

Bioplastique™: A New Biphasic Polymer for Minimally Invasive Injection Implantation

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Abstract. The search for prosthetic materials that are biocompatible, nontoxic, and permanent led the authors to develop a micronized, inert, biphasic polymer particle for permanent soft tissue augmentation which neither migrates nor is absorbed by the body. Placed in a bioexcretable gel carrier, these textured microparticles are easily implanted using a specially designed blunt-tipped cannula with local anesthesia on an outpatient basis. Research using this implant material, Bioplastique™ (Bioplasty, St. Paul, MN), in rabbits has shown that when the textured particle size is maintained within a critical range, neither particle migration nor storage disease occurs. The gel carrier is rapidly phagocytized and replaced by fibrin matrix within a few days. Host collagen then gradually forms a fibrotic capsule around each textured particle, making use of the naturally occurring foreign body reaction to create a stable implant. After being followed for over two years, Bioplastique has proven to be useful in many clinical applications with few complications.

Key words: Bioplastique—microparticle implantation—rabbit studies

Background

Historically, soft tissue deficiencies have presented some of the most challenging problems for plastic surgeons. Over the years, inadequate skin coverage for defects has prompted development of the flap, tissue expansion, and other plastic procedures,

Note: The authors are inventors of Bioplastique and have a financial interest in it.

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while a truly satisfactory material to supplement deficient soft tissue mass remained unfound. Early attempts to augment soft tissue deficiencies involved transplantation of autologous fat [7], oils [II], mica [I], and ivory [13]. Recent renewed attempts at fat grafting have proven unsatisfactory as well [3].

Inorganic injectables—including teflon, silicone gels, and silicone fluid—although generally bioinert and permanent, have been found to migrate from the site of implantation to distant parts of the body [10]. The full implications of this migration are, as yet, unknown.

Although bovine collagen has been found useful for correcting small tissue defects, results are temporary [12]. Research to prolong the "life" of organic injectables included the harvesting of host serum crosslinked fibrinogen combined with alpha-amino caproic acid from Fibrel™ (Mentor, Minneapolis, MN) [6]. However, this too is autodigested in a matter of months.

The Ideal Soft Tissue Implant

What, then, constitutes an ideal soft tissue augmentation/replacement system? The authors consider the following characteristics desirable in a soft tissue implant:

- (1) bio-inert
- (2) permanent
- (3) particle size large enough to prevent migration after implantation
- (4) particle size small enough to allow implantation by minimally invasive blunt cannula procedure
- (5) not resulting in "storage disease"
- (6) light in color

(7) moldable following implantation, but stable after remolding

Work with a variety of alloplastic materials has revealed that tissue ingrowth can occur when implant surfaces are textured or patterned [3, 5, 9, 14]. This ingrowth prevents host/prosthesis micromotion at the interface and a more intimate mechanical bond is formed between implant and host [9]. As a result, the scar capsule that forms around a textured implant is thinner and less reactive than capsules formed around smooth-surfaced implants in the same mammalian subject at the same time [9]. Thus, it seems reasonable that texturing the microparticles would lead to a more permanent implant result.

Preventing Particle Migration

Implant particles $<60 \mu\text{m}$ have been found to be engulfed by macrophages and transported to regional lymph nodes [2]. Particles that are sufficiently small may remain intracellular indefinitely. However, those that approach the size of a macrophage (20-60 μm) may cause the death of a cell when engulfed. The dead cell releases intracellular enzymes, attracting other phagocytes and causing a chronic inflammatory response.

Since particles $>60 \mu\text{m}$ have never been found within a cell or the lymph nodes, we postulated that the critical particle size to prevent migration is $>80 \mu\text{m}$. From these conclusions, it was anticipated that implanted particles $>100 \mu\text{m}$ with a textured surface should be interspersed in a host-generated fibrotic tissue matrix within a few weeks. For soft tissue augmentation, a useful upper limit for microimplant dimensions was determined to be 1 mm, because particles larger than this may be perceived as surface irregularities on palpation.

