Cranioplasty performed with a new osteoconductive, osteoinducing hydroxyapatite-derived material

ALFREDO POMPILI, M.D., FABRIZIO CAROLI, M.D., LIVIO CARPANESE, M.D., MAURO CATERINO, M.D., LAURA RAUS, M.D., GIANCARLO SESTILI, B.S., AND EMANUELE OCCHIPINTI, M.D.

Divisions of Neurosurgery and Diagnostic Radiology, “Regina Elena” National Cancer Institute, Rome, Italy

Object. Cranioplasty is required to protect underlying brain, correct major aesthetic deformities, or both. The ideal material for this purpose is autogenous bone. When this is not available, alloplastic or artificial materials may be used. These materials should be malleable, strong, lightweight, inert, noncarcinogenic, nonferromagnetic, and, if possible, inexpensive. The authors reviewed their surgical experience with a new bone substitute and discuss outcomes in patients in whom it was used.

Methods. The 11 patients presented in this series had bone defects resulting from bone-involving tumor (eight cases), trauma (two cases), or aesthetic deformity due to repeated craniotomies (one case). The defects were repaired using Osprogel, a bone substitute that consists of calcium hydroxyapatite combined with synthetic, human bone–derived gelatin, glycerol, and water. Osprogel is not only a bioinert material but also an osteoconductive and osteoinducing substrate; when it is placed in contact with healthy cancellous bone, it induces osteogenesis and angiogenesis, thus permitting the regrowth of nearly normal bone. The sheet of Osprogel was modeled onto the cranial defect intraoperatively and was kept in place either by using a titanium micronet secured to surrounding bone with microscrews (first two cases) or by using a single- or double-layer titanium mesh secured with stitches. No complications due to the procedure were observed.

The results, evaluated at least 6 months after surgery by using three-dimensional (3-D) reconstructed computerized tomography scans, were excellent in seven patients, good in three, and fair in one. In the patient with a fair result, the repair was unsatisfactory because there was lack of experience in using the material. In part of the area to be repaired, the Osprogel was used as filler; here it was washed out and resorbed. The cases deemed as having a good result had good bone replacement; however, the curvature was faulty.

Conclusions. In the near future, this technique may be refined to achieve good or excellent results either without the use of supporting material or with the use of individual, computer-designed 3-D prostheses.

KEY WORDS • cranioplasty • hydroxyapatite crystal • skull fracture • skull defect • cranial trauma • brain neoplasm

Acquired cranial defects usually result from trauma, infection, or bone removal because of craniomeningeal neoplastic disease. The indication for cranioplasty arises from cosmetic or brain-protection concerns. Many patients suffer tremendously when they realize that part of their cranial bone is missing, whereas for others this may not be a problem. The presence of large defects may jeopardize the underlying brain in cases of direct trauma, although this is a rare event.1,3,15,20

Cranioplasty is recommended when cranial defects give rise to major aesthetic deformities and whenever it can relieve the symptoms of the patient and improve his or her quality of life.

Clinical Material and Methods

Between September 1995 and March 1997, 11 patients with acquired cranial defects underwent cranioplasty that was accomplished by using a synthetic material composed of calcium hydroxyapatite (HA) combined with gel. This material, Osprogel (Tech-Medical S.R.L., Bologna, Italy), consists of 70% active membrane (HA); 15% synthetic, human bone–derived protein gelatin; 14% glycerol; and 1% water. The material, unlike HA alone, has an intercommunicating porosity, with a pore diameter of 250 to 300 μ, enabling the migration of vascular and bone tissue. In the period immediately following implantation, the
bone-derived gelatin ensures progressive resorption of biological fluids and provides morphogenetic proteins; afterwards, the gelatin is replaced by bone and vascular tissue, which finally embodies HA granules (unpublished data). It follows that this gel is not only a bioinert hetero-plastic material but also, at least, an osteoconductive substrate. Angiogenesis and osteogenesis were histologically demonstrated in specimens obtained 6 and 24 months after implants for bone defects in maxillofacial surgery (unpublished data).

Titanium mesh or micronets were used either to support the sheet of Osprogel and ensure that the implant would retain the desired curvature or to provide protection during the repair procedure.

Three-dimensionally (3-D) reconstructed computerized tomography (CT) scans were obtained preoperatively and at least 6 months postoperatively in all patients.

Surgical Technique

The defect is exposed and the dura is checked for possible lesions, which should be carefully repaired with peri-craniol grafts. The bone margins should be sharpened to expose healthy cancellous bone with which the Osprogel must be in contact. The implant, whose thickness ranges from 2 to 4 mm, is wetted with saline, modeled and cut with scissors to the appropriate shape and curvature, and inserted into the defect, taking care not to press it but to place its edges in contact with healthy cancellous bone (Fig. 1 upper).

Osprogel is supplied with one side covered by a net of Dacron to facilitate suturing or fixation, as in our cases, to overlying titanium net or mesh.

