Bioresorbable Skeletal Fixation Systems in Craniofacial Surgery

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Today the use and advances of bioresorbable biomaterials in skeletal fixation is in a process of major evolution in the applications and understanding of all fixation devices. Craniofacial skeletal fixation is an essential element in the stabilization of the different components of any bony components in the biological system. The rigid fixations of the craniofacial skeletal represent a major biological region in the human skeleton where such applications produce the desired stability with maximal advantages and minimal disadvantages to any existing systems in present use. This shift in the evolutionary status, from overusing metallic components to a move of avoiding the use of metallic implants, particularly in infants and in children, to the total applications of resorbable material in all applications in the craniofacial skeleton and in all age groups, is because of the complications and safety to the patients. The metallic implants, once popular and in wide variety of uses in the 1980s, are falling by the wayside as the application and sophistication in the resorbable components become more accepted by the practicing surgeons working, in particularly, on all components of the craniofacial skeleton. The craniofacial skeleton is a unique component of the skeletal system for its proximity to the central nervous system on one hand and to the contaminates oropharyngeal airway on the other hand.
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Today the use of bioresorbable biomaterials in skeletal fixation is in a process of a major evolution in the applications and understanding of all fixation devices.[1] The advances made in the last decade made the utility and applications in the clinical situations possible. Skeletal fixation is an essential element in the stabilization of the different components of any bony system. This shift in the evolutionary status from using metallic components to a move of avoiding the use of metallic implants particularly in infants and in children with the total applications of bioresorbable material in all applications in the craniofacial skeleton and in all age groups is to be noted as advancement in technology.[2] The metallic implants, once popular and in wide variety of uses in the 1980s, are falling by the wayside as the application and sophistication in the resorbable components becomes more accepted by the practicing surgeons working, in particularly, on all components of the craniofacial skeleton. Added to it is the safety to the patients, in the form of avoiding the need for a second operation to remove these implants and the avoidance of the passive internal migration and growth disturbances, particularly in children.[3] These bioresorbable implants are also invisible on radiographic analysis, thus make their use in oncological clinical situations an added clinical advantage.

Biomaterial

The introduction and use of the polylactide and its different components as a resorbable utility biomaterial for suture material in the mid-1960s, followed by the extensive use for many applications, and culminating in a high standard of safety records, was the main impetus for the desire of basic research scientists and technology engineers to get into the development and later the production of resorbable fixation devices for use in the craniofacial skeleton.[4] The basis of the standard unites is the poly lactic acid in its levo and dextro forms to produce the desired form and shape needed as a copolymers of the biomaterial to be used in the craniofacial skeleton. Interest in expanding the horizons and widening applications have been mounting so as to improve the clinical applications of the bioresorbable material. Many laboratories around the world have been looking into changing the chemistry and producing different combinations to produce a compounded biomaterial that is used in skeletal fixation of the craniofacial skeleton. These different combinations being produced are made so as to vary the two different characteristics of the produced biomaterial, that is longevity versus strength. These are the basis of all the materials systems today that are marketed for use by the surgeons,[5] because there were many questions that had arisen regarding the validity and the side effects of the widely practiced applications of metallic implants to stabilize the craniofacial skeleton. The poly lactides base and molecular weight are the basis of all the copolymers used in the skeletal fixation systems. The key issue is that for the skeletal fixation the components that are used must have an understanding of longevity and mechanical strength expressed in sheer pressure at different parts of the skeleton. The craniofacial skeleton have two unites: the static nonmovable units as the orbito-cranium, and the constantly moving unit as the jaws. The static components on the nonmovable parts as the cranium and the dynamic parts that are in constant motion such as the mandible both have different biology in their inherent understanding of their fixation systems particularly the requirement of sheer stress for the needed biomaterial.[5]

