

The Effect of New Technologies on Plastic Surgery

Thomas A. Mustoe, MD; Hongshik Han, MD

Plastic surgery has always been a technique- and technology-driven surgical discipline, given that there is no regional anatomic focus. There has been a remarkable evolution in technique over the last 25 years with an increased understanding of anatomy leading to a whole host of new and more reliable flaps, which has transformed reconstructive surgery, breast reconstruction being one notable example. The development and maturation of microsurgery has led to the full fruition of anatomic principles. With better understanding of blood supply to the skin, fascia, muscle, and bone, many traditional reconstructive procedures are constantly being superseded by the new, ingenious use of various tissue flaps. Advances in technology will accomplish another transformation of the specialty, notably the recent advances in tissue engineering, the potential of gene therapy, new alloplastic materials, and computer-assisted imaging technology. It would be impossible to address all of the recent advances in this rapidly expanding field of surgery in a short article. We have selected a few topics that we thought would be the most interesting to all surgeons to give a wide view of a variety of challenges addressed by the modern plastic surgeon. Major advances in surgery often come from cross-fertilization between specialties, and plastic surgeons have frequently been involved in this process.

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GROWTH FACTORS IN WOUND HEALING

Wound healing is no longer considered to consist of 3 distinctive phases (inflammation, proliferation, and remodeling). It is now recognized that the process is a dynamic, overlapping sequence of coordinated cellular processes involving multiple cell types with a highly orchestrated complex soup of growth factors controlling the processes of cell migration, proliferation, matrix synthesis and breakdown, inflammation, and the resolution of the process with programmed cell death. The potential for therapeutic interventions arose from the observation that in many chronic wounds there was a deficiency of growth factors, and in animal models, even when healing was progressing in normal fashion, it could potentially be accelerated.

Over the last 12 years, the potential for therapeutic interventions in wound healing have evolved from basic surgical principles to the recognition that a dozen or more growth factors, made available by recombinant gene technology, can promote wound healing in animal models. New growth factors are being isolated, cloned, and tested each year with no slowing in pace. Nevertheless, the tremendous excitement over the potential for therapeutic intervention in wound healing that existed 5 years ago has been tempered by the failure of several large studies to see a significant therapeutic effect in the treatment of chronic wounds. Acute surgical wounds have tremendous potential for intervention, but owing to the low rate of surgical complications and the consequent need for very large numbers of patients to show a therapeutic effect, this area has not yet been looked at with any notable attention by pharmaceutical companies.

Currently, although multiple growth factors have been tested clinically, the only

From the Department of Plastic and Reconstructive Surgery, Northwestern University Medical School, Chicago, Ill.

growth factor approved by the Food and Drug Administration, Washington, DC, for clinical use is recombinant human platelet-derived growth factor-BB (rhPDGF-BB). Testing of PDGF occurred over a 7-year period from the first phase 1/2 studies^{1,2} in pressure sores to a substantive trial³ in diabetic foot ulcers, culminating in 3 pivotal trials involving more than 1000 patients. In patients with diabetic ulcers, a consistent 10% improvement over controls in the complete healing of diabetic ulcers was demonstrated in double-blind prospective studies.⁴ Marketed as 0.01% Regranex gel (Ortho-McNeil Inc, Raritan, NJ) (becaplermin), PDGF is currently only approved for the indication of diabetic ulcers, although other studies are ongoing. The variability in healing and the multiple factors that impair healing (ischemia, bacteria, aging, and suboptimal nutrition) undoubtedly explain much of the difficulty in demonstrating a therapeutic effect with growth factors.

Nevertheless, as experience has been gained in conducting prospective randomized trials in wound healing and new formulations and growth factors are being tested, there exist some other promising growth factors in clinical trials and several others in animal studies.⁵⁻⁸ Wound healing has evolved from a scientific backwater, in which sound surgical principles were the main approach, to a certainty that other products with demonstrated clinical efficacy that is superior to basic optimal wound care will follow PDGF.