In the first two cases, the titanium honeycombed micro-net (thickness 0.6 mm) was first affixed to the implant and then to the craniectomy borders with microscrews (Aesculap AG, Tuttingen, Germany) (Fig. 1 lower). In other cases, to cut costs, a titanium mesh was used. This mesh was cut to the appropriate size and shape, curved where necessary, and affixed with stitches to the implant and bone (Fig. 2). The mesh may be supplied with an incorporated Osprogel sheet (Osprotitantex; Tech-Medical S.R.L.). In two cases, we used this preformed material; in the remaining cases, we preferred to prepare the combined implant in our operating theater, by using either single- or double-layer mesh.
Results

A summary of cases and their results is listed in Table 1. No complications arising from the procedure were recorded. All patients were discharged within the first 10 postoperative days.

Illustrative Cases

Case 1

This 22-year-old man presented with a grossly triangular left-sided parietal defect measuring approximately 18 cm$^2$ resulting from a comminuted, depressed fracture sustained in a road accident that had occurred 3 months earlier (Fig. 3 left). Cranioplasty was performed using Osprogel and a 6 × 4-cm titanium micronet, which was affixed with 13 self-tapping titanium microscrews. The result was impressive: the defect was completely repaired, leaving normal curvature of the skull, as shown on the 3-D reconstructed CT scan obtained 6 months postoperatively (Fig. 3 right).

Case 3

This 49-year-old woman had undergone surgery for brain tumor in the early 1970s. On that occasion, her right parietal flap had been removed. The patient did well in the following years, leading a normal life, except for seizures that occurred when she did not take her anticonvulsant medications. No radiological investigation had been performed during the last 10 years.

Because the patient suffered from recurrent seizures, she underwent CT scanning, which revealed a left frontal meningioma. She was thus scheduled for surgery both to remove the tumor and repair her old cranial defect, the estimated size of which was approximately 50 cm$^2$ (Fig. 4 upper). The frontal meningioma was removed without any problem. The old craniectomy area was exposed and the bone margins were edged with a punch drill to obtain healthy cancellous bone. A large sheet of Osprotitantex was used.

The 3-D reconstructed CT scan obtained 8 months afterward showed the repaired defect (Fig. 4 center and lower). However, skull curvature was not as satisfactory as expected. This was probably because of the large size of the defect and the fact that the titanium mesh that we used was not rigid enough to retain the shape given during the surgical procedure.

Case 9

One year before admission, this 12-year-old boy had suffered from electrical shock, leading to amputation of his right forearm and thermal necrosis of the cranial skin and bone of his left-sided parietooccipital area. His neurological functions and meningeal layers were intact. He had undergone emergency skin repair with a flap taken from a thigh, giving rise to a large bone defect (Fig. 5 upper). At our institution, plastic surgeons inserted an inflatable balloon to obtain enough cranial skin to cover the defect (Fig. 5 center). Three months afterward, the final repair was performed: the old skin graft was removed and the bone edges were prepared to receive the implant (Fig. 2 upper).
Osprogel and double-layer titanium mesh were used to cover the cranial defect (Fig. 2 lower). Skin repair was achieved by rotating the prepared cranial flaps (Fig. 5 center). The patient’s postoperative course was uneventful. Computerized tomography scanning performed 6 months after the procedure showed very good filling of the defect (Fig. 5 lower).

**Case 10**

This 38-year-old man was admitted to the hospital because he had been suffering from a slowly progressive right-sided frontoorbital swelling for 1 year, which had caused exophthalmos and proptosis. The 3-D reconstructed CT scan and other neuroimaging studies revealed a huge bone mass that was diagnosed as fibrous dysplasia (Fig. 6 upper).

At surgery, all of the diseased bone was removed, including the anterior most portion of the orbital roof. The resulting defect was repaired using Osprogel and double-layer titanium mesh with excellent cosmetic results (Fig. 6 lower).

**Discussion**

The ideal material for cranioplasty is obviously autogenous bone, whose survival is expected to be secured by
osteoblasts and vessels of the surrounding bone. Autogenous bone grafts may consist of: 1) when available, bone removed during craniectomy; 2) split calvarial grafts; or 3) endochondral grafts obtained either from a rib or from the iliac crest. The use of the latter grafts practically demands a second surgical procedure, although not all patients and/or surgeons share this philosophy.

Material selected for allograft cranial bone replacement should be: 1) malleable, to achieve a good cosmetic result; 2) as strong as bone, to secure adequate protection; 3) lightweight, to avoid patient discomfort; 4) chemically inert, noncarcinogenic, and nonferromagnetic, to allow CT scanning and magnetic resonance imaging to be performed; and 5) as inexpensive as possible.

In a recent, excellent historical review of cranioplasty, Sanan and Haines listed the materials and techniques that have been used from ancient times to very recent years. They conclude that allografts, which have been used practically for centuries, carry resorption and infection rates that are too high. Use of metallic and nonmetallic substitutes may also lead to several problems.

