Biomaterials have become an integral component of craniofacial reconstruction. Their increasing ease of use, long “shelf-life,” and safety enables them to be used effectively and play an important role in reducing operating times [1]. The ideal biomaterial is biocompatible with surrounding tissue, radiolucent, easily shaped or molded, strong enough to endure trauma, stable over time, able to maintain volume, and osteoactive [1–5]. There are various biomaterials currently available and specific usages have been characterized well in the literature. This article reviews different biomaterials that can be used in craniofacial reconstruction, including autogenous bone, methyl methacrylate and hard tissue replacement, hydroxyapatite, porous polyethylene, bioactive glass, and de-mineralized bone.

Autogenous bone

The first documented bone autograft was described by Walther in 1821 where he replaced the bone plug after trephination and noted partial healing [6,7]. Full healing of the wound was prevented by subsequent wound suppuration. In 1885, Macewen [8] reported a successful reimplantation of bone pieces into a cranial defect. Other donor sites have been attempted for repairing cranial defects, including the tibia (1889), cranium (1890), fascia (1906), rib (1911), scapula (1912), ilium (1914), and sternum (1915) [6,9–15].

Today, many physicians believe that autogenous bone remains the biomaterial of choice for craniofacial reconstruction. In a series of 73 cranioplasties reconstructed with autogenous bone with no subsequent infection, Wolfe [16] describes the safety and efficacy of autogenous bone graft reconstruction. It has been noted that resorption of autogenous bone graft can be particularly problematic in certain situations, particularly in reconstruction of the malar eminence in patients with Treacher Collins Syndrome, and when bone grafts are placed for augmentation of the chin [1]. However, difficulties may also be encountered with the use of alloplastic materials in these reconstructive situations, as they may result in erosion of the underlying recipient bone.

In experimental studies in which alloplastic implants were removed, it was noted that the underlying recipient bone underwent transformation to a trabecular architecture with decreased bone density [17]. This may be particularly troublesome if an alloplastic implant must be removed following infection or dislodgment, which would result in greater deformity than was initially present. Although some cite the morbidity involved in harvesting cranial bone, it has been documented that with proper training, plastic surgeons can harvest bone grafts easily and comfortably with minimal morbidity [18].

Cranial bone, iliac bone, ribs, and tibia are the most commonly used bone graft donor sites. In certain clinical circumstances, vascularized bone grafts, such as free fibula or free iliac bone, provide distinct advantages over nonvascularized bone grafts. The clinical setting in which vascularized bone grafts have been used most frequently has been for reconstruction of large segments of the mandible. However, vascularized bone grafts require greater amounts of time and skill and are not necessary in most clinical circumstances. Disadvantages of the autogenous bone grafts that are not seen with other biomaterials are the potential morbidity of the donor site and the additional time required to harvest the graft. In addition, autogenous bone graft often undergoes signi-
significant resorption when used for augmentation of the facial skeleton, rendering it unreliable for long-term augmentation.

**Methyl methacrylate**

Methyl methacrylate is an acrylic-based resin that has found many uses in today’s craniofacial reconstruction. Its use in craniofacial reconstruction was first described during the early stages of World War II when there was a growing interest in acrylic resins [6,19]. Its first reported human use was in 1940 by Zander [6,7]. Unlike autogenous bone, which can have variable resorption of between 25% and 40% of the bone graft over time, methyl methacrylate is resistant to absorption [20]. A meta-analysis reviewing 45 studies of routine cranioplasty with methyl methacrylate showed an infection rate of approximately 5%. In a series of 42 cranioplasties by Manson and colleagues [20], isolated cranioplasties showed no infection. However, patients who had undergone simultaneous reconstruction of the cranial vault, the orbital walls, and nose had an infection rate of 23%. All patients who had infection with methyl methacrylate had experienced a previous infection, indicating that a history of infection in the region is a significant risk factor for subsequent infection. Methyl methacrylate was found to be stronger than the adjacent skull bone to compression and torsion testing. In addition, they found that cranial orbital reconstruction adjacent to previously infected ethmoidal sinuses were more directly related to infection than was the material used for reconstruction. The authors cited an additional advantage of methyl methacrylate to be low cost, predictable resultant shape, ready availability, and suitability for complex defects.. The authors concluded that methyl methacrylate is the cranioplasty material of choice in adults with good soft tissue quality who have not had previous infection. However, criticism of methyl methacrylate is that it is an inert and fixed substance that will not adapt to the changing craniofacial skeleton. This is particularly important if one is considering skeletal reconstruction in a growing child. An additional disadvantage of methyl methacrylate is that there is no bone incorporation or ingrowth, making it susceptible to infection or dislodgement through the duration of the reconstruction.

