

Bioplastique: A New Textured Copolymer Microparticle Promises Permanence in Soft- Tissue Augmentation

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Bioplastique: A New Textured Copolymer Microparticle Promises Permanence in Soft-Tissue Augmentation

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Migration, absorption, or toxicity of prosthetic materials has always plagued the plastic surgeon attempting to ameliorate soft-tissue deficiencies and other contour abnormalities. Our previous work to develop textured-surface breast prostheses has led to the development of micronized, inert, biphasic copolymer particles that neither migrate nor become absorbed by the body. These particles are textured, of critical dimension, and, when mixed with a bioexcretable gel vehicle, can be implanted using a special blunt-tipped cannula.

Our experimentation in rabbit ears has shown that the bioexcretable gel component is rapidly phagocytized and is replaced by fibrin-like matrix within 3 days. The fibrin is then replaced by host collagen that gradually converts into a fibrotic encasement around each texturized particle. Clinical use of the substance in a variety of soft-tissue deficiencies has been generally effective, with only a few complications, when followed for 1 year.

Since the beginnings of plastic and reconstructive surgery, deficiencies of appropriate tissue, especially replacement of the damaged nose and other facial parts, have presented the most challenging problems for surgeons. In Dieffenbach's work,² where the term *plastic surgery* may first have been used, it was a deficiency of tissue in a cleft lip and palate that prompted special techniques of flap, graft, and tissue forming and shaping that have become the province of skilled plastic and reconstructive surgeons.³ Through the years, the acute problem of adequate skin coverage for defects has been addressed by the evolution of flap, tissue expansion, and other plastic procedures, while the replacement of deficient parts remained unresolved.

The first attempts to overcome soft-tissue de-

ficiencies involved transplantation of organic substances such as autologous fat⁴ and ivory,⁵ mica,⁶ and oils,⁷ and more recently, inorganic substances, including silicone gels and fluid.^{8,9} In breast augmentation procedures, bizarre remedies such as cadaver fat, Ivalon, and polyethylene strips¹⁰ were even used. Most of the foreign substances resulted in inflammatory responses. Some were accompanied by temporary fibrosis that appeared to improve the deficiency. Some inert alloplastic materials remained for decades without significant alteration."

Injections of minute quantities of liquid silicone have been successful in the treatment of Romberg's disease and several other specific soft-tissue deficiencies where minimal mechanical stress was placed on the recipient site.⁴ Liquid silicone, however, has lent itself to widespread abuse by untrained practitioners who injected vast amounts of fluid that subsequently migrated to distant body parts and caused a variety of well-known problems.^{12,13}

In the 1970s, reconstituted bovine collagen became available in an injectable form. Although expensive, this approach to soft-tissue augmentation held great promise and appeared to be an effective treatment for small tissue defects. However, over time, these benefits proved to be transitory, and more permanent materials were sought. Attempts to prolong the life of injected organic substances included the harvesting of host serum, cross-linked fibrinogen with alpha-aminocaproic acid to develop Fibril.¹⁴ This also was autodigested in a few months.

A variety of implanted alloplastic materials

have been rendered more effective by texturing their surfaces, allowing tissue ingrowth: orthopedic implants,¹⁵ dialysis shunts,¹⁶ heart valve sewing rings,¹⁷ peritoneal access devices,¹⁸ and more recently, silicone breast implants.^{19,20} Tissue ingrowth prevents host-prosthesis interface micromotion, resulting in a more intimate mechanical bond between the mammalian host and an inert implant. The use of textured surfaces has resulted in a thinner, less reactive encapsulation than smooth-surfaced implants in the same animal at the same time, as shown by Taylor and Gibbons,²¹ Whalen,⁷ Ersek,²⁰ and others.

PARTICLE SIZE

It has been observed in a variety of clinical situations that particles less than 60 μm in diameter can be engulfed by macrophages and transported to regional lymph nodes. Submicrometer-sized particles may be the most easily transported and may remain intracellular indefinitely. However, particles that approach the size of a macrophage (from 20 to 60 μm) may cause the death of a cell when engulfed. The dead cell releases its intracellular enzymes (cytokines), and these attract other phagocytes. While destroying and engulfing this cellular debris, the phagocytes again encounter and engulf the particle, and a vicious cycle of "choke and die, choke and die"

continues as a chronic inflammatory response. This has been observed in perigraft pseudoarthrosis around polymer joints.²²

No particle greater than 60 μm has ever been seen within a cell or within lymph nodes. The critical particle size is therefore determined to be greater than 80 μm . It was anticipated from these conclusions that implanted particles greater than 100 μm in size with textured surfaces should be covered in 3 weeks, interspersed with host-generated fibrotic tissue. Theoretically, there is no upper limit to the size of the textured particles (as evidenced by sintered-surface hip implants, textured breast implants, and others). Textured nose and chin implants may be considered to be macroparticles as herein described. The useful upper limit of microimplant dimensions is 1 mm because particles greater than 1 mm may be perceived as surface irregularities when palpated.