Materials and Methods

Bioplastique is a biphasic polymer consisting of a gel phase and a permanent polymer particle phase. The gel carrier is a member of the plasdone family. The gel is scavenged by the reticuloendothelial system and excreted by the kidneys, unchanged, within a matter of days. The gel carrier has a molecular weight between 15,000 and 30,000; a molecular formula of $(\text{C}_6\text{H}_8\text{LiNO})_n$, and an appearance and consistency similar to honey. The plasdone has been used as vehicles and extenders for a variety of medications without ill effect for nearly 50 years [8].

Small textured microparticles of biocompatible polymer measuring between 100 and 600 μm were fabricated and then mixed 38% by weight with 62%

of the polymer gel carrier. The solid phase of this new substance was made of fully polymerized, vulcanized polydimethylsiloxane: $(\text{CH}_3)_2\text{SiO}$. This solid elastomer has been used successfully since 1960 for nose and chin prostheses, pacemaker leads, heart valves, and vascular and hydrocephalus shunts.

The polymer mixture was diluted with deionized water, osmotically balanced, and mixed until the solid microimplant particles were evenly dispersed. The mixture was then gelled and placed in 1-cc syringe cartridges and sterilized prior to implantation. To implant the substance, we developed a specially designed cannula with a tapered blunt tip and a blunt hole on the taper. To assure control in injection, an altered injection gun was used to deliver precise amounts of Bioplastique through the cannula in a measurable and predictable manner.

Twenty large adult New Zealand white rabbits were selected for initial testing. The animals were provided by a licensed supplier. Their ears were anesthetized with xylocaine (1%) and epinephrine (1: 100,000) in the subcutaneous plane to receive the implants. A remote puncture was made with a sharp 20-gauge needle, about 1 cm from the planned test site. The injection site was pretunneled using a pencil-tipped cannula. Test material was injected carefully while the blunt cannula was withdrawn (Fig. 1A). The rabbits were monitored, and test sites were periodically measured by micrometer. Transillumination, photos, and histological sections were performed at two days, four days, one week, three weeks, six weeks, three months, and six months.

Sections of each implant area were performed with hematoxylin-eosin and Mason's trichrome stain.

Controls

Commercially available collagen derivatives (Fibrel, Zyderm [Collagen Corp., Palo Alto, CA], and Zyplast [Collagen Corp., Palo Alto, CA]) were obtained and injected subcutaneously in adjacent sites in the rabbit ears using 20-gauge (for Fibrel) and 27-gauge (for Zyderm and Zyplast) needles and syringes provided by the respective manufacturers. By transillumination with cold light, the size and density of the areas of injection were easily and atraumatically monitored for each individual rabbit.

Prior to the humane sacrifice of each test animal, their ears were anesthetized with xylocaine and then subcutaneously injected with methylene blue dye in order to define the lymphatic system. Careful dissection was then carried out at the base of each ear to remove regional lymph nodes for histologic section. Histologic sections were prepared from the base of each ear, whether or not lymph nodes were palpated.