Background Information

The interest in skeletal fixation to produce the required stability for the healing process needed for the craniofacial skeleton started after the First World War, even though scattered reports

of a need for such stabilization systems were noted many years before the war in the literature. The Second World War brought the importance of that need to the forefront, particularly that some of the survivors of the war needed their faces worked on after multiple injuries during their rehabilitation. It was not accepted any more to have a deformed face and a functional derangement that can be repaired easily by the practicing surgeon if the appropriate technologies were available. That was the start of the collaboration between the industry and the clinicians to achieve the best outcome for the patients.[7]

The first stage in the evolution process involved just manipulation to place the craniofacial structures together, in conjunction with some techniques that were still practiced by some surgeons until a few years ago. That no fixation approach was fraught with the noted observations that most of such structures collapsed into a nonfunctional position that need to have a secondary repair afterward and maybe a tertiary repair. The instability was the result of the myofunctional components of the facial skeleton. The muscle pull on the unstable bones caused the bones to shift. The craniofacial bones are membranous bones, and the healing is devoid of the presence of a callous formation, as in long bones.

The second stage involved the use of external fixator apparatus for the patients. That gave an initial superior result to the previously practiced repair. However, after the external fixator in the form of an external apparatus was removed, the patients' repaired segments collapsed. The relapse, which is discussed in many chapters, was a result of a similar process related to stability without the presence of a primary healing in these components that are either fractured or osteotomies. The third stage involved the use of wire fixation that set the stage for the use of the metallic implants systems that were the predecessors of the resorbable plating systems in use today. That evolution has progressed slowly since the Second World War. The wars bring about many casualties, and the rehabilitation of such patients spill to the activities in the civilian population.

Safety Factors

The applications and use of the biomaterials in the biologic system is always associated with a major question: are those biomaterials safe to use or are they harmful to the individual patient? Also, are there any by-products that are harmful to the patients under any circumstance? The safety issue became the fundamental focus of the Food and Drug Administration (FDA) and its similar administration in Europe. These scientist panels look at all the biomaterials that are to be used.[8] The scientific study of the efficacy and the animal studies that are required before the premarket studies, referred to in the biomaterial circles as the PMS, are designed to collect data from clinical applications over a period of time. The data are analyzed and, if the biomaterial is found to be safe and efficacious, it is then released in the marketplace for wholesale and retail shops, doctors offices, and hospitals. All the biomaterials referred to have passed through that mill and the final applications after release is the focus of discussion in this section.

Historical Perspectives

A review of the history of skeletal fixation is helpful to the understanding of the situations in which we work today. Skel-
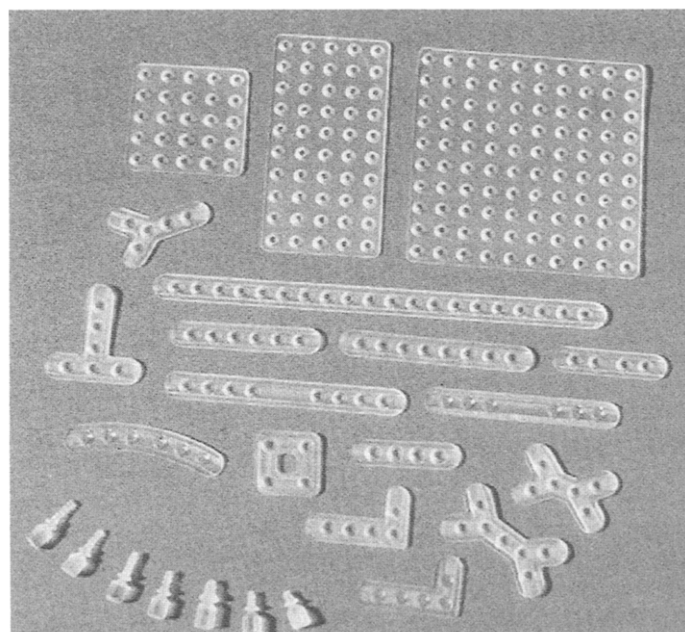