IMPLANT MATERIALS IN PLASTIC SURGERY

The use of alloplastic materials to alter soft tissue or bony appearance has undergone tremendous advances. The ideal implant materials must meet several stringent criteria. They must be nonallergenic, non-foreign body-reaction forming, noncarcinogenic, resistant to stress and strain, and sterilizable. They must also match the biomechanical characteristics of the tissue they are replacing. No such material that perfectly satisfies all of the criteria yet exists, although the current advances in material science continually improve implant properties. Implants have been in the armamentarium of plastic surgery for thousands of years. However, it was not until the 1940s that advances in material science allowed for the development of several implantable materials that led to widespread implant use. Continued advances in biomaterials have led to their increased use, both for hard and soft tissue.

Bony fixation has traditionally been accomplished with metal plates and screws. With the recognition that the same principle could be applied in the hand and facial skeleton with miniplates and microplates, they became useful for a much broader range of indications. Currently, the best available metal plating systems for these uses are made of titanium alloy and vitallium. Titanium alloy is composed of titanium, aluminum, and vanadium, while more rigid vitallium is an alloy of cobalt and chromium. Both have very low bioreactivity and corrosivity, and both have no magnetic properties, making the systems safe when using magnetic resonance imaging. Titanium, in particular, has minimum radiographic scatter artifact, allowing for postoperative computed tomog-

raphy (CT) with minimal distortion of surrounding tissues. Light weight and ease of bending has allowed their widespread use. In complex facial fractures, more than 10 microplates might be used. Although these small plates infrequently require removal, the recent introduction of biodegradable polyesters as plating material conveniently solves the potential problems of foreign body reaction, implant extrusion, delayed infection, and altered bone remodeling on pediatric facial skeleton. The 2 most commonly used absorbable plate systems are composed of polyglycolic acid and poly-L-lactic acid, both of which become hydrolyzed and degraded in the body at physiological pH levels. The absorbable minifixation system has tensile strength equal to titanium and holds the craniofacial bones together as strongly as those made of titanium, resulting in the same rate of consolidation.⁹ Poly-L-lactic acid miniscrews offer fixation stability for 6 months and polyglycolic acid for 2 months.¹⁰ The new generations of bioabsorbable miniplating systems (Bionx Implants Inc, Blue Bell, Pa) are reinforced with copolymer, making it possible to bend and reshape the plates to fit the skeletal contour. The follow-up study of patients who underwent mandibular osteotomy fixed with the absorbable screws demonstrated normal clinical recovery and radiological osteotomy healing after 2 years.¹¹

The advance in biomaterial technology has direct implications for tissue engineering, which uses an alloplastic biodegradable scaffold to grow human cells. Polyglycolic acid and poly-L-lactic acid have been used to create absorbable scaffolds for tissue-engineered cartilage and bone.¹² The recent clinical application of the absorbable vascular stent made of similar materials shows a high patency rate comparable to the microsuturing technique and potentially offers a promising alternative to the conventional small-vessel anastomosis.¹³

Hydroxyapatite has replaced calcium phosphate and methyl methacrylate as the new bone substitute material in recent years. The material properties of hydroxyapatite, chemical composition $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$, are similar to those of bone and teeth, and its strength is a function of its pore size and degree of pore continuity.¹⁴ The newly developed hydroxyapatite synthesis technology enables the material scientists to determine the implant pore size and the degree of pore continuity.¹⁵ By controlling these parameters, it is possible to manufacture the hydroxyapatite with nearly identical biomechanical characteristics as human cancellous bone.^{14,16}