**Hard Tissue Replacement**

Hard Tissue Replacement (HTR; Walter Lorenz Surgical, Jacksonville, FL) is another polymeric composite consisting of a polymethylmethacrylate substrate sintered with polyhydroxyethyl and a calcium hydroxide coating shielding the polymethylmethacrylate from the external surface. It has a 20% to 30% material porosity (150 to 350 microns), holds a negative surface charge (−8 to −15 mV) and has substantial compressive strength (50,000 lb/in² in particulate form and 5000 lb/ in² in molded form) [21]. Its porosity promotes vascular ingrowth. The hydrophilic surface diminishes bacterial adhesion following preimplantation soaking in antibiotic solution. In addition, the negative surface charge further deters adhesion of bacteria to the implant.

The implant can be prefabricated in custom shapes for facial augmentation. When placed in a subperiosteal position, the implants can be adequately held in place by closure of the overlying pericranium. Guyuron has extensive experience in the use of these implants for malar augmentation, chin augmentation, and augmentation of the temporal regions for correction of the “hourglass” facial deformity [22]. The hourglass facial deformity may occur following temporal atrophy following elevation of the temporalis muscle and as the result of bilateral irradiation of the orbits and anterior cranial base during infancy. Custom implants of HTR polymer can be placed in the temporal region for augmentation. A recent report of four such cases demonstrates the successful correction of the hourglass deformity using this technique [22].

Eppley et al [23] described the successful use of computer-generated HTR for cranial reconstruction in fourteen patients who had large (greater than 150 cm²) preexisting defects of the cranium or cranio-orbital region. They used a preoperative high-resolution 3D CT scan to reconstruct the defect. The manufacturer then used this reconstruction to fabricate the HTR implant with less than 1 mm accuracy. At the time of surgery the implant was secured using metal or resorbable fixation. To minimize the risk of infection in cases where the frontal sinus was in proximity to the implant, the sinus was cranialized, covered with a pericranial flap, or obliterated with hydroxyapatite cement paste. The authors reported no postoperative complications or infections and good reconstructive results. This technique simplifies the reconstruction and reduces operative time by eliminating the need to harvest bone graft and to shape the graft intraoperatively [23].

**Hydroxyapatite**

Hydroxyapatite is the primary mineral component of teeth and bone and comprises up to 70% of the
calcified skeleton. It is a calcium phosphate compound arranged in a hexagonal structure and can be produced synthetically as a ceramic by a process called sintering. It is one of the more common forms of calcium phosphate in clinical use. It has excellent tissue compatibility and the advantage of being osteoinductive, osteoconductive, and readily available. Osteoactivity is the ability of the biomaterial to be replaced with bone formation either through osteoinduction or osteoconduction. Hydroxyapatite is a porous material that promotes osteointegration, or the formation of a bond between the implant and adjacent bone. In addition, it is biocompatible and does not produce a chronic inflammatory response [4,24–26].

Hydroxyapatites have traditionally been available in ceramic forms, which are nonresorbable. Hydroxyapatite has also been made available for clinical use in cement paste form since 1992 [3] and in granular form since 1993 [27]. Hydroxyapatite cement paste is formed when tetracalcium phosphate and dicalcium phosphate react in the presence of water to form hydroxyapatite [28]. The two calcium salts undergo an isothermic reaction to form a dense paste that has been claimed to be resorbable over time. Mixing the powder in a sodium phosphate buffer solution can accelerate the setting time of the cement [29]. Initial studies by Constatino [3] and associates in feline cranial defects showed that new bone comprised 77% of the tissue replacing the hydroxyapatite cement 1 year after implantation. The authors have also used this material for obliteration and reconstruction of the cat frontal sinus [30] and for reconstructing a fronto-orbital craniotomy in 12-week-old kittens [31]. Whereas there were some subtle growth differences in kittens reconstructed with the cement paste, excellent contour reconstruction was achieved in all animals [31].