MATERIALS AND METHODS

Small particles with average diameter of 150, 100 and 600 μm were fabricated with a textured surface from an inert biocompatible polymer and were mixed 38 percent by weight with 62 percent of a biocompatible solution of water and organic polymer gel with lubricating properties and a viscosity similar to that of honey (Fig. 1). Although we experimented with microimplants

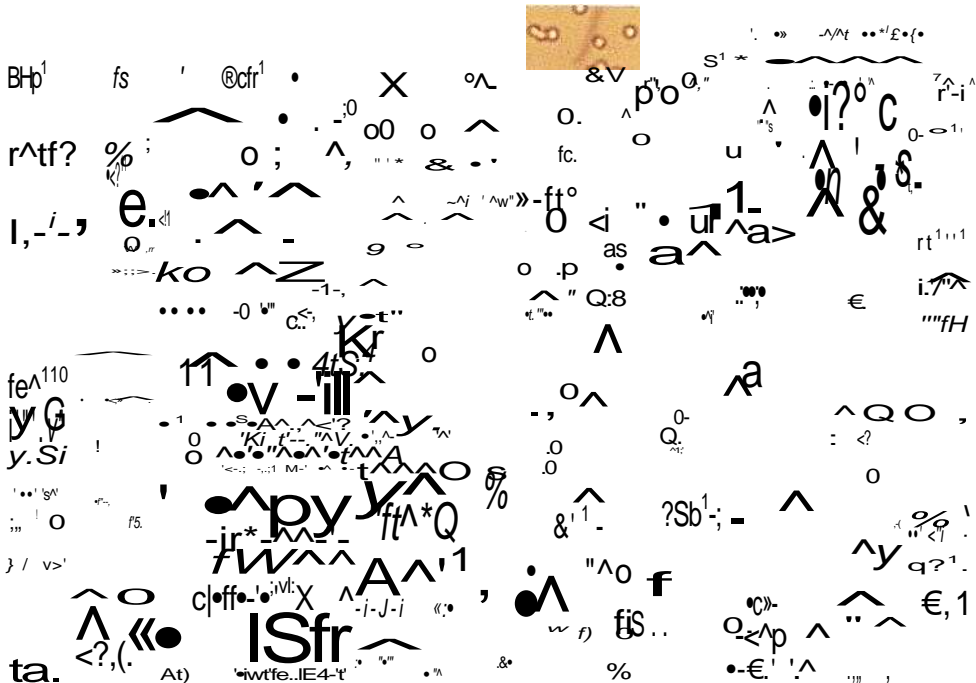


FIG. 1. A bioplastic, multifaceted, textured particle is seen here in a high-powered view (approximately 400X). We have shown the particle, which is three-dimensional, on a field of human red cells. The diameter of the textured microimplant is obviously eight to ten times the diameter of the red cell. The human red cells in this slide are approximately 8 μm in diameter.

made from several suitable biocompatible solids and with several suitable viscous lubricating gels, this study concerns itself only with Bioplastique.

The solid phase of this biphasic copolymer was made of fully polymerized and vulcanized methyl methylpolysiloxane $[(CH_2-SiO)]$, the same rubber-like polymer that has been used for vascular shunts, heart valves, pacemaker leads, and nose and chin prostheses since 1960.

The hydrogel is of the family of plasdone, having an average molecular weight of approximately 13,700 and an empirical formula of $(CHCH_2)_2N(CH_2)_3CO$. Polymers of this family have been used as binders, extenders, and vehicles for a variety of medications for nearly 50 years. They are freely transported through tissue fluids and excreted unchanged by the kidneys.²³

The copolymer mixture was diluted with deionized water, mixed until the inert particles were evenly dispersed, and then placed in 1-cc cylinders with small pistons placed in the proximal ends. The distal end of each cylinder could then be attached to a 1-cc syringe with a Luer lock on the end, and a piston member could be inserted in the proximal barrel.