Hydroxyapatite is commercially available in 2 forms. As a plate or block, it can be sculpted into the desired shape in the operating room; as granules, it is mixed with Avitene (Davol Inc, Cranston, RI) (microfibrillar collagen hemostat) and autologous blood to form a paste, which then can be contoured as needed. Animal studies have shown that hydroxyapatite can reach full integration with living cortical bone.¹⁷ It provides the osteoconductive extracellular matrix environment in which the native osteocytes can migrate and, eventually, replace these synthetic scaffolds. The highly interconnected porosity of hydroxyapatite allows for easy ingrowth of surrounding tissue, resulting in new bone formation and implant incorporation. The use of hydroxyapatite ceramic plates in place of autologous bone grafting has been highly suc-

successful in craniofacial surgery, with no foreign body reaction and an infection rate no higher than in a study¹⁸ using grafted bone while saving considerable time and potential complications of bone grafting. Follow-up post-operative CT scans have documented the complete bony substitution of the hydroxyapatite granules used in pediatric cranioplasty after 2 years.¹⁹

The recent application of cyanoacrylates to substitute suture to close small skin wounds may have opened the door for myriad other potential tissue adhesives. There are several cyanoacrylate derivatives in clinical use, but no measurable differences have been found in their clinical efficacy.²⁰ The most widely available cyanoacrylate in clinical use is the Food and Drug Administration–approved tissue glue octylcyanoacrylate (Dermabond; Ethicon Inc, Somerville, NJ). Despite the initial limitations of its use on the low-tension wound alone, with the appropriate use of splints to restrict the movement of the affected area, cyanoacrylates have been successfully employed on high-tension skin lacerations.²¹ They form a strong, permanent bond in tissues, particularly in skin and tendon, and have also been used in bone, cartilage, fascia, retina, and cornea. One study²² concludes that the cosmetic outcome of small traumatic wounds closed with cyanoacrylate is superior to suture-closed wounds at 1-year follow-up with high patient satisfaction. Currently, its most widespread use in plastic surgery has been for the closure of pediatric lacerations in which suture removal can be problematic. Surgically, its indications are still evolving. It clearly works, but the need for meticulous closure of the dermal layers to avoid deeper penetration has somewhat limited the potential for saving time. Nevertheless, it seems clear that this area will evolve, and sutureless wound closure will become more common in the future.

TISSUE ENGINEERING

The recent advances in cell biology and molecular physiology contribute to the parallel advances in tissue engineering. With the better understanding of the fundamental cellular response to external stimuli and the tissue culture technique, medical scientists are able to manipulate the behavior of cell lines in vitro, and wound care is one of the first fields to recognize the benefit of tissue engineering. Although this area is being covered by other authors,²³ it is important to discuss specific indications in wound healing and burn therapy. It has been recognized that a functional bilayer structure of both dermis and epidermis is required for a permanent skin substitute, and the newer generations of tissue-engineered synthetic skin are composed of such a construct.

Tissue-engineered skin has had several developmental pathways, but currently the bilayer structure is essentially insoluble dermal extracellular matrix components populated with cultured epidermal cells. The extracellular matrix is composed of fibroblast-embedded collagen gel interspersed with glycosaminoglycan and hyaluronic acid.²⁴ The recent success in adding residential Langerhans cells to the synthetic skin may potentially lead to the development of synthetic skin able to fight off infections.²⁵ Ultimately, the tissue-engineered skin

may contain all of the necessary cellular components to modulate rapid healing with minimal scarring in a construct structurally equivalent to human extracellular matrix and retain all of the characteristics of natural skin.

Coverage of open wounds is one of the fundamental problems plastic surgeons face. For large burns in which the traditional split-thickness skin graft is not available, topical antibiotic dressings and porcine skin have been used extensively. However, the use of xenograft was limited as a temporizing measure owing to intense foreign body reaction and eventual rejection, accompanied by a high rate of graft infection. The new generations of synthetic skin equivalents have been shown to be far superior, with a considerable reduction in the partial-thickness burn healing rate and hospitalization in a clinical trial.²⁶

In the application of chronic wounds, the first Food and Drug Administration–approved skin equivalent came into clinical use in 1998 for the indication of venous ulcers (Apligraf; Novartis, East Hanover, NJ). Apligraf, like other skin equivalents, has a bilayered structure with live keratinocytes on an acellular dermal matrix,²⁷ which was shown to enhance the healing of venous ulcers present for longer than 1 year in a pivotal trial²⁸ involving about 200 patients. Integra (Integra LifeScience, Plainsboro, NJ) is another commercially available bioengineered skin substitute introduced this year. It is made of reconstituted collagen and danaparoid sodium (chondroitin sulfate) backed by a polymer layer and used as a biological dressing for the coverage of large burn wounds.