Fig 1. Display of the components of the system in use plates and panels get soft with heat so that they can be contoured, to the configuration of the site to used on, a major advantage for their use.

etal fixation in the craniofacial region has gone through many advances in the past few decades. Most of these advances have followed major international conflicts involving the complex treatment of large numbers of casualties.[10]

Initially, fractures of the craniofacial skeleton were treated without fixation by allowing the bones to heal in open soft tissue, then performing the repair at a later time. Fractures were also treated with closed reduction after manipulation. The next development was the use of an external apparatus for fixation. This method was useful until the external fixation was removed and the repaired structures collapsed again. Those procedures were accompanied by a lack of success and were the impetus for the development of the techniques of open reduction and internal fixation in all-skeletal clinical problems. That was the background for the development of the biomaterials to be used in these situations.[11]

Internal fixation then came into practice and required the use of rigid fixation. Use of the plating system began at the turn of the century, with the use of stainless steel plates. The popularity of the applications came after the wars and in the mid-1970s. The use of first vitalium and then titanium as the plating systems followed the major applications of the stainless steel system, which were accompanied by many complications. In the latter part of the last century, the use of resorbable plating systems evolved and has advanced to their present status. Resorbable plating systems remain state-of-the-art for skeletal fixation in the craniofacial region, particularly in infants and children (Fig 1).

The evolution of biocompatible resorbable polymers offers surgeons of today a new array of options for craniofacial skeletal fixation.[12] Some of the potential benefits of resorbable polymers include greater ease and accuracy of contour adaptation, clear radiographic presentation because of the absence of X-ray scatter, elimination of the need for secondary surgeries for device removal, and reduced risk of stress shielding of the
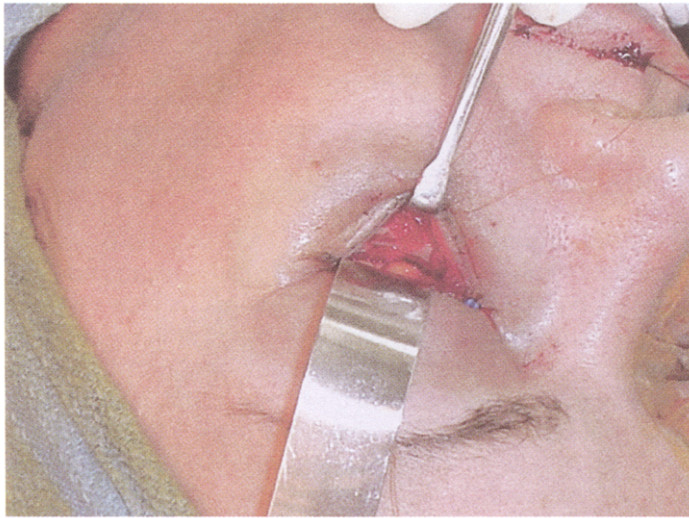
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Fig 2. Repair of the orbital floor where as a small panel contoured into the orbit via a transconjunctival approach to the orbit.

underlying bone. Known as polyesters, these copolymers have chemical, physical, material, mechanical, and biologic properties different from those of metal fixation devices. Knowledge of these differences will facilitate the utilization of resorbable implants in fixation for craniofacial trauma (Fig 2).

Among the bioresorbable polyester craniofacial fixation devices approved for clinical use by the FDA, copolymers of lactides and glycolides are available. The first copolymer of l-lactide and glycolide (LactoSorb, W. Lorenz, Jacksonville, FL) was approved by the FDA in 1996. The lactide in LactoSorb is a homopolymer of the levo form. The ratio of the l-lactide monomer to the glycolide monomer is 82:18 in poly (l-lactide-coglycolide), to take advantage of glycolide's rapid degradation time. Strength declines to approximately 70% by 6 to 9 weeks, and resorption is complete by 12 months.[14]