Cannula

A special cannula was fabricated to dispense the copolymer mixture, employing a tapered blunt tip with a blunt hole on the taper. The hole portion occupies less than 50 percent of the cross-sectional diameter of the cannula, and the

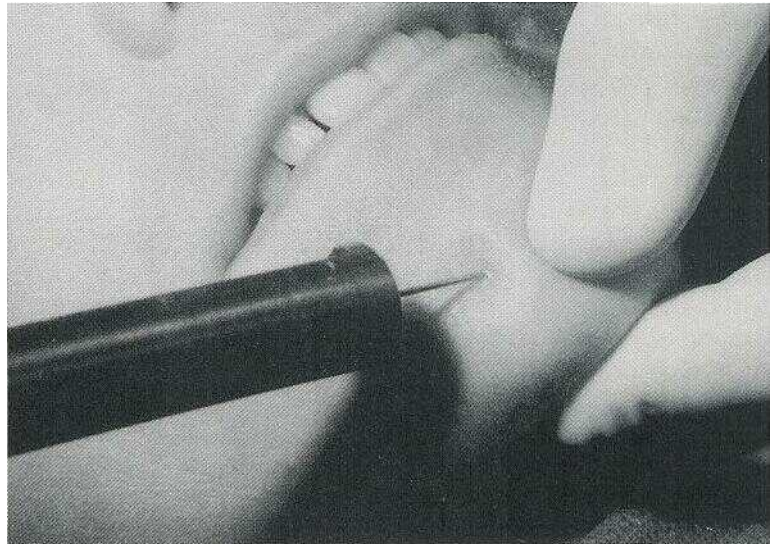


FIG. 2. (Left) A blunt-tipped dissection/injection/aspiration biopsy cannula was developed that has an offset hole on the taper of the tip so that the blunted forward end will push aside the noble structures of arteries, nerves, and veins. Because the blunt tip goes up greater than 50 percent of the cross-sectional diameter and the wall of the hole is deburred and smooth, center punching is not likely. (Right) Cannula tip being used to inject biphasic copolymer microimplants in a chin augmentation.

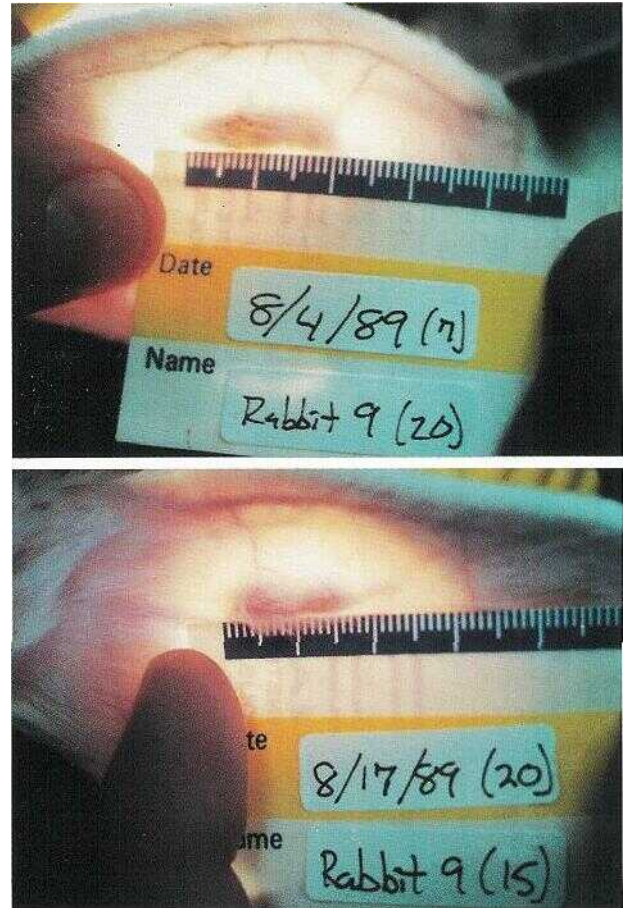


FIG. 3. The rabbit's ear is easily transilluminated so that the injection site to receive the biphasic copolymer can be measured carefully and accurately for length, thickness, width, and phototransmission. In these views, the injection site is approximately equal when seen at 1 (above) and 3 (below) weeks.

blunted bullet tip portion is greater than 50 percent of the cross-sectional surface (Fig. 2).

Injection Gun

A special highly leveraged injection ratchet mechanism with a significant mechanical advantage was utilized to accept the syringe cartridges

and deliver precise amounts of the gel mixture through the cannula in a dependable and predictable manner.