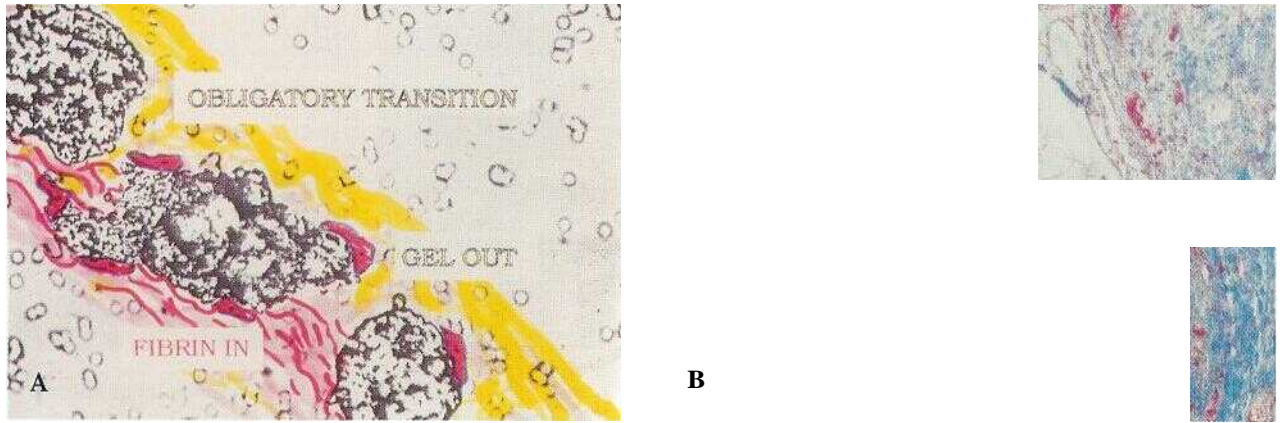


Fig. 1(A) Immediately after implantation the hydrogel is rapidly dispersed by the body's tissue fluids. Because of the osmotic gradient, there is an obligatory transition. All of the gel is removed within a matter of hours. The tissue fluid contains fibrinogen, and the gel is replaced by fibrin as it is removed (artist's rendering). **(B)** (Day 2) Fibrin stains pink and collagen stains blue in Masson's trichrome stain, seen here after injection in the rabbit ear. At one day, all of the gel has been replaced by fibrin

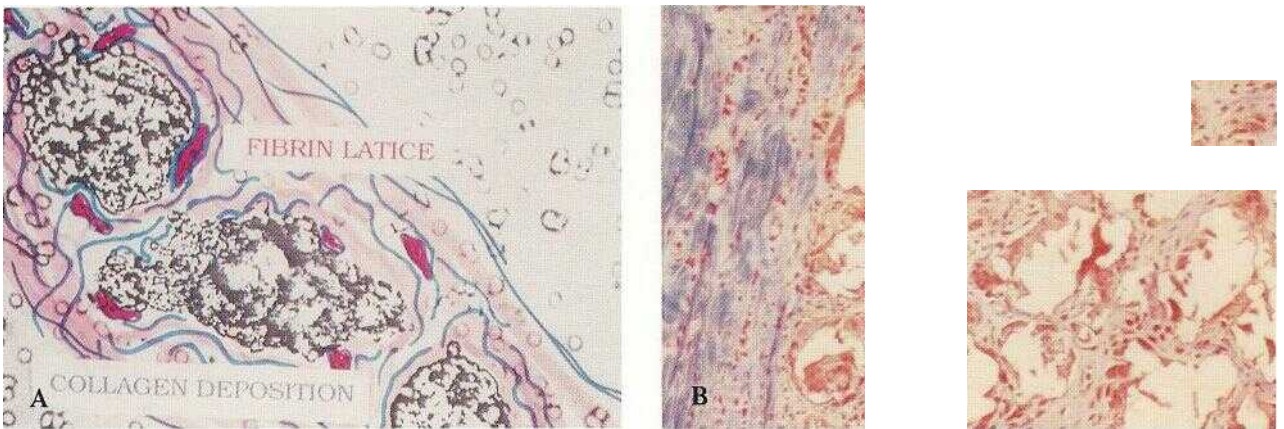


Fig. 2(A) Between days 1 and 3 the fibrin lattice is populated by fibroblasts that excrete collagen and begin to polymerize it extracellularly (40X) (artist's rendering). **(B)** A rabbit ear at day 4; most of the pink staining fibrin is being converted to blue staining collagen (100X)