Approved more recently in 1998 is a copolymer produced from a mixture of 70% l lactide monomer and 30% d,l lactide monomer (MacroPore, MacroPore Biosurgery, Inc., San Diego, CA). This 70:30 ratio in poly (l-lactide-cod,l-lactide) DLLA retains approximately 70% of its initial strength after 9 months and approximately 50% after 12 months, with resorption completed by 24 to 36 months. Additional resorbable polyesters from Bionx, Leibinger (delta system and the new delta system); Synthes (resorbable system); KLS Martin (resorb-X); and Inion (two systems) are all FDA-approved and available for surgeons to use. The differences among these systems are the ratios of the copolymers used in the compositions that affect their longevity, a consideration of importance to surgeons. The deciding factor in which system to use is the individual surgeon's preference and ease in clinical application. In children, the surgeon wants the system to resorb much faster than in the adult. A patient going into radiation therapy has slower healing, so the systems used must stay longer to allow for better bone healing. Thus the surgeons have more options, based on the need of the patient and the long-term applications needs.[15,16]

In view of these considerations, the primary focus is on the use of poly (l-lactide) for skeletal repair and fixation, due to its wide range of acceptance among practicing surgeons. The acronym (DLLA) will also be utilized to designate a copolymer of the two monomers, l-lactide and d,l-lactide, a combination needed

for strength to stabilize the bony components if it is because of fractures or controlled fractures as in facial osteotomy.[16]

Biophysics

Poly (l-lactide), which has a high crystallinity, is characterized by its strength and long degradation time. Conversely, a polymer created from d,l-lactide has little strength and degrades rapidly. Combining l-lactide and d,l-lactide results in a copolymer with the intermediate characteristics of strength for 6 to 9 months and resorption in 24 to 36 months. In addition, the copolymer is optically clear and noncrystalline, resulting in minimal foreign body reactions by tissue. It should be noted that, even within a given copolymer, strength and degradation characteristics could vary according the degree of polymerization.[18,19] Therefore, the manufacturer must maintain this within the desired range. A common measure of the degree of polymerization is called intrinsic viscosity (IV) and, for any given polymer, the IV correlates with molecular weight. To measure IV, the polymer is dissolved in a standardized known amount of chloroform and then passed through a viscometer. The length of time that it takes for passage is used to calculate the IV.

At sufficiently high temperatures, all materials change from hard to soft and finally to liquid. The temperature at which a material changes from hard to soft is known as the glass transition temperature (Tg). For 70:30 poly (l-lactide-cod,l-lactide), the Tg is 55°C (131°F), thus allowing heat to be utilized for contouring these implants.[20]

Contouring an orbital floor liner illustrates this property. After making a template of the orbital floor, the template is held against the orbital floor liner (Fig 1A), then placed in a water bath and heated above Tg. The floor liner becomes soft in a few seconds and simply drapes over the template when lifted from the water bath. In a few more seconds, the floor liner cools below Tg and can be removed from the template. The liner is then ready to be placed in the patient. It is useful to note that 70:30 poly (l-lactide-cod,l-lactide) has shape memory and, if placed back in the water bath, it will return to its original contour, thus enabling additional opportunities to raconteur it (Fig 2). If only a portion of an implant needs to be recontoured, only that portion needs to be placed back in the water bath. Cyclic heating of 70:30 poly (l-lactide-cod,l-lactide) to 70°C can be performed multiple times with no change in material strength (Fig 3).

Biochemical

When lactic acid undergoes polymerization, ester bonds are formed and H_2O is released. Therefore, lactide copolymers are also known as polyesters. Resorption of lactide copolymers takes place as a reversal of this process, with sorption of H_2O and scission of the ester linkages. This bulk hydrolysis of lactide copolymer implants continues until single lactic acids molecules are released, which are then metabolized into glucose or into CO_2 and H_2O via the Krebs tricarboxylic acid cycle.