Hosts

Twenty large adult white rabbits were selected for the initial experiments. The rabbits were

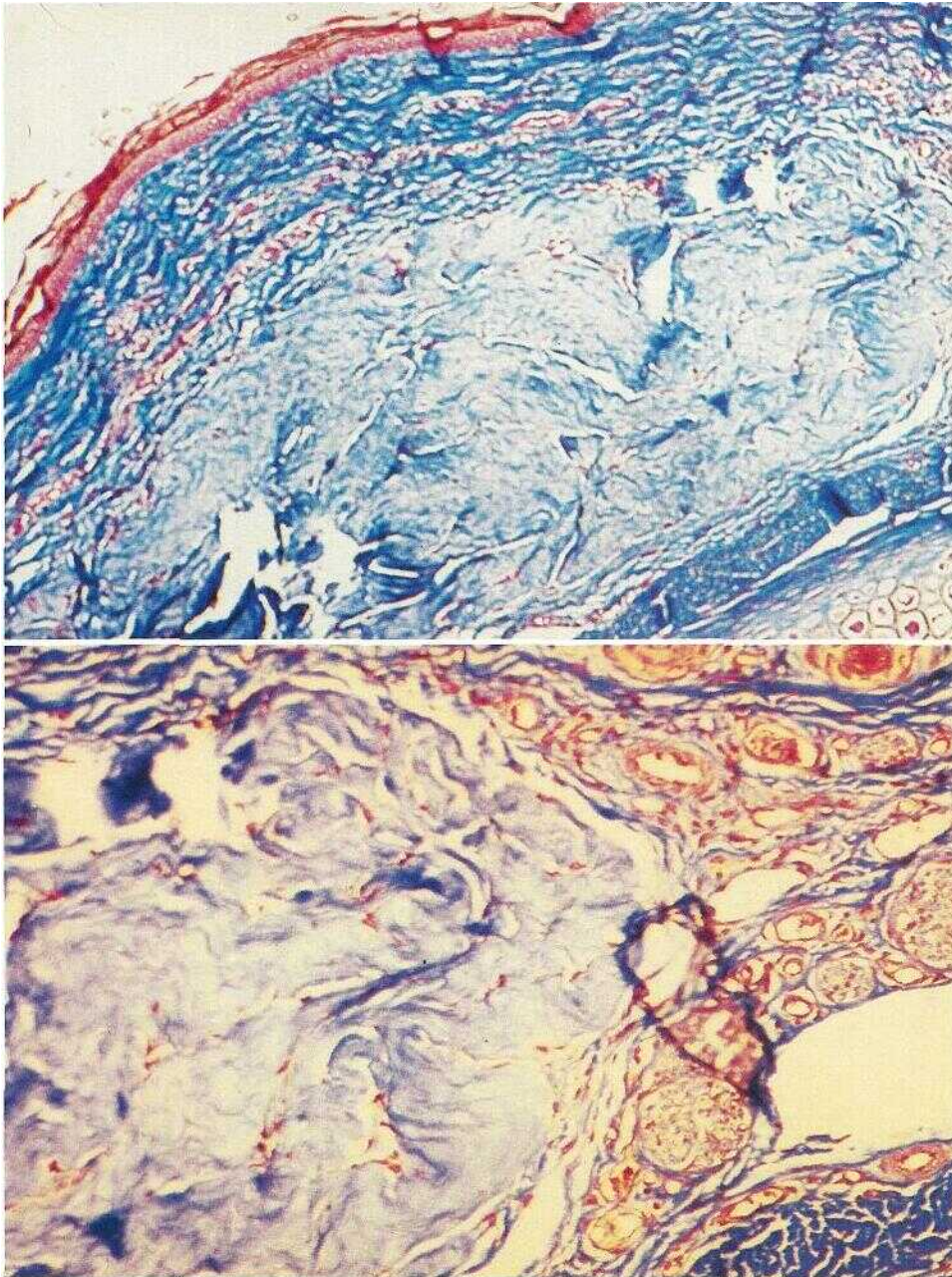


FIG. 4. (*Above*) This trichrome stain of a cross section of the rabbit ear shows the site of injection of commercially available collagen-containing material (Zyplast). Here, at 3 days, can be seen the swirls of collagen fibrils as they are delivered from the needle. The collagen fibrils can be seen staining a bright blue that is characteristic of a trichrome stain (X 100). (*Below*) At approximately 200X magnification, the injection of collagen (Zyplast) can be seen to have developed capillary ingrowth. The bright blue staining of the collagen fibrils is degenerating to a lighter blue on trichrome stain.