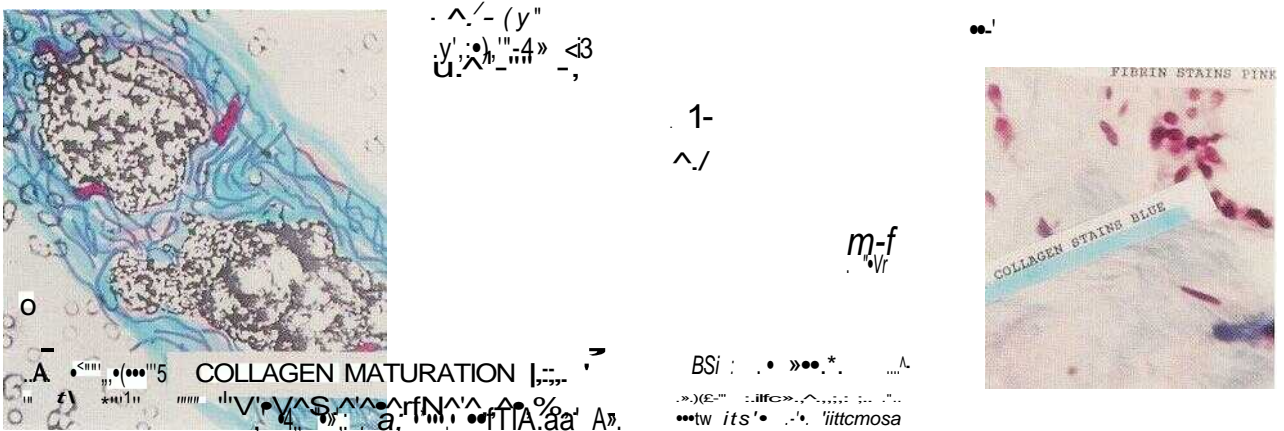


Fig. 3(A) After most of the fibrin is replaced by collagen. Collagen deposition is completed within about three weeks and the particles are then engulfed in a stable collagen-containing matrix. Then the stage of collagen molding and maturation begins. During this phase of wound healing, collagen deposition and degradation are approximately equal (artist's rendering). **(B)** A high-power view (400X) of textured Bioplastique solid polymer particles after implantation in rabbit ears. At 382 days it reveals a quiescent, tolerant encapsulation



Fig. 4(A) Forty-year-old white female, one year following overzealous liposuction that left two similar indentations in the lateral thigh. **(B)** Immediate postoperative result after injection treatment with 3 cc of Bioplastique used to correct one dent, leaving the other dent as a control and light index. **(C)** Eleven months following Bioplastique treatment, showing that the untreated dent remains essentially the same as prior to treatment, whereas the treated dent is substantially improved