A major advantage of the cement paste over the ceramic form of hydroxyapatite is that it can be easily shaped during surgery [32]. The cement paste form of hydroxyapatite has been used extensively for adult craniofacial reconstruction [33,34]. It has also been used in growing children for cranioplasty and for treatment of temporal hollowing following cranial vault remodeling [35]. Friedman and associates [36] have reviewed a number of clinical applications in which they report excellent results using hydroxyapatite cement paste for craniofacial reconstruction.

A large animal sheep model, however, has not demonstrated significant bone ingrowth into hydroxyapatite cement paste cranioplasty when studied over a 1-year period. In this study, Gosain et al [37] investigated craniofacial augmentation using autogenous bone graft versus nonceramic (cement) and ceramic forms of hydroxyapatite. The authors found that cranial bone grafts were not reliable for long-term augmentation, with complete bone graft resorption observed in each of the facial recipient sites. The volume maintenance of the hydroxyapatite composites was much more predictable, with no significant resorption noted in either the cement paste or ceramic forms of hydroxyapatite over 1 year. Bone replacement was greater within the ceramic forms than within the cement paste forms of hydroxyapatite. Increased bone replacement within the center of the ceramic implants was attributed to the porosity of the implants. The cement paste implants used for facial augmentation demonstrated a lip of bone, which surrounded the implants and blended into the adjacent facial bone cortex. However, there was little or no bone within the center of the implants. A similar result was observed in a clinical example of a 3-year follow-up on the use of hydroxyapatite cement as an onlay to an area of frontal bone depression in a 4-year-old girl. Biopsy demonstrated that the implant had minimal bone ingrowth, with significant bone noted only at the periphery of the implant [5]. The hydroxyapatite cement paste remained largely nonresorbed, with minimal bone entering the center of the implant material. Clinical experience to date indicates that although hydroxyapatite cement paste appears to provide an excellent biomaterial for cranial vault reconstruction, to date there is no histologic evidence of significant bone ingrowth or resorption of this biomaterial in humans.

In a series of 56 pediatric and five adult patients, Burstine et al [38] showed excellent results over a mean follow-up of 20 months using hydroxyapatite cement paste, without any adverse affect on orbito-cranial growth with. They reported seven (11%) complications, including seroma formation (n = 4), visible irregularities requiring reoperation (n = 2), and a case in which a drain placed in contact with the hydroxyapatite became fixed within the cement and required operative removal. The authors reported no visible loss of implant volume or gross resorption of the implant, no visible thinning of the overlying skin or visible edges at the implant-bony interface, and no implant migration. Intraoperative curing time was reported to be 20 minutes, compared with 5 days following reconstruction with hydroxyapatite granules. Curing time for the cement paste was further reduced to 10 minutes when sterile water with monosodium phosphate solution was mixed with dry cement [38].

Byrd and colleagues [39] reported their use of porous granular hydroxyapatite for craniofacial augmentation (Interpore 200, Cross International, Irvine,
The granules are mixed intraoperatively with blood to give them an adhesive consistency and held in place with clot formation. The authors originally reported the results for facial augmentation in 43 patients. Twenty-six patients were followed for over a year, and all achieved excellent results. Areas of the craniofacial skeleton that benefited from augmentation with hydroxyapatite included the skull, zygomatic-maxillary, lateral mandible, perialar, periorbital, and temporal regions. The authors felt that their technique achieved a predictable result with minimal migration of the granules. No cases of infection were reported, and only two patients required minor revisions. Interpore 200 is a nonabsorbable form of hydroxyapatite, and no clinical evidence of resorption was noted. Byrd and Hobar [39] updated this experience in 1996, reporting on more than 200 patients operated over an 8-year period.