obtained from a licensed supplier. Their ears were anesthetized with lidocaine 1% and epinephrine 1:100,000 in the areas to receive the copolymer. The cannula was then passed subcu-

taneously through remote puncture sites, and the test material was injected in a carefully controlled manner—only during the withdrawal of the cannula. These rabbit ears were subsequently mon-

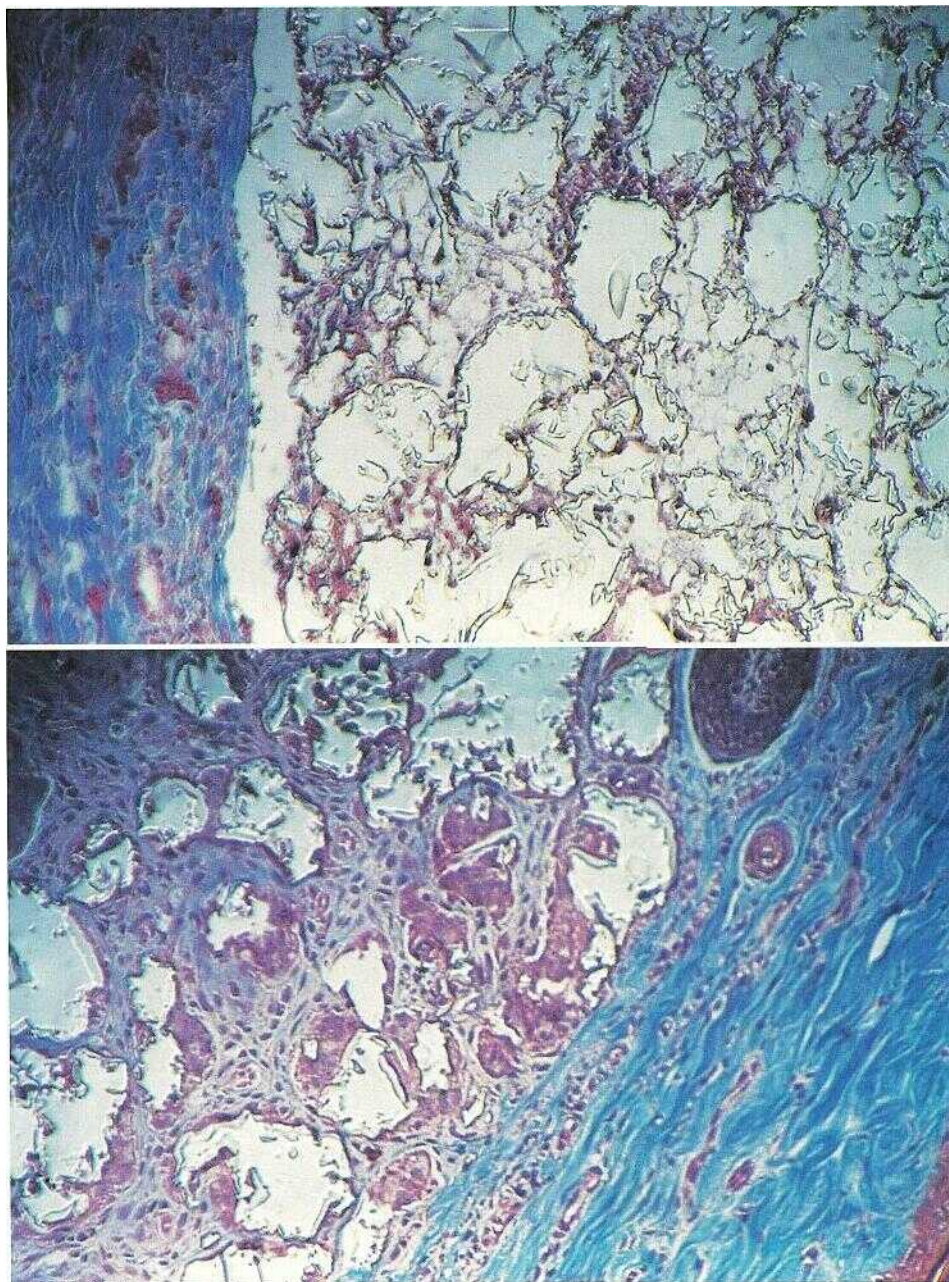


FIG. 5. (*Above*) Bioplastique copolymer microparticles injected into rabbit ear seen here 3 days after injection (trichrome stain; X200). The biphasic copolymer can be seen with the gel phase of the copolymer having been scavenged by the host inflammatory cells and here being replaced by the pink-staining fibrin. The voids are spaces occupied by the permanent textured microparticles. (*Below*) By 3 weeks, the pink-staining fibrin has been almost completely replaced by pale blue-staining collagen. Each particle is engulfed by its own host-prosthesis interface of host collagen. This controlled fibrosis extends throughout the area of implantation, and every single particle is individually encased in host collagen. Note that the surrounding blue-staining connective tissue has no migrant or errant particles. They are all contained within the implantation site.

itored and measured by micrometer. Transillumination, photographs, and histologic sections were done at 1, 3, and 6 weeks and 3 and 6 months (Fig. 3).

Controls

Commercially available collagen derivatives (Zyplast, Zyderm, and Fibril) were obtained and injected in the subcutaneous plane in adjacent sites in the rabbit ears using the 27-gauge (for Zyderm and Zyplast) and 20-gauge (for Fibril) needles. The needles and syringes used were those provided by the respective manufacturers.

Nodes

Prior to the sacrifice of each of these experimental rabbits, their ears were injected with methylene blue dye in the subcutaneous plane 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. In addition, histologic sections were prepared from the base of each ear, whether or not lymph nodes were palpated.

RESULTS

Histologic sections taken at 1 week showed that the initial collagen-containing injections (Zyplast, Zyderm, and Fibril) had resulted in collagen-containing boli, as demonstrated on trichrome stain as blue, indicating collagen (Fig. 4, *above*). Within 2 weeks, these areas had become vascularized. At 3 weeks, no residual collagen could be found (Fig. 4, *below*).