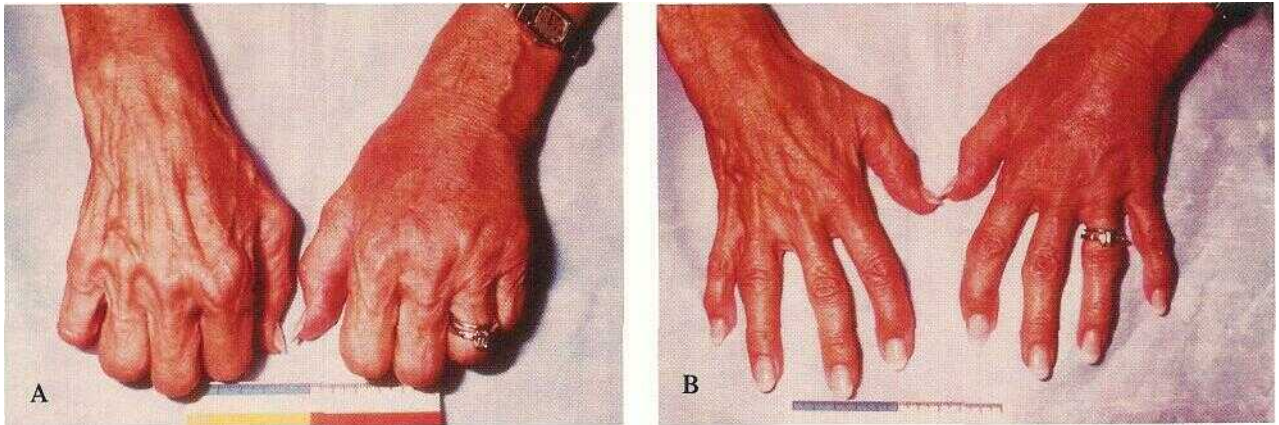


Fig. 5(A,B) Sixty four-year-old white female had 2 cc of Bioplastique injected in the subcutaneous plane of the left hand only. The right hand serves as a control and lighting index. This procedure was done under local anesthesia and the patient is seen two months after surgery

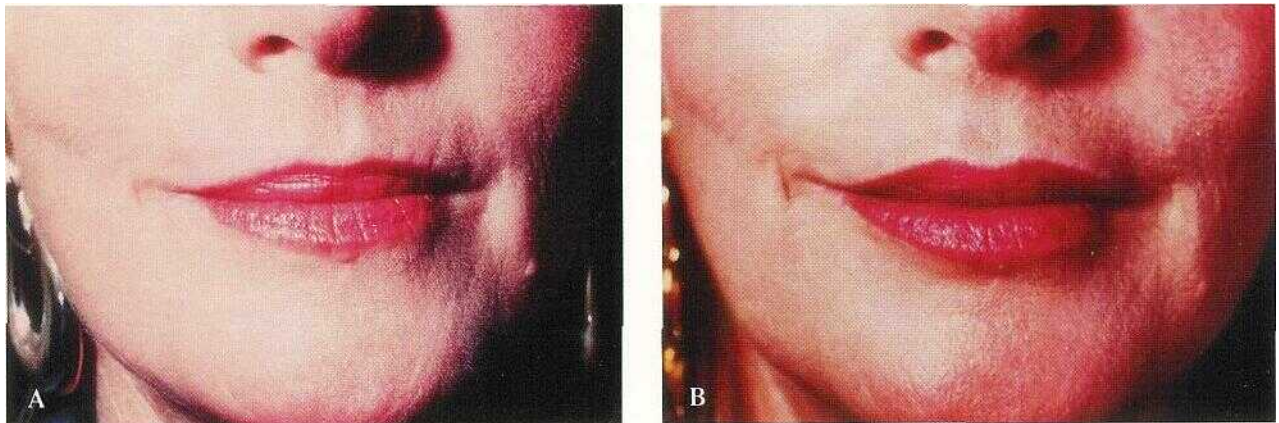


Fig. 6(A) This 40-year-old female has fine lines in the skin above her upper lip. She has requested lip augmentation. 0.2 cc of Bioplastique were added to the upper lip, and 0.2 cc were added to the lower lip. **(B)** Postoperative view showing increased thickness of the lips. The Bioplastique is only in the muscle in the region of the vermillion. It is not subcutaneous or submucosal. The slight thickening of the muscle provides improved appearance in the wrinkles. No attempt is made to inject the skin itself