Holmes [40] reviewed his experience in experimental and clinical applications of ceramic forms of hydroxyapatite. He initially demonstrated bone regeneration within an implanted hydroxyapatite replica of a coral skeletal structure placed within mandibular defects in dogs. By 6 months postimplantation, 88% of the implant areas were filled with the regenerated bone. This regenerated bone was a woven type at 2 months and changed to a lamellar type by 6 months. The coralline hydroxyapatite implants were biodegradable, and 29% resorption of the implants was noted in two implanted defects examined at 12 months. Holmes and colleagues subsequently studied porous hydroxyapatite ceramics as bone graft substitutes. Dog models were established to use this material in alveolar ridge augmentation [41] and in cranial reconstruction [42]. In both models bone ingrowth extended across the entire extent of the implant. Bone growth was noted throughout the pores of the implant, and the bone appeared mature and well vascularized. In contrast, little bone ingrowth was seen in reconstruction of similar defects using autogenous bone grafts. One-and-a-half years postoperatively the implant specimens consisted of 45% bone in the alveolar ridge, and 40% bone in the cranial defects. These studies confirmed the applicability of nonresorbable porous form of hydroxyapatite as a bone graft substitute material for facial reconstruction. Holmes and colleagues [43] also found that bone induction within porous hydroxyapatite could be accelerated through the addition of an osteogenic protein. The authors found that there was significantly more bone ingrowth within implants treated with osteoinductive protein. By 3 months postimplantation, the new bone within the implants treated with osteoinductive protein was predominantly lamellar, whereas that within untreated implants was predominantly woven. Thereafter, increasing amounts of lamellar bone gradually appeared in the untreated implants. In another study, Holmes and colleagues [44] found that demineralized bone matrix filled within coralline hydroxyapatite resulted in enhanced new bone formation and an increase in the rate of healing of cranial defects within rabbits compared with defects reconstructed with coralline hydroxyapatite alone [44]. The authors also emphasized the role of backscatter electron microscopy for the analysis of bone ingrowth within hydroxyapatite implants, stressing improved accuracy of the technique over conventional histology.

### Porous polyethylene (Medpor)

Porous polyethylene (Medpor; Porex Surgical, College Park, GA) is commonly used for facial augmentation and to restore continuity to craniofacial skeletal defects. Polyethylene resins are straight-chain aliphatic hydrocarbons that are inert and promote little tissue reactivity. Unlike bone grafts, porous polyethylene shows little evidence of implant degradation. Like HTR, this is a porous (100 to 250 μm) biomaterial that permits bone and soft tissue ingrowth when placed on facial skeletal defects. There are reports of sufficient soft tissue ingrowth with sufficient vascularity to allow skin grafts to be placed directly over the implant [45].

Dougherty and Wellisz [46] compared Medpor to silicone implants for reconstruction of orbital floor defects using rabbits. The authors created 8-mm defects bilaterally in the maxillary sinuses that included bone and mucosa. They reconstructed one side with Medpor and the other with silicone. One surface of the implant was exposed to the open maxillary sinus. They studied the implant sites for 5 months postimplantation through serial sacrifice of animals. The porous polyethylene implants showed vascular and soft tissue ingrowth in the pores in the first week and bone ingrowth by 3 weeks. The use of Medpor implants resulted in more rapid closure of the obturated defects with soft tissue and bone fixation, whereas the silicone implants developed a fibrous tissue capsule without fixation to the adjacent skeleton.

In a recent review, Yaremchuk [47] described his 11-year clinical experience in which 370 porous polyethylene implants were placed in 162 patients. The implants were used in various clinical scenarios, including acquired tumor-related and congenital defects, aesthetic procedures, secondary posttraumatic reconstruction, and orbital wall reconstruction following acute trauma. The distribution of implants
Bioactive glass particulate (Nova Bone)