The histologic sections of Bioplastique (the microparticles under study) evidenced a dynamic transition in which the gel phase of the copolymer was replaced by a fibrin and protocollagen matrix surrounding each of the microparticles (Fig. 5, *above*). At 3 days, the fibrin matrix was complete, with all the gel having been removed by the host. Connective-tissue cells had developed and had begun to replace the matrix with collagen fibrils, which stained bluish by trichrome (Fig. 5, *below*). By the sixth week, this fibrosis was complete, and each individual textured particle appeared to be encased in its own individual interconnected covering of fibrous tissue (Fig. 5, *below*).

Histologic examination of the regional lymph nodes at the base of the rabbit ears revealed no migration of particles. Cross sections of the ear below the injected area showed no particles. Through transillumination, the size and density



FIG. 6. (*Above*) The subcutaneous injection through a remote puncture site of this deficient cleft lip along the philtral ridge was accomplished on an outpatient basis under local anesthetic. (*Below*) The result is seen here at 4 weeks.

of the areas of injection were easily and atraumatically monitored for each rabbit. No textured microimplants were found at the base of the ears or in the regional lymph nodes of any of the rabbits under study.

The dimensions of the subcutaneous deposits of textured microimplants remained approximately the same throughout the period of study, as was evidenced by transillumination, photographic record, and micrometer measurement (Fig. 10). Opacity was noted to decrease over the first few weeks as transillumination became brighter but then appeared to stabilize between the end of the first and the sixth months.

DISCUSSION

Although injection of the collagen-containing materials (Zyderm, Zyplast, and Fibril) created immediate soft-tissue augmentation, these substances—which are only 3.5 to 6.5 percent solid collagen material—soon became invaded by host capillaries and were absorbed. In these rabbit



FIG. 7. (Above, left) This 42-year-old white woman has had previous cheek augmentation with solid implants. She has now complained of hollowness of the cheeks beneath the implants. She is happy with the malar prominence but would like the cheeks filled in. (Above, right) Seen here at 1 month following injection of Bioplastique biphasic copolymer microimplant particles, there is a reasonable improvement. (Below, left) Patient seen 10 months postoperatively. (Below, right) At 1 year, correction is maintained.

ears, collagen was seen to degenerate from the blue stain (indicating collagen) seen on initial injection to a pink stain (indicating fibrin matrix) within 2 weeks. In rabbit ears (which may be a highly vascularized site), injected reconstituted bovine collagen disappears within a matter of weeks.