An exciting future potential for tissue engineering is in the area of cartilage. Its absence of an intrinsic blood supply makes it the ideal grafting material. Using the basic approach of seeding living cells onto a biomaterial synthetic matrix, ear cartilage frameworks seeded with human chondrocytes have been successfully implanted in athymic mice, which in turn grew human elastic cartilage.²⁹ The future for tissue engineering in plastic surgery for other soft tissue forms, such as breast reconstruction with fat cells, holds tremendous promise and excitement for the future.

MINIMALLY INVASIVE ENDOSCOPIC APPROACHES IN PLASTIC SURGERY

The use of endoscopy has been widely adapted from gynecology and orthopedic surgery to abdominal and thoracic surgery over the last decade. In plastic surgery, which does not involve body cavities, the advantages of minimally invasive procedures are less in terms of decreasing morbidity, but nevertheless are potentially still substantial. In addition, there is a necessity to create an optical cavity in soft tissue dissection (rather than working in a preexisting space, such as the abdominal, pleural, or joint cavity), and this has necessitated the development of endoscopes that also hold tissues apart. Since then, the techniques of limited-incision surgery have been widely adapted, with the endoscope frequently serving as an assist or adjunct, but nevertheless an important one. It is worthwhile discussing the areas in which minimally invasive endoscopic surgery has found its broadest applications in plastic surgery.

Nowhere are the benefits of endoscopic surgery more apparent than in the selected cosmetic procedures of the face, particularly the browlift. The classic forehead rejuvenation with coronal incision has been largely supplanted by the endoscopic browlift with considerable reduction of incision scars, reduction in postoperative scalp sensory changes, and faster recovery. The procedure has also been advanced by new fixation techniques such as bony anchors that allow soft tissues to be anchored and elevated to fixed bony points with subsequent skin re-draping without the need for skin excision. It has also been applied to aid the subperiosteal tissue dissections in the face-lift.³⁰

Another plastic surgery procedure in which endoscopic surgery approaches widespread use is in the carpal tunnel approach, which avoids a scar across the proximal palm. There has been a notable shortening of the postoperative recovery owing to the reduction in pillar pain, with an associated earlier return to normal activities. Modifications of the limited-incision surgery without the use of the endoscope have also found widespread use.

Other procedures in which the endoscope have had definite applications but have not yet found widespread use have been in the placement of tissue expanders and breast implants. The advantages of hiding incisions and still allowing optimal visualization of dissection planes have been substantial in some surgeons' hands. A particularly exciting use has been in craniofacial surgery for the release of craniosynostosis, pioneered by F. Vicari, MD (oral communication, April 17, 1997). There are multiple other procedures in which the advantages of limited incisions have some applications that are still not widely employed: elevation of flaps, nerve dissections, and the elevation of omental flaps. The basic limitations are difficulties in maintaining an adequate optical cavity (it is hard to keep carbon dioxide insufflation in an artificial cavity, and retractors are not yet optimally designed), as well as the more limited reduction in morbidity. The advantage in some of these cases is limited to the benefit of a shorter incision, which can be offset by the increased length of the procedure and the need for all the additional equipment.