Bioactive materials are defined as those that elicit a specific biological response at the interface of the material that results in the formation of a bond between the tissue and the material [48]. This minimizes the formation of a fibrous capsule around the implant. Bioactive glasses have been shown to form a surface apatite layer in vivo that enhances the formation and attachment of bone. Nova Bone (Porex Surgical, College Park, GA) is a synthetic bioactive glass particulate consisting of 45% silica dioxide, 45% sodium oxide, 5% calcium, and 5% phosphate, which is believed to be bioactive toward the production of new bone within the biomaterial. It was first introduced in 1971 by Hench and colleagues [49]. The bioactivity in glass particulates begins when they are mixed with saline or blood [50]. The silicon-oxygen bonds are broken to release silicic acid, which condenses to form a negatively charged gel at the surface of the particles. This gel serves to hold the glass particles in a cohesive mass. Within several hours, calcium phosphate is produced within the gel to crystallize into a new surface apatite layer. Bioactivity is initiated within this surface layer when collagen, mucopolysaccharides, and glycoproteins from surrounding bone are incorporated into the apatite layer to mediate a direct chemical bond with the host bone, facilitating early bone formation at the biomaterial-bone interface. The growing apatite layer further serves to stimulate osteogenic progenitor cells to produce TGF-β by release of silicon from the glass surface. TGF-β serves as an osteogenic cytokine, leading to a rapid proliferation of bone in contact with the glass particles [51].

Most biomaterials, including bioactive glasses, are osteoconductive, serving as a biocompatible interface along which bone cells migrate. In addition, bioactive glasses are osteoinductive, which is defined as the process whereby a bioactive surface is colonized by osteogenic stem cells from the defect environment as a result of surgical intervention [52]. Bioglass particles range in size from 90 to 710 microns. Resorption of bioglass particles of 150 microns or less occurs as silica is released within the apatite gel layer. Larger bioglass particles are incorporated in the growing bone matrix and eventually broken down by osteoclasts. As a result of their bioactive properties, the interfacial bonding strength of most bioactive materials is equivalent to or greater than that of bone [53]. Unlike nonbioactive alloplasts, failure under mechanical stress does not occur at the bone interface, but rather occurs in the host bone or within the biomaterial. This absence of failure at the bone interface is a unique and defining feature of bioactive materials [54].

We have recently reviewed the role of bioactive glass in craniomaxillofacial reconstruction [55]. Most clinical experience with bioactive glass has focused on the repair of periodontal and alveolar ridge defects [56–60]. However, there are reported uses with varying degrees of success for reconstruction of other areas of the head and neck. Bioactive glass has been used for the repair of orbital floor fractures with maintenance of globe position in studies that have followed patients for up to 1 year [61,62]. A composite of bioactive glass (80% to 90%) and autogenous iliac bone (10% to 20%) resulted in accelerated bone regeneration healing time compared with bone graft alone for elevation of the floor of the maxillary sinus floor [63]. Cordioli et al [64] have used these principles in 27 patients who would otherwise have insufficient maxillary bone for implant placement. They achieved simultaneous bone augmentation of the maxillary sinus floor and placement of titanium implants for dental restoration.

The authors have reported on bioactive glass particles (Nova Bone, Porex Surgical) mixed with autogenous bone particles harvested from cranial burr holes as an adjunct to cranial vault reconstruction [5,55]. This was done to reconstruct full-thickness defects in two patients 5 years and older, when minimal spontaneous bone regeneration was expected. On follow-up CT scan, these patients demonstrated conversion of most of the reconstructed defect to bone density within 6 months. In a 4-year follow-up, both patients have had stable reconstruction with no need for reoperation or biopsy of the biomaterial.

Some complications of bioactive glass have been reported when used as a ceramic implant for contour...
restoration of the facial skeleton. Duskova et al [65] have found extrusion rates in 20% of cases, requiring reoperation with implant size reduction or soft tissue coverage.

**Demineralized bone**

Demineralized bone is another alternative for reconstruction of the craniofacial skeleton. Salyer and associates have studied the use of cortical demineralized perforated bone for reconstructions (produced by Pacific Coast Tissue Bank) in animal models and in the clinical setting [66–70]. One study evaluated the use of demineralized bone for reconstruction of calvarial defects in beagles [68]. The authors verified that the demineralized bone implants were well-accepted within calvarial defects with little tissue reaction and remarkably little osteoclastic activity. There was evidence of new bone growth by 8 and 12 weeks following implantation of the demineralized bone. Bone growth tended to occur more frequently on the dural aspect of the calvaria and formed a continuum with the implant. Fragmentation of the implanted material was observed in the presence of new bone formation by 12 weeks postoperatively. This fragmentation occurred in the absence of multinucleated cells, and the authors hypothesized that a hydrolytic enzyme was responsible for the degradation. No marked differences were found between demineralized bone grafts of calvarial origin and those of tibial origin.