CONCLUSIONS

The subcutaneous injection of the biphasic copolymer microimplant material Bioplastique reveals a prompt replacement of the biocompa-

tible gel by host fibrin or procollagen within a day or two. As this fibrin substitution is completed, some new capillaries penetrate the space between the solid particles, and fibroblasts appear within the matrix and begin fabricating host collagen by the sixth day. As evidenced by the modification of the stain from pink (fibrin) to blue (collagen), the transformation is complete within 3 weeks. It can thus be concluded that these inert textured microimplants stimulate a host-collagen matrix that anchors them in place, resulting in permanent soft-tissue augmentation.

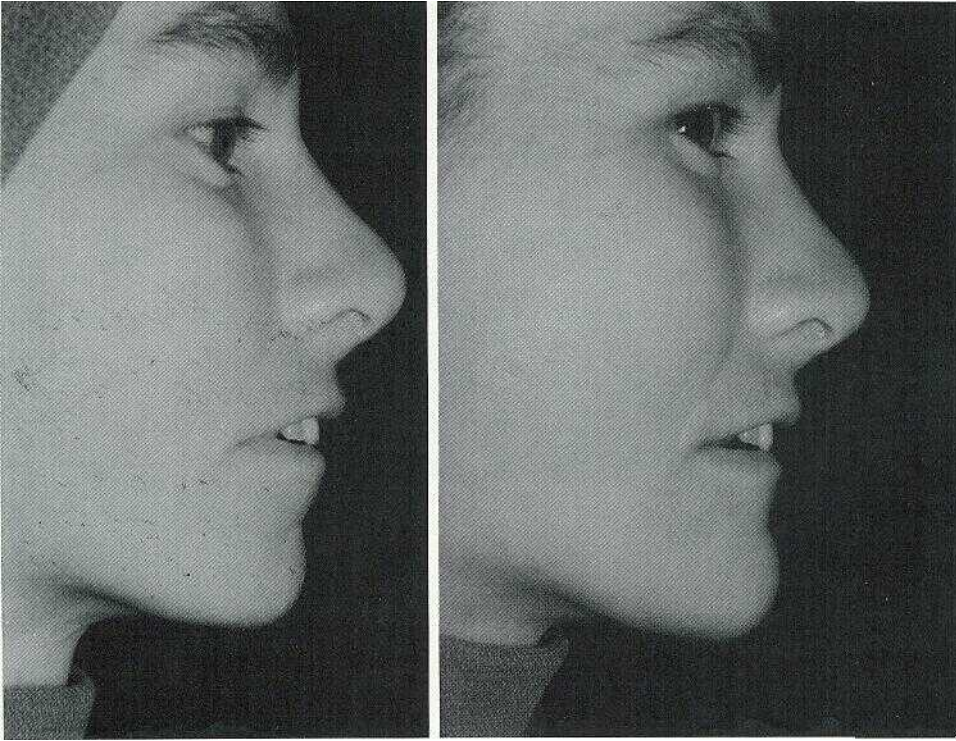


FIG. 8. (Left) Cosmetic chin augmentation is easily accomplished with Bioplastique injection surgery. Patient is seen here immediately prior to injection. (Right) Chin augmentation patient shown immediately after injection.