A variety of factors are known to affect the rate of lactide copolymer resorption. A higher IV or molecular weight means there are more ester linkages that undergo scission and these processes result in a longer resorption time. A larger implant size or volume will also require more scission before implant resorption can be completed. If the polymer is packed more
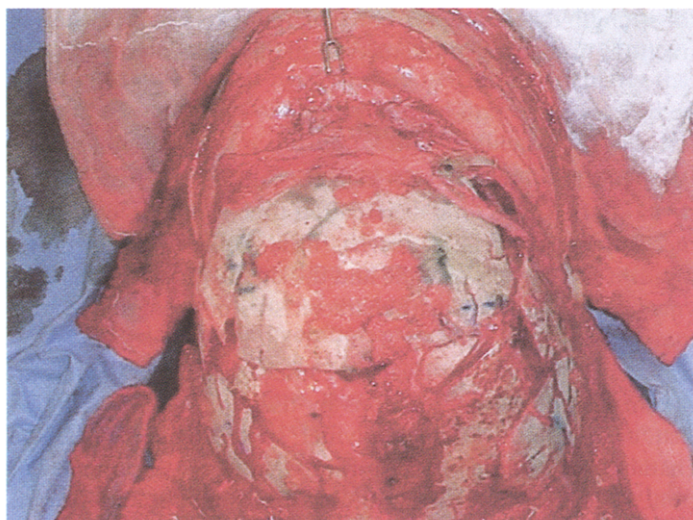
Fig 3. Total fixation of a craniofacial components of a child after corrective surgery for a birth defect in the craniofacial region. All biomaterial used were bioresorbable.

tightly in an orderly crystalline pattern, there is less space for H_2O access and resorption will take longer than for noncrystalline implants. Because hydrolysis occurs both on the implant surface and within its interior, implant porosity will increase surface area, facilitate H_2O access, and decrease resorption time. The molecular configuration of copolymers may alter resorption time. Greater vascularity of the implant host site, as well as flexural bending from functional loading, appears to be associated with an increased rate of hydrolysis.

Biotoxicology

The toxicology of lactides has been of minimal concern, because of the relatively small volumes of implant material, slow degradation rates, and short serum half-lives. The serum half-life of the levo form is 15 minute; for the d,l form it is 22 minute. The normal resting blood lactate level is 1.1–2.8 mmol/L/L. After muscular activity it will rise 10-fold to 10–23 mmol/L/L. If the assumption is made that degradation occurs over 2 months, with first order kinetics and a half-life of 74 hours, a 100 g implant would release 0.18 mmol/L/L of lactide acid in the first minute, far less than the changes resulting from muscular activity. Two of the largest sheets of 70:30 L-La/D-La copolymer weigh only 18 g, and degradation actually takes

place over a much longer 18 to 36 month time interval. Even with first order kinetics starting instantly, the 18 g of lactide copolymer would result in an increase in blood lactate levels of only 1.1%.

Pathology

The histological responses to 70:30 L-La/D-La copolymer have been well studied. There is an initial acute inflammatory response following implantation. By 72 hours there is a narrow zone of fibrinous exudate, edematous granulation tissue, and a modest degree of fibroblast proliferation. By 7 to 14 days the granulation tissue has matured into a thin, cellular, fibrovascular capsule. Measurements of in-vivo tissue pH adjacent to 70:30 L-La/D-La copolymer implants have detected no change during degradation.

Biomechanics

The mechanical properties of 70:30 L-La/D-La copolymer, bone, and steel are well known. The tensile strength of lactide is approximately 30% of the strength of bone. With a tensile strength of 70%, lactide materials can readily be designed to accommodate the failure loads for nonweight-bearing bones. When designed as 1.0 mm thick plates, the tensile strength is approximately 190 N or 45 lbs. When metal screws are over-torqued, the threads strip the bone. When lactide screws are overtorqued, the heads sheer off. The sheer strength of 2.0 mm screws is approximately 85 N or 20 lbs. As the 70:30 L-La/D-La copolymer undergoes hydrolysis, its mechanical strength will decrease. At 3 months, strength remains near 100%, decreasing to 90% at 6 months, 70% at 9 months, 50% at 12 months, and 0% by 18 months.