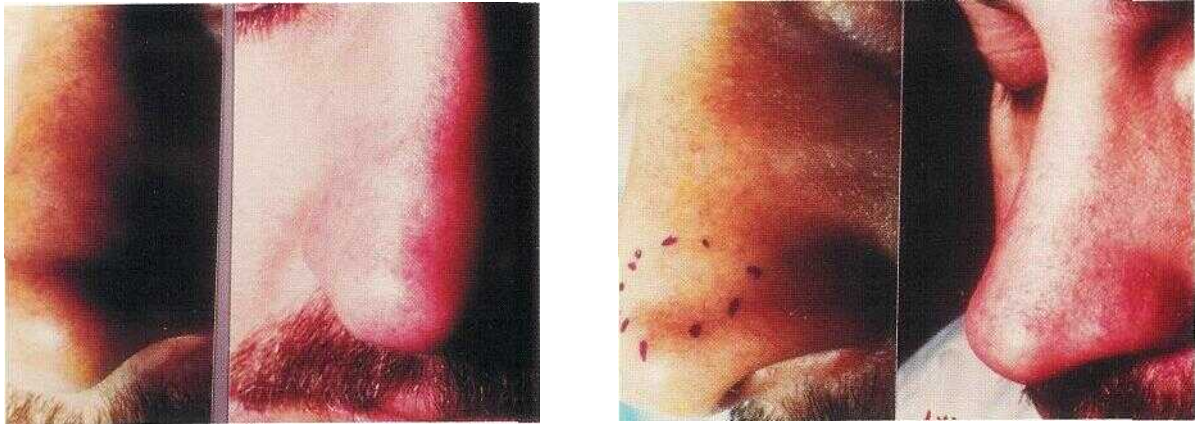


Fig. 7(A-D) This 40-year-old male has a congenital indentation at the level of the alar dome on just one side of his nose. 0.2 cc of Bioplastique were injected through a 20-gauge blunt cannula after pretunneling through an injection site within a nostril. Postoperative pictures at one year. No material or indentations are palpable



-A
Hife-

B

Fig. 8(A) Preoperative photo of 50-year Oriental female who complained of a deficient bridge of the nose. **(B)** Postoperative view following injection of 2.5 cc of Bioplastique through a 20-gauge blunt cannula using an injection site within the mucosa of the nostril. Treatment was done in three sessions, adding a little more at each session

Animal Test Results

Exogenous Collagen Injections

Histologic sections were taken at one week. These revealed that use of the collagen-based materials (Fibril, Zyderm, and Zyplast) had resulted in initial collagen-containing boh. Within two weeks these areas had become vascularized. After three weeks had passed, no residual collagen could be found histologically. The micrometer and transillumination measurements demonstrated a steady decline to pre-injected levels within one month.

Bioplastique

At two days, histologic sections of Bioplastique revealed that a dynamic transition had occurred in

which the gel carrier was replaced by a fibrin, and a protocollagen matrix surrounded each of the micro-particles (Figs. 1B, 2A). At just four days, the fibrin matrix was complete (Fig. 2B). All the carrier gel had been removed by the host. Connective tissue cells had developed and had begun to replace about 30% of the matrix with host collagen fibrils which stained blue by trichrome (Fig. 3A). AT day 382, fibrosis was complete and each individual Bioplastique microimplant particle appeared to be encased in its own fibrous capsule (Fig. 3B).

Histologic examination of the regional lymph nodes at the base of the rabbit ears revealed no particles. Cross-sections of the ear below the injected area showed no particles. No microimplant particles were found at the base of any of the ears or in the regional lymph nodes in any of the rabbits under study.

The thickness of the subcutaneous deposits of Bi-

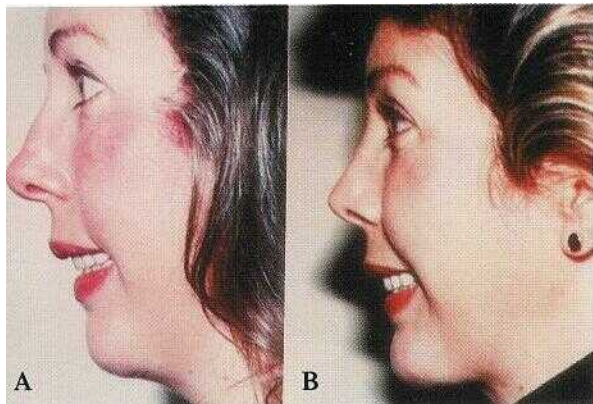


Fig. 9(A,B) This 40-year-old white female had a rhinoplasty and a chin augmentation using 1.5 cc of Bioplastique injected percutaneously through 20-gauge blunt cannula

