

Injectable Hyaluronic Acid Gel for Soft Tissue Augmentation

A Clinical and Histological Study

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BACKGROUND. Several biomaterials are available for the purpose of soft tissue augmentation, but none of them has all the properties of the ideal filler material. The recent development of hyaluronic acid gels for dermal implantation give the physician new possibilities of effective treatment in this field.

OBJECTIVE. This study provides a clinical and histological evaluation of safety and efficacy of a cross-linked stabilized non-animal hyaluronic acid gel (Restylane, Q-Med, Uppsala, Sweden) to determine its characteristics, advantages, disadvantages, and side-effects.

METHODS. 158 patients were treated with facial intradermal implant of hyaluronic acid gel for augmentation therapy of wrinkles and folds, and for lip augmentation and/or recontouring. The results were evaluated in all patients by subjective judgement by the physician and the patient, and by photographic method at time 0 and after 1, 2, 4 and 8 months from the procedure. In addition, a smaller histological study was carried out in five volunteer patients for a term of 52 weeks to determine the interaction and duration of the material in human healthy skin.

RESULTS. Clinically, both the physicians' and patients' evaluations revealed very satisfactory results, with a global 78.5% and 73.4% respectively of moderate or marked improvement after eight months, independent of the treated area. The photographic evaluation revealed even better results with a 80.4% of moderate or marked improvement after 8 months. The safety evaluation showed a 12.5% of postoperative immediate adverse events, that were localized and transient. There was no evidence of major systemic side effects. Histologically, the product was shown to be long-lasting and well tolerated as judged by histological techniques.

CONCLUSIONS. Stabilized, non-animal, hyaluronic acid gel is well tolerated and effective in augmentation therapy of soft tissues of the face. This material presents several advantages in comparison to previously used injectable biomaterials and expands the arsenal of therapeutic tools in the field of soft tissue augmentation. © 1998 by the American Society for Dermatologic Surgery, Inc. *Dermatol Surg* 1998;24:1317-1325.

The search for the ideal augmentation material for facial soft tissues has been an ongoing effort for many years. Injectable soft tissue substitutes provide an affordable, non-surgical alternative for correcting contour defects in facial skin. A safe and effective material for this purpose should respect certain characteristics: it should be biocompatible, non-antigenic, nonpyrogenic, noninflammatory, nontoxic, easy to use, stable after injection, non-migratory, long-lasting but reabsorbable, natural looking and not too expensive.^{1,2} Although many biomaterials are currently on the market, none meets all the above criteria. The recent development of hyaluronic acid gels for dermal implantation is therefore particularly interesting for the cutaneous surgeon involved in treating the aging face.

Hyaluronic acid is a glycosaminoglycan biopolymer composed of alternating residues of the monosacchar-

ides D-glucuronic acid and N-acetyl-D-glucosamine linked in repeating units. This substance has an enormous ability to bind water and form hydrated polymers of high viscosity. Hyaluronic acid is naturally occurring, in the same identical form, in the intercellular matrix of dermal layers of the skin of all species, and has an extraordinarily high biological compatibility. The amount of hyaluronic acid in the skin decreases with age, and loss of this substance results in reduced dermal hydration and increased folding.³

Exogenous hyaluronic acid is rapidly cleared from the dermis and degraded in the liver to carbon dioxide and water.^{4,5} Hyaluronic acid products reside no longer than some days in the dermal tissue and have no significance in augmentation therapy: for this reason, it is therefore essential to use a modified hyaluronic acid that yields a long lasting effect while maintaining good biocompatibility.

When the hyaluronic acid chains are chemically cross-linked, the solubility and the rheological properties of the material change to become more viscous and water-insoluble as gels. The physical properties of hy-

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Table 1. Response to Hyaluronic Acid Gel Implant: Glabella

Glabella (n 56)	Time 0			Month 1			Month 2			Month 4			Month 8		
	Ps	Pt	Ph	Ps	Pt	Ph	Ps	Pt	Ph	Ps	Pt	Ph	Ps	Pt	Ph
No improvement	0	0	0	0	0	0	1	2	1	3	4	2	8	5	4
Slight improvement	0	1	0	2	4	1	5	2	3	9	9	4	8	12	7
Moderate improvement	8	11	7	11	16	11	12	23	16	12	22	25	18	23	26
Marked improvement	47	44	48	43	36	44	38	29	36	32	21	25	22	16	19
Overcorrection	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0

Ph = Photographic evaluations; Ps = Physician; Pt = Patient.

treated area was performed in order to correct possible uneven beading of the product. A different technique is used for the lips, where recontouring is obtained by linearly injecting the vermilion border and volumetric augmentation is obtained by directly injecting into the vermilion.