Metallic cranioplasty in which tantalum plates were used became very popular after World War II. Apart from other problems, tantalum is no longer used because it interferes with current neuroradiological tools.

Polymethylmethacrylate is still very popular and has long been used at our institution. Its advantages are malleability and fairly low cost. Nonetheless, this foreign material may cause excessive inflammation, producing a membrane at the interface between the host bone and the cranioplasty device, thus increasing the risk of infection. Lately, the use of miniplate struts has been suggested to improve the performance of acrylic implants.

In the past, surgeons using cranioplasty techniques have relied on the principles of osteoconduction: the auto- or allograft provides the structure that allows the surrounding bone, osteoblasts, and vessels to grow into it. Osteoinduction is a different process, in which osteoblasts do not migrate from surrounding bone but are stimulated and produced in the implant. This production is mediated by bone morphogenetic proteins.

Currently, the use of new materials such as HA-based ceramics, which may induce bone growth into the implant, is becoming increasingly widespread, particularly in maxillofacial and oral surgery. Angiogenesis and osteogenesis were histologically demonstrated in specimens collected 6 and 24 months after implants for
Cranioplasty with osteoinducing material

Bone defects in maxillofacial surgery (unpublished data). Hydroxyapatite is naturally found as a mineral in bone and teeth and can be produced synthetically. It acts as an osteoconductive material and binds easily to bone. Porous HA greatly facilitates the migration of osteoblasts and vessels. The human bone-derived protein gelatin also serves as a “storehouse” of morphogenetic proteins.

The main requirement for bone regrowth is that the implant must be in contact with healthy cancellous bone. In most of our patients, HA appeared to be replaced by new bone, as documented by CT scans, to a much larger extent than previously reported in dental or maxillofacial surgery, and also far beyond our expectations.

To the best of our knowledge, this is the first series of calvarial repairs performed using this material. The sheets of Osprogel were first wetted with saline and then molded and cut with scissors to the approximate shape and curvature. They were inserted into the defect, taking care not to press them but to place their edges in contact with the healthy cancellous bone (Fig. 1 upper). For the first two patients, we used a honeycombed titanium micronet (thickness 0.6 mm) to prevent the HA granules from being washed out and to ensure that the implant would retain the desired curvature (Fig. 1 lower). We achieved the same result in all the following cases by using less expensive titanium mesh, single or double layers. In repairing small defects (<10 cm²), the commercial preparation that includes Osprogel and titanium mesh (Osprotiinantex) is also suitable. However, it does not retain its curvature over time when used in larger defects (Cases 3 and 7). Our worst result was obtained in Case 2. Here, a large round-shaped midline bifrontal defect, caused by metastatic tumor, was repaired by using a rectangular micronet as support for the underlying Osprogel. The follow-up 3-D reconstructed CT scan (Fig. 7) displayed good filling of the defect in the area in which Osprogel had been secured to the micronet. In the area where it had been used alone, however, the Osprogel had fallen into the underlying empty space, and the granules had been washed out.

In all but one case in which a double-layer mesh was used, the results were excellent. A double-layer mesh was used in the woman in Case 11; however, the pterional concavity was not well modeled by the surgeon, resulting in faulty curvature.

It must be emphasized that the role of the net or mesh was either to help retain curvature of the skull or to ensure protection during the repair procedure. Titanium is a well-known material, widely used for cranioplasty. It is a radiolucent, nonferrous metal of low atomic number that allows very clear CT and magnetic resonance images to be obtained. Strength, biocompatibility, and easy handling are other features of this material.

The most important limitation of the material used for this series is that, at present, it needs to be titanium supported. However, the results are impressive and, in our opinion, superior to those we have obtained in the past by using methylmethacrylate. This is due, above all, to the biocompatibility of the materials and to the absence of inflammatory reactions. We believe that further efforts are justified to refine the technique and materials, including laboratory investigations on experimental models, to eliminate the concurrent use of titanium nets or meshes. More-over, the combination of software models and preformed prostheses is expected to improve the technique and yield excellent results in cases in which good cosmetic results are mandatory.

Acknowledgments

The authors express their thanks to Ms. Stefania Saraceni for revising the English text and to Ms. Marzia Piccoli for editing the manuscript. Very special thanks are given to Mr. Eugenio Giglio and Mr. Maurizio Ballarotto for their valuable technical work and help at the CT scan board.

References


Manuscript received March 25, 1997. Accepted in final form March 9, 1998. This paper was presented in part at the poster session, “Technology—Miscellaneous” at the 11th International Congress of Neurological Surgery, Amsterdam, The Netherlands, July 6–11, 1997. Address reprint requests to: Alfredo Pompili, M.D., Division of Neurosurgery, Istituto Regina Elena, Viale Regina Elena 291, 00161 Rome, Italy.