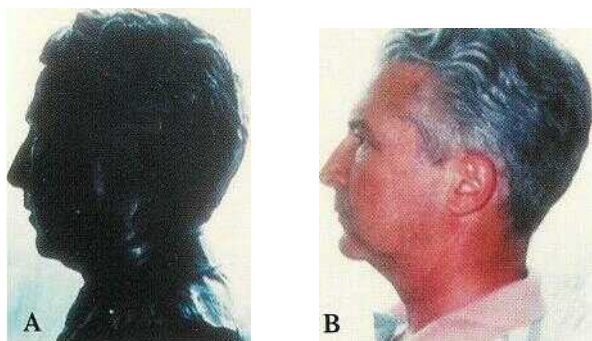


Fig. 10(A,B) This 50-year-old white male had a deficient chin. On the left is a preoperative CAD/CAM (computer-assisted design machine) bronze portrait. On the right patient is seen 6 months after injection of 1 cc of Bioplastique to the pogonion. The procedure was performed under local anesthesia from two lateral injection sites

oplastique increased about 10% between weeks 1 and 3, and then remained thicker until day 30-40 when it returned to the week 1 level and remained approximately the same throughout the balance of the study period. This was evidenced by transillumination, photographic records, and micrometer measurement.

Discussion

The control materials—Fibrin, Zyderm, and Zyplast—successfully create immediate soft tissue augmentation. However, these substances are only 3.5-6.5% solid collagen material and are soon ab-



Fig. 11. The microparticles can be removed with some of the scar encasement by standard biopsy technique. Here, an 18-gauge needle has been used with suction applied to the syringe, rotating as in a core drilling sample. Because these particles are textured, it is not possible to remove the particles alone. Some of their encasing scar tissue must be removed also.

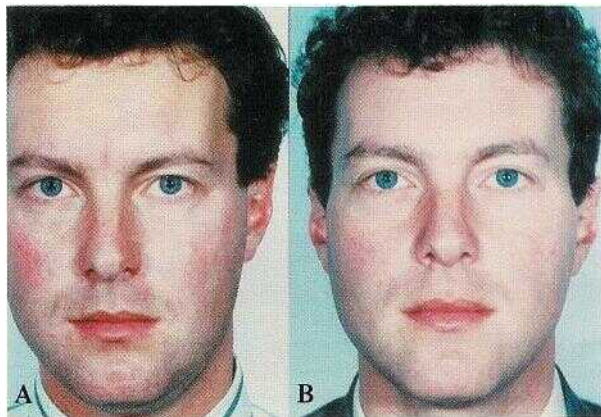


Fig. 12(A,B) This 29 year old white male has a prominent glabella crease shown in Figure 12-A. This was filled with 0.2 ccs of Bioplastique through a remote puncture site after pre-tunneling. Although the crease remains because the corrugator muscles are still intact, its ability to trap the light has decreased by perhaps 50% (Figure 12-B). Further correction may be indicated in this case.

sorbed by the host. In rabbit ears, collagen was found to degenerate from the blue stain seen on initial injection (and indicating the presence of collagen) to a pink stain (indicating fibrin matrix) within just two weeks. By week 3, all of the exogenous collagen appeared to have been digested or degraded and had disappeared.

When Bioplastique is injected subcutaneously, prompt replacement of the carrier gel by host fibrin or protocollagen occurs within a day or two. As the fibrin substitution is completed, some new capillar-

ies penetrate the space between the solid implant particles and fibroblasts appear within the matrix. These begin fabricating host collagen by the sixth postoperative day. This transformation is complete within three weeks—as is evidenced by the modification of the stain from pink (fibrin) to blue (collagen).

Conclusions

Inert, textured microimplants stimulate development of a host-collagen matrix that anchors them in place and surrounds each particle in a thin (0.50 μ m) encapsulation that results in permanent soft tissue augmentation. Based on these animal experiments, clinical studies in humans were begun in 1989. Since that time, the authors have found Bioplastique useful in treating cleft lips, thin lips, depressed scars, hollow cheeks, Oriental noses, chins, correction of overzealous liposuction, and other subcutaneous applications (Figs. 4-12).

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