DISTRACTION OSTEOGENESIS

The principles of bony distraction have been borrowed from the orthopedists and applied to craniofacial surgery with increasing success. Since the first application of distraction osteogenesis in craniofacial surgery in 1992,³¹ there has been an explosion of ingenious applications of distraction osteogenesis to treat various craniofacial skeletal deformities. The system consists of the initial corticotomy with placement of gradual distraction apparatus connected to the percutaneous pins through the osteotomized segments. Within the last 5 years, it has gone through several improvements from the initial large, external devices derived from orthopedic distraction equipment to the new, modular internal distraction system with a single percutaneous activation screw.³² Distraction devices can be categorized by their application methods, internal vs external, and the direction and

location of distraction. The external devices are capable of applying distraction forces in multiplanar direction, but they are large and cumbersome with serious compromise in cosmesis during the treatment period. The internal or intraoral devices, while smaller and less discomforting to the patient, can only distract in one direction. Although initially applied only for the lengthening of the mandible, the technique of distraction osteogenesis finds new applications in plastic surgery daily.

The use of distraction osteogenesis in plastic surgery has expanded to all aspects of craniofacial surgery, and several groups are studying the feasibility of bony distraction without the formal osteotomies. Maxillary distraction after an incomplete Le Fort I-osteotomy on patients with cleft lip and palate repair has shown impressive improvements to correct maxillary retrusion.³³ The same technique has been applied to distract hypoplastic maxilla on patients with facial clefts,³⁴ and the postdistraction cephalometric analysis has shown the correction of maxillary hypoplasia with positive midfacial skeletal convexity and dental overjet.³⁵ The distraction technique has also been used to correct the coronal craniosynostosis in rabbits without corticotomy³⁶ and to successfully advance the entire midface in an experimental animal model.³⁷ The newly generated bone from distraction cannot be differentiated from the surrounding, normal bone after 1 year.³⁸ The majority of craniofacial skeletal reconstruction in the pediatric population may someday be replaced by these gradual distraction methods to achieve facial balance and symmetry.

COMPUTER-ASSISTED IMAGING, COMPUTATIONAL MECHANICS, AND PLASTIC SURGERY

The recent advancement in medical computer-assisted imaging technology is transforming the field of plastic surgery, and nowhere is its effect more apparent than in craniofacial surgery. Craniofacial surgery is a newer plastic surgical subspecialty to correct the skeletal deformity by repositioning and reassembling the various elements of the cranium and facial bones. It requires meticulous and precise preoperative determination of osteotomy sites to reposition the bony segment in 3-dimensional space. Even a deviation of a few millimeters could result in an unnatural outcome, making the normal facial balance impossible to obtain. Given these unique and unforgiving requirements, craniofacial surgery is benefiting tremendously from the recent advances in computer-assisted imaging technology.

Craniosynostosis is the premature fusion of skull sutures in early infancy, restricting the normal growth of the brain. If not corrected in infancy, it results in mental retardation, blindness, deformed facial structures, myriad other functional impairments, and death. The corrective surgery involves removing the child's skull and reassembling it to give a normal shape and volume to allow unrestricted growth of the brain and other vital craniofacial structures. The traditional surgical planning involves conducting CT of face and skull. The 2-dimensional CT-derived pixel elements are stacked together to reconstruct a 3-dimensional image. Plastic

surgeons then mentally visualize the osteotomy sites, the shape of the resected bony elements, and the 3-dimensional repositioning and reassembling of the pieces to form the appropriately shaped cranial vault while avoiding damaging the brain, orbits, and other nearby vital craniofacial structures. In reality, however, most decisions are made in the operating room owing to difficulty in accurately assessing the 3-dimensional regional contour on the 2-dimensional films, and the actual osteotomy sites are made based on the surgeon's experience and intuitive sense of normal form. In more complicated cases, laser stereolithography is used to replicate a plastic model of the child's craniofacial skeleton from the CT to better grasp the 3-dimensional nature of the deformity. The model also helps to determine the possible combinations of skull elements that can be transposed to recreate a normal shape of the cranial vault. However, these models are expensive and not reusable, allowing only a single "practice" surgery. The new computer-assisted imaging technology provides the solution.