Evaluation

The efficacy of hyaluronic acid gel implant was evaluated in all patients by subjective judgement of the physician and the patient, and by photographic method at time 0 (before and immediately after the first or the touch up implant) and 1, 2, 4, and 8 months postoperatively.

Photos were taken using a 135 mm Nikon SLR together with a 60 mm Nikkor macro lens. The film used was Fuji Super-G ISO 800. The distance to the patients was one meter. The lighting consisted of an electronic flash, diffused with a bouncer. The lighting was identical on both the before and the after pictures.

The physician's and patient's evaluations were graded as: no improvement, slight improvement (1-33% correction), moderate improvement (34-66% correction), marked improvement (67-100% correction), and overcorrection.

The photographic evaluation has been done for all patients by the same physician (MLR) using the same rating scale as

above. The results presented are those at the eighth month after treatment.

Results

All patients included in the study were white caucasian women with a mean age of 36.8 (range 26-68). Tables 1-4 show the efficacy evaluation data for anatomic location in the physician's, patient's and photographic evaluation. Figures 1-4 graphically show the mean results among the three evaluation methods for anatomic location. Naso-labial folds and lips turned out to be the most effectively treated areas with respectively 82.2% and 79.9% of moderate or marked improvement at eighth month (Figures 5-10).

Independently of the treated area, the overall percentage of moderate or marked improvement after 8 months is very satisfactory: 78.5% in the physician's evaluation, 73.4% in the patient's evaluation, 80.4% in the photographic evaluation, as shown in a graphic comparison among the three evaluation methods (Figure 11).

The safety evaluation (Table 5) showed a 12.5% (34 cases) of immediate adverse events, that were localized and transient: the most commonly reported were bruising, tenderness, discomfort, edema and erythema at the treatment site. All of these adverse events, which were related to the implant,

Table 2. Response to Hyaluronic Acid Gel Implant: Naso-labial Folds

Naso-labial folds (n 99)	Time 0			Month 1			Month 2			Month 4			Month 8		
	Ps	Pt	Ph	Ps	Pt	Ph	Ps	Pt	Ph	Ps	Pt	Ph	Ps	Pt	Ph
No improvement	0	0	0	0	1	0	0	4	0	1	6	2	7	8	7
Slight improvement	0	0	0	2	8	1	4	10	3	7	9	7	10	8	11
Moderate improvement	2	1	0	6	14	5	17	20	16	20	30	17	37	45	40
Marked improvement	97	97	99	91	76	93	78	65	80	71	54	73	45	38	41
Overcorrection	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0

Abbreviations as in Table 1.

Table 3. Response to Hyaluronic Acid Gel Implant: Oral Commissure Folds

Oral Commissure Folds (n 36)	Time 0			Month 1			Month 2			Month 4			Month 8		
	Ps	Pt	Ph	Ps	Pt	Ph	Ps	Pt	Ph	Ps	Pt	Ph	Ps	Pt	Ph
No improvement	0	0	0	0	0	0	0	0	0	0	2	1	3	5	4
Slight improvement	0	1	0	0	4	0	1	4	1	4	3	3	6	6	5
Moderate improvement	3	4	1	8	5	7	9	11	10	11	15	13	16	15	15
Marked improvement	30	31	33	28	27	29	26	21	25	21	16	19	11	10	12
Overcorrection	3	0	2	0	0	0	0	0	0	0	0	0	0	0	0

Abbreviations as in Table 1.

aluronic acid gels are controlled by the molecular weight and the concentration of the material and by the degree of cross-linking.⁶ An enhancement of the physical properties of the substance can be therefore obtained by modifying these parameters in order to produce highly concentrated cross-linked high molecular weight derivatives that keep the biological compatibility of the native polymer but show a lower dissolution rate and longer residence time when injected into the dermis.⁶⁻¹¹

The most commonly used sources of hyaluronic acid are rooster combs, the umbilical cord, the vitreous humour, tendons, skin and bacterial cultures.^{4,12}