Salyer and colleagues [67] published their first clinical report on the use of demineralized bone in 1992. They have since reported on a number of innovative clinical applications of demineralized bone, including that of skull reconstruction in Siamese twins who had previously been separated from union at the skull vertex [69]. The implants were processed with microperforations, which are believed to be centers of new bone formation. The demineralized bone has been biopsied 4 years following initial reconstruction in one of the Siamese twins. Most of the specimen represented large areas of nonvital bone, lacking living bone cells. In several areas there appeared to be fragmentation of the autogenous bone matrix. However, active resorption was not observed, osteoclasts were not seen, and there was no inflammatory or fibrotic reaction in the adjacent soft tissues. Remodeling was seen in several areas contiguous with nonvital bone. The authors also stressed the technical advantages in using cortical demineralized perforated bone—the material is pliable and can be shaped intraoperatively to suit the specific cranio-facial defect. The authors stress that this material affords the advantage of nearly limitless supply without the risk of donor harvesting, which is particularly useful in the pediatric population.

Recently, demineralized bone paste has become commercially available (Synthes Maxillofacial, Paoli, PA). An advantage of this biomaterial is that it is porous and is easily molded to fit the defect. The material does not harden but remains as a paste intended to serve as a matrix for bone ingrowth. It is therefore well-suited to reconstruct defects in the craniofacial skeleton. However, demineralized bone paste is not suited to reconstruct load-bearing regions in the skeleton because it will not harden to bear significant load until significant bone ingrowth is complete.

**Summary**

This review highlights some of the recent developments in biomaterials that are suited to reconstruction of the craniofacial skeleton. Although there is no ideal biomaterial, numerous alternatives are available to practicing surgeons that provide attractive alternatives to autogenous bone graft in the appropriate clinical settings. Biomaterials are a particularly well-suited for skeletal augmentation, as autogenous bone can often undergo unpredictable resorption in these applications. Although all of the biomaterials discussed in this article seem to maintain their volume over time, porosity of the biomaterial may be a significant factor in determining bone ingrowth into the implant. Methyl methacrylate is nonporous, and no bone ingrowth is expected. Cement paste implants tend to contain micropores, and experimental and clinical evidence indicates that there is less long-term bone ingrowth into these biomaterials than in implants with macroporous architecture. Biomaterials presently reviewed that have a macroporous architecture and have demonstrated bone ingrowth in clinical or experimental studies include ceramic and granular forms of hydroxyapatite, Hard Tissue Replacement (HTR) polymer, porous polyethylene (Medpor), bioactive glasses (Nova Bone), and demineralized bone paste. Prefabricated biomaterials and those that set as a cement are not designed to change dimension over time and are therefore best-suited for cranial vault reconstruction after completion of skull growth [71].

Rubin and Yaremchuk [72] conducted an exhaustive review of the complications and toxicities of implantable biomaterials used in facial surgery. They reviewed nearly 200 clinical studies reporting series of patients with implantable biomaterials in the face. Polymer and ceramic materials in the face had an
overall infection rate of 3% and an exposure/extrusion rate of 1.2%; 4.6% of implants were removed because of implant-related complications. The authors concluded that it is difficult to attribute many of the complications solely to the implant material itself, and that there is much overlap between surgical technique, host response, and potential toxicity of the implant. The authors also noted that the biocompatibility of a material can vary depending on the conditions under which the implant is placed. Proplast had been used for implants in the malar, chin, nasal, and orbital floor regions with acceptable complication rates. However, when it was used as an interpositional disk implant in the temporomandibular joint, complication rates were significantly higher. Nearly all of the Proplast implants fractured over time under the load of the temporomandibular joint, and particulate fragments of Proplast would elicit a vigorous foreign body reaction and contribute to erosion of the joint. Therefore, alloplastic implants used for facial augmentation may have a different outcome when placed in positions subject to stress loading. Although current implant materials have favorable complication rates in most craniofacial applications, a biomaterial that fairs well in one clinical circumstance may not be ideal for all applications in facial reconstructive surgery.

References

[29] Costantino PD, Friedman CD, Jones K, Chow LC,


[59] Thronson RR, Sexton SB. Grafting mandibular third molar extraction sites: a comparison of bioactive glass