With the improved computing power providing ever-increasing image resolution, the plastic surgeon can now look at the 3-dimensional CT image of the patient's skull in "cyberspace" and rotate it to view it from any angle. It provides accurate 3-dimensional regional contour and thus helps the surgeon to better understand the nature of the deformity. Several computer graphics research groups (Fakespace, Mountain View, Calif) are currently working on incorporating these images with immersive image display technology in which one can actually pick up the projected image in cyberspace, perform practice osteotomies, and manipulate the resected elements within the computer-generated 3-dimensional space with a tactile feedback mechanism. This can be done repeatedly until an optimal result is obtained. These advances in imaging technology are being applied to produce the patient-specific prefabricated implant. One Japanese group³⁹ has employed the full-scale laser lithographic molding model of a patient's craniofacial skeleton to produce the clay template to fit the calvarial defect. They then produced the thermoplastic implant built from the template and used it to reconstruct complex calvarial contour deformity.

The computer graphics technology is also used to predict the postoperative soft tissue change as a function of changes in underlying skeletal geometry in craniofacial surgery. Borrowing the techniques from forensic anthropology, a graphic program is in development at Northwestern University, Chicago, Ill, to determine the interpolated shape of the facial reconstruction from the 3-dimensional CT data (H. H., P. K. Patel, MD, written communication, June 1, 1999). A mathematical model, predicting the minimal number of osteotomies of any given shape to provide a 3-dimensional skull shape with predefined curvature, has been developed by the same group. Routine cephalometric analysis is now being done using a graphics program instead of manually tracing and measuring the individual distances and angles between various skeletal landmarks (Dentofacial, Toronto, Ontario). Using a similar mathematical algorithm and the normal cephalometric craniofacial growth model, we are also writing a program that can predict the skeletal growth process in children as a function of

time once the corrective operations are completed. The postoperative objective assessment of cleft lip repair has applied computer-assisted imaging technology to quantify the degree of correction and to minimize the interobserver variations.⁴⁰

The recent rise of computing power allows the computational stress mechanics calculations, once only afforded by those who had access to supercomputers, to run on micro-workstations and, for simpler mathematical models, on a high-end desktop computer. Borrowing from the automobile and aerospace industries, plastic surgeons have used the technique of finite element analysis to calculate the stress and strain on craniofacial skeletons under various loading conditions. A patient-specific model has been developed and used to preoperatively simulate the gradual correction of skull deformities using the external distraction device.⁴¹ The finite element simulation of acute loading (trauma) on the craniofacial skeleton predicting a fracture pattern is also being studied at Northwestern University (H. H., P. K. Patel, MD, written communication, June 1, 1999).

Corresponding author: Thomas A. Mustoe, MD, Division of Plastic and Reconstructive Surgery, Department of Surgery, 707 N Fairbanks Ct, Suite 811, Chicago, IL 60611-3042 (e-mail: t-mustoe@nwu.edu).

