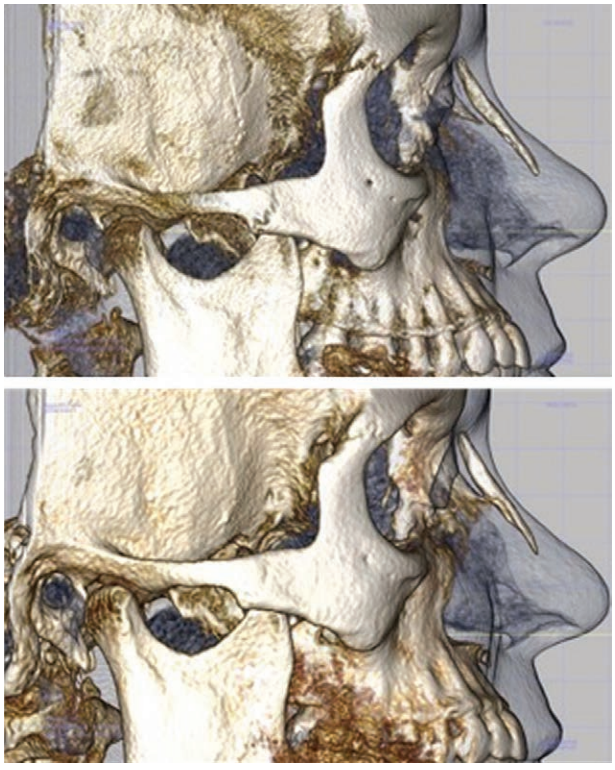

Fig. 8. Case 5. (*Above*) Cone beam computed tomographic scan obtained in 2010, 1 year after nasal dorsal and premaxillary augmentation with allograft bone. (*Below*) Cone beam computed tomographic scan obtained in 2016, 7 years after nasal dorsal and premaxillary augmentation with allograft bone.

forming new vessels from circulating progenitor cells (vasculogenesis).[58]

Neovascularization brings into the graft osteoclasts, which are derived from pluripotential cells, which are derived from circulating monocytes and macrophages and capillary pericytes.[53] The osteoclasts follow Haversian canals, resorbing allograft bone and releasing embedded bone morphogenetic protein and growth factors, and then change to osteoblasts and eventually to osteocytes.[35,55,59–65] The process of new bone formation and remodeling initiated by osteoclastic resorption has been called reverse creeping substitution.[57]

Revascularization, whether by osteoconduction or osteoinduction, is dependent on the quality and vascularity of the host bed. We have had success with both primary (48 percent) and secondary or multiple revision rhinoplasty (52 percent). Of the allograft resorptions, 55 percent were primary and 45 percent were revision, which suggests that a virgin versus a scarred recipient bed was not a factor in this study.

Perhaps more important than the recipient site is the quality of the donor bone. There is variation of growth factors between donor individuals based on genetics and health,[66] perhaps influencing the success of osteoinduction and osteoconduction.[67] Bone morphogenetic protein and growth factor may deteriorate during the time

window allowed between demise and icing and allograft processing.

Although one study found no correlation between donor age and the levels of measured bone morphogenetic proteins,[51] a more recent report concluded that BMP-4 undergoes an age-related decrease that may contribute to the reduction of bone volume observed with aging.[68] There is perhaps less bone morphogenetic protein and growth factors in older bone, and osteogenesis appears to be age-dependent.[69] Two of our patients demonstrating resorption within 2 years had donors older than 60 years. Each had a successful replacement allograft from a donor younger than 40 years. Even so, because the average age for all donors was 52 years and that for the nine failures was 56 years, donor age was not significant in this study.

The success of allograft bone will improve with advances in bone engineering. Simply leaving the periosteum intact would provide more rapid revascularization.[35,70] Bone morphogenetic protein added to allograft bone may improve the take rate but is currently too expensive. Allogenic bone graft healing is enhanced in rabbits by autologous mesenchymal stem cells and platelet-rich plasma, suggesting that recipient sites could be enriched with autogenous adipose-derived stem cells.[71] Osteoclastogenesis may improve by coating allograft with a polymer releasing BMP-2 and vascular endothelial growth factor.[72] Because cortical bone revascularization is hampered by its dense architecture,[57] laser perforation may promote ingrowth of new bone without changing structural integrity.[59] Partial demineralization of cortical bone grafts may accomplish two things: (1) release encased bone morphogenetic protein and growth factors to foster osteogenesis and (2) soften the bone somewhere between rock hard and powder to where strength is maintained but grafts can be shaped by scalpel carving in the operating room.

The irradiated allografts used in this study were purchased from American Association of Tissue Banks–certified bone banks that used a standard of terminal irradiation of 15 to 20 kGy. Intuitively, one would suspect significant loss of efficacy with irradiation, but in a study of dry demineralized bone, the application of 15 to 20 kGy resulted in only a small loss of activity.[73] Irradiation did not appear to negatively impact our results, because 16.3 percent of the nonirradiated allografts resorbed and only 8 percent of the irradiated allografts resorbed. It is possible that the mineralized form of the allograft bone that is used in our study may protect the bone morphogenetic protein and growth factors during irradiation.

In an effort to develop an office tool for accurate assessment of graft survival, we modified a soft-tissue cephalometric concept introduced by Guyuron.[74] [**See Figure, Supplemental Digital Content 6,** which shows (*left*) preoperative traumatic collapse of nasal bone and cartilage. (*Center*) Acetate overlay planning technique based on full-size photograph. This office-available, photographic technique may prove applicable to follow persistence of dorsal projection. (*Right*) Early 7-month postoperative result (patient not part of this study). The acetate overlay technique can now be used to follow and detect changes in allograft resorption, ***http://links.lww.com/PRS/D161***.] When used for preoperative planning, an acetate tracing of a full-size photograph is redrawn to the desired result and, when aligned over the original photograph, exact measurements of reduction or augmentation can be made. Postoperative use of this technique may prove an inexpensive tool for objective serial postoperative assessment of maintenance of dorsal projection.

CONCLUSIONS

Freeze-dried allograft cortical bone has equal success in augmentation rhinoplasty that is comparable to mainstream alternatives, without the donor-site morbidity, and should be considered for nasal dorsal augmentation. Further studies are needed to corroborate or refute the finding of this report and to obtain 20-year data on duration of allograft and its suitability for use in young patients.

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PATIENT CONSENT

Patients provided written consent for the use of patients' images.

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