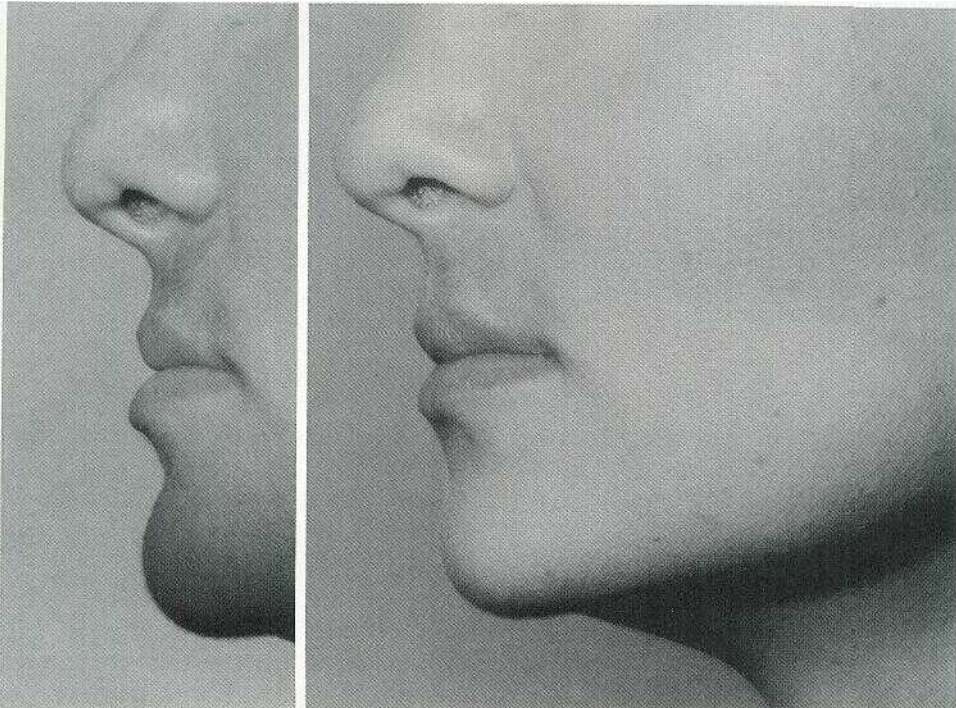


FIG. 9. This patient was treated for cleft lip and nose. (Left) Patient prior to procedure. (Right) Patient after injection with approximately 0.6 cc of Bioplastique biphasic copolymer.

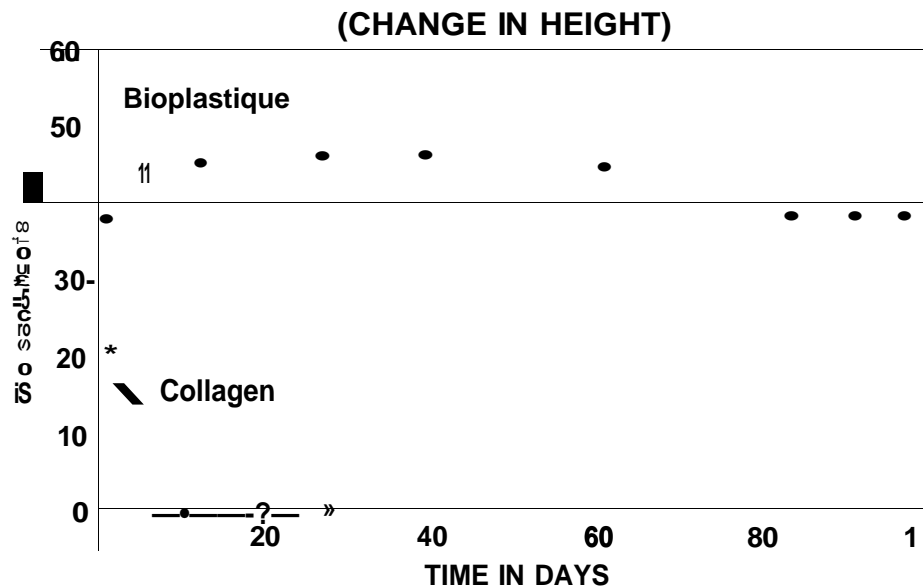


FIG. 10. Implant thickness change. Rabbit ears injected with Bioplastique copolymer micro-particles and collagen (Zyplast).

Transillumination

The decreased light transmission seen in the initial days following injection may be due to some subcutaneous bleeding or hematoma formation as a result of needle trauma. Since the dimensions of the subcutaneous implantation did not change appreciably during the period of study, and since replacement of the relatively translucent gel by the relatively opaque host collagen would not explain the progressive opacity decrease, the trauma (minimal bleeding) of the injection appears to be the more likely explanation.

Host Suitability

Despite our encouraging results, rabbit ears may not be a good experimental model to test how such subcutaneous injections will behave in the rest of the mammalian body. The cartilage framework and the shape of the ear hold it in a reasonable position with little stress or pressure on the injected subcutaneous prostheses. It would appear that splinting the surrounding area or otherwise minimizing the tension and motion would be a useful technique in the effective clinical use of such an injectable subcutaneous soft-tissue augmentation system, especially in this biphasic configuration. Since effective formation of the collagen matrix requires the particles to remain separated as they originally are when interspersed, any motion, bending, or stress on the area of injection may cause migration of the

particles before fibrosis is complete. It is anticipated that injecting the copolymer mixture in many fine tunnels, in many different planes, in many different directions within the treated area may minimize this migration.

Based on these animal experiments, clinical studies have begun. We have found this substance useful in cleft lips, depressed scars of chicken pox, indentations resulting from overzealous liposuction, glabella frown wrinkles, and soft-tissue augmentation of thin lips. Since developing these special dispersion and fixation techniques, we have had reasonable clinical results for over 1 year, as seen in Figures 6 to 9.

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