REFERENCES

1. Robson MC, Phillips LG, Thomason A, Robson L, Pierce GF. Platelet-derived growth factor-BB for the treatment of chronic pressure ulcers. *Lancet*. 1992;339:23-25.
2. Mustoe TA, Cutler NR, Allman RM, et al. A phase II study to evaluate recombinant platelet-derived growth factor-BB in the treatment of stage 3 and 4 pressure ulcers. *Arch Surg*. 1994;129:213-219.
3. Steed D. Clinical evaluation of recombinant human platelet-derived growth factor for the treatment of lower extremity diabetic ulcers. *J Vasc Surg*. 1995;21:71-78.
4. Mustoe TA. Status of growth factors and devices in wound healing. Paper presented at: Wound Healing Society and Wound, Ostomy, Continence Nurses Meeting; June 21, 1999; Minneapolis, Minn.
5. DaCosta RM, Jesus FM, Aniceto C, Mendes M. Randomized, double-blind, placebo-controlled, dose-ranging study of granulocyte-macrophage colony stimulating factor in patients with chronic venous leg ulcers. *Wound Repair Regeneration*. 1991;7:17-25.
6. Galiano RD, Zhao LL, Clemmons DR, Roth SI, Lin X, Mustoe TA. Interaction between the insulin-like growth factor family and the integrin receptor family in tissue repair processes: evidence in a rabbit ear dermal ulcer model. *J Clin Invest*. 1996;98:2462-2468.
7. Robson MC, Steed DL, McPherson JM, Pratt BM. Use of transforming growth factor β_2 (TGF- β_2) in treatment of chronic foot ulcers in diabetic patients. Paper presented at: Joint Meeting of the European Tissue Repair Society; August 24-28, 1999; Bordeaux, France.
8. Xia Y, Zhao Y, Marcus JR, Jiminez P, Mustoe TA. Effect of keratinocyte growth factor-2 (KGF-2) on wound healing in ischemia-impaired wound healing animal model and scar formation. *J Pathol*. In press.
9. Peltoniemi HH, Tulamo RM, Toivonen T, Hallikainen D, Tormala P, Waris T. Biodegradable semi-rigid plate and miniscrew fixation compared with rigid titanium fixation in experimental calvarial osteotomy. *J Neurosurg*. 1999;90:910-917.
10. Peltoniemi HH, Hallikainen D, Toivonen T, Helevirta P, Waris T. SR-PLLA and SR-PGA miniscrews: biodegradation and tissue reactions in the calvarium and dura mater. *J Craniomaxillofac Surg*. 1999;27:42-50.
11. Kallela I, Laine P, Suuronen R, Ranta P, Iizuka T, Lindqvist C. Osteotomy site healing following mandibular sagittal split osteotomy and rigid fixation with polylactide biodegradable screws. *Int J Oral Maxillofac Surg*. 1999;28:166-170.
12. Cao Y, Vacanti CA, Paige KT, Upton J, Vacanti CA. Transplantation of chondrocytes utilizing a polymer-cell construct to reproduce tissue-engineered cartilage in the shape of a human ear. *Plast Reconstr Surg*. 1997;100:297-302.