Clinical Experience

As with all fixation systems, clinical experience eventually determines the efficacy of any implant design that is most likely to produce a lasting and successful outcome. As a starting point, it is recommended that the surgeon select a copolymer design one size of the currently desired system to be employed. An example from our experience is that the substitution of titanium with PLA systems for all repairs is imperative. The traditional metal plate with two holes on each side and 2.0 mm screws would normally have been used; however, the patient insisted on resorbable over metal fixation, so four hole plates are necessary.

TABLE 1. Five Years Experience with the Bioresorbable Plating System

Category	Patient	Plates	Screws	Panel	E
Congenital	176	923	2405	121	3449
Trauma	65	103	368	35	506
Tumor	54	294	653	46	993
Cosmetic R	29	00	58	00	58
Total	324	1320	3484	202	5006

Follow up in months: (1–42) arithmetic mean 22
Complications: No Major Complications
average/patient = 15.4 compt./pt.
Edema +2 Age range . . . (1mo—94y) sem. 5.5
Age
Palpable +2 Average age 11.8y
Extrusion children 1 screw/1pt. Standard of care for infants and
Infection 1 salvage acomp.
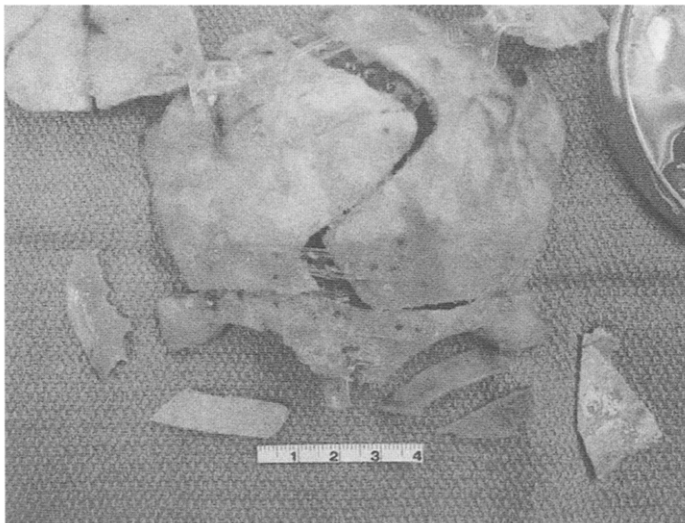
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Fig 4. Multiple components of a cranio-orbital rigid fixated together with a resorbable plating system to regain the patient contour after correction of a congenital deformity on the patient. This is done on the side table before placing it in the patient's forehead and stabilized with a plate and screws.

To assure adequate stability, the copolymer plate was contoured from a piece of 1.0-mm thick mesh with four holes on each side and attached with 2.4 mm screws (Fig 3). While this design may be excessive in strength, it is appropriate to be conservative until more clinical experience is acquired (see Table 1), for an overall experience in the first 5 years of utility of the biomaterial implants. The screws in all the systems available today need to have the hole made first, then tapped with a second metallic device to establish the troughs the biomaterial resorbable screw has to go in, an extra step from the routine systems used by the metallic counterpart. That may take a few minutes at the beginning of the application, but it is a fast learning phase for all those who apply the system.

The next comprises a review of the author's clinical experience with biomaterial use in craniofacial fixation, as shown in Table 1. We have noted minimal complications in all the patients used, and the follow-up time is enough to allow us to note that there is minimal soft tissue reaction and no mishaps or danger to the patients, particularly in children (Fig 3). These plates are not visible to the diagnostic techniques available today (Fig 4). We can only see the screw holes for about a year before the fill-up by the regenerating bones.

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