13. He FC, Wei LP, Lanzetta M, Owen ER. Assessment of tissue blood flow following small artery welding with an intraluminal dissolvable stent. *Microsurgery*. 1999; 19:148-152.
14. Shigeru K, Oku T, Takagi S. Hydraulic property of HA thermal decomposition product and its application as a biomaterial. *J Ceramic Soc Jpn Int Ed*. 1989; 97:96-103.
15. Ono I, Takeshita T, Nakajima N, Ogawa T. Determinations of strength of synthetic HA ceramic implants. *Plast Reconstr Surg*. 1998;102:807-811.
16. Salyer KE, Hall CD. Porous HA as an onlay bone-graft substitute for maxillofacial surgery. *Plast Reconstr Surg*. 1989;84:236-244.
17. Jallot E. Correlation between hydroxyapatite osteointegration and Young's modulus. *Med Eng Phys*. 1998;20:697-701.
18. Ono I, Tateshita T, Satou M, et al. Treatment of large complex cranial bone defects by using hydroxyapatite ceramic implants. *Plast Reconstr Surg*. 1999;104: 339-349.
19. Choi SH, Levy ML, McComb JG. A method of cranioplasty using coralline hydroxyapatite. *Pediatr Neurosurg*. 1998;29:324-327.
20. Osmond MH, Quinn JV, Sutcliffe T, Jarmuske M, Klassen TP. A randomized, clinical trial comparing butyl-cyanoacrylate and octyl-cyanoacrylate in the management of selected pediatric facial lacerations. *Acad Emerg Med*. 1999;6: 171-177.
21. Saxena AK, Willital GH. Octyl-cyanoacrylate tissue adhesive in the repair of pediatric extremity lacerations. *Am Surg*. 1999;65:470-472.
22. Quinn J, Wells G, Sutcliffe T, et al. Tissue adhesive versus suture wound repair at 1 year: randomized clinical trial correlating early, 3-month, and 1-year cosmetic outcome. *Ann Emerg Med*. 1998;32:645-649.
23. Kaihara S, Vacanti JP. Tissue engineering: toward new solutions for transplantation and reconstructive surgery. *Arch Surg*. 1999;SSA9012.
24. Boyce ST. Skin substitute from cultured cell and collagen-GAG polymers. *Med Biol Eng Comput*. 1998;36:791-800.
25. Regnier M, Patwardhan A, Scheynius A, Schmidt R. Reconstructed human epidermis composed of keratinocytes, melanocytes, and Langerhans cells. *Med Biol Eng Comput*. 1998;36:821-824.
26. Demling RH, DeSanti L. Management of partial thickness facial burns. *Burns*. 1999;25:256-261.
27. Falanga V, Margolis D, Alvarez O, et al. Rapid healing of venous stasis ulcers and lack of clinical rejection with an allogenic cultured human skin equivalent: human skin equivalent investigators group. *Arch Dermatol*. 1998;134:293-300.
28. Sabolinski ML, Alvarez O, Auletta M, Mulder G, Parenteau NL. Cultured skin as a "smart material" for healing wounds: experience in venous ulcers. *Biomaterials*. 1996;17:311-320.
29. Rodriguez A, Cao YL, Ibarra C, et al. Characteristics of cartilage engineered from human pediatric auricular cartilage. *Plast Reconstr Surg*. 1999;103:1111-1119.
30. Ramirez OM, Pozner JN. Subperiosteal minimally invasive laser endoscopic rhytidectomy. *Aesthetic Plast Surg*. 1996;20:463-470.
31. McCarthy JG, Schreiber J, Karp N, Thorne CH, Grayson BH. Lengthening the human mandible by gradual distraction. *Plast Reconstr Surg*. 1992;89:1-8.
32. Cohen SR. Craniofacial distraction with a modular internal distraction system: evolution of design and surgical techniques. *Plast Reconstr Surg*. 1999;103: 1592-1607.
33. Swennen G, Colle F, DeMay A, Malevez C. Maxillary distraction in cleft lip patients: a review of six cases. *J Craniofac Surg*. 1999;10:117-122.
34. Polley JW, Figueroa AA. Rigid external distraction: its application in cleft maxillary deformities. *Plast Reconstr Surg*. 1998;102:1360-1372.
35. Figueroa AA, Polley JW. Management of severe cleft maxillary deficiency with distraction osteogenesis: procedure and results. *Am J Orthod Dentofacial Orthop*. 1999;115:1-12.
36. Losken HW, Mooney MP, Zoldos J, et al. Coronal suture response to distraction osteogenesis in rabbits with delayed-onset craniosynostosis. *J Craniofac Surg*. 1999;10:27-37.
37. Haluck RS, Mackay DR, Gorman PJ, Saggars GC, Manders EK. A comparison of gradual distraction techniques for modification of the midface in growing sheep. *Ann Plast Surg*. 1999;45:476-480.
38. Geany T. What constitutes an adequate bone formation in the craniofacial skeleton? *J Craniofac Surg*. 1995;6:356-357.
39. Ono I, Gunji H, Suda K. Method for preparing an exact-size model using helical volume scan computed tomography. *Plast Reconstr Surg*. 1994;93:1363-1368.
40. Hurwitz DJ, Ashby ER, Lull R, et al. Computer-assisted arthropometry for outcome assessment of cleft lip. *Plast Reconstr Surg*. 1999;103:1608-1623.
41. Remmler D, Olson L, Duke D, Ekstrom R, Matthew D, Ullrich CG. Presurgical finite element analysis from routine CT studies for craniofacial distraction. *Plast Reconstr Surg*. 1998;102:1395-1404.

Surgical Anatomy

Injury to the long thoracic nerve of Bell during an axillary dissection results in loss of innervation to the serratus anterior muscle resulting in a winged scapula.

1. Blackburne LH, Fleischer KJ. *Advanced Surgical Recall*. Baltimore, Md: Williams & Wilkins; 1997:35.