Currently, there are two hyaluronic acid gels for dermal augmentation in Europe, Hylaform (Biomatrix Inc., USA), produced by extraction from rooster combs, has a higher molecular weight but a lower concentration (6 mg/mL), and its visco-elastic properties have a more elastic tendency; Restylane (Q-med, Sweden), produced by bacterial fermentation, has a lower molecular weight but a higher concentration (20 mg/mL), and its visco-elastic properties have a more viscous tendency.¹² Both gels are very pure and contain only low levels of impurities; these are avian proteins for Hylaform and fermentation byproducts for Restylane. The impurities are included in the hyaluronic acid molecular network and are reported to be neither toxic nor to elicit immunological response.^{8,11,13}

The value of a material that has physical and mechanical properties particularly suitable for soft tissue augmentation and biological characteristics similar to those of dermis is worth investigation.

Materials and Methods

Our study was designed to evaluate safety and efficacy of a cross-linked stabilized non-animal hyaluronic acid gel (Restylane, Q-Med, Uppsala, Sweden) by determining its characteristics, advantages, disadvantages and side effects. We also performed a smaller histological investigation to determine the duration of the implanted material and the tissue response as compared to a standard degradable collagen implant (Zyplast, Collagen Corp., USA).

Materials

Restylane is a medical device currently in use in Europe, where it is approved under the rules of Council Directive 93/42/EEC Annex II accordingly to the requirements of the standards SS-EN ISO 9001, SS-EN 46001 and SS-EN 556. The material is not FDA-approved.

Restylane is produced in cultures of equine streptococci by fermentation in presence of sugar; the fermentation material is then alcohol-precipitated, filtered and dried. The hyaluronic acid chains are then chemically stabilized through permanent epoxidic cross-links that the manufacturer reports to alter only about 1% of the hyaluronan molecular network.¹⁰ The resulting viscoelastic transparent gel, suitable for intradermal

injection, has a concentration of 20 mg/mL and is no longer water-soluble but retains its affinity for water and its ability to swell and form hydrated copolymers. The material is heat sterilized in its final container. It is delivered in disposable syringes (0.7 ml) ready for use. The implantation syringe contains only hyaluronic acid gel and water; no local anesthetic is added in order to keep the material free of any component that could lessen the safety of the implant.

Restylane, although potentially free of animal peptides, could be associated with fermentation byproducts or bacterial toxins. For this reason we always performed a preliminary skin test at the beginning of our experience. The skin test was a double test as it is usually done before collagen implants; in no case did we record immediate or delayed hypersensitivity nor local or systemic allergic reactions. The material is reported not to have yet elicited humoral or cell-mediated immune reactions.^{10,13}

Zyplast is a bovine skin collagen 35 mg/ml that is purified and cross-linked by glutaraldehyde and aseptically dispensed in a suspension of normal saline with 0.3% lidocaine. It has been in use for more than ten years and is considered as the reference injectable material for soft tissue augmentation.¹¹

Clinical Study

Patients and Study Design

In this open study, 158 consecutive patients were treated with facial intra-dermal implant of hyaluronic acid gel (Restylane) for a total of 273 areas.

The inclusion criteria were: 1) Request of cosmetic treatment for correction of wrinkles and/or folds, and for lip augmentation and/or recontouring, 2) Patients willing to return for follow-up, 3) Informed consent. The non inclusion criteria were: 1) Bleeding disorders, 2) Antiplatelet or anticoagulant therapy, 3) Pregnancy or lactation, 4) Patients not willing to return for follow-up.

Follow-up evaluations were made at month 1, month 2, month 4 and month 8 postoperatively. The anatomic locations treated are: the glabellar lines (n 56), the naso-labial folds (n 99), the oral commissure folds (n 36), and the lips for augmentation and/or recontouring (n 78). Furthermore the material has been used to treat depressed acne scars (n = 4). Fine or superficial lines have not been treated. Patients requiring further implants (n = 11) or lost of follow-up (n = 4) were excluded from the study.

The implant procedure has been single or a touch up has been done after 8-10 days. No further procedure has been done. The average amount of material used for a single patient was 1.4 ml.

Implantation Technique

A local anesthetic cream (lidocaine-prilocaine) could be administered before the injection, while nerve block anesthesia of the infraorbital and mental nerves (mepivacaine 3%, 4 ml) has always been used when treating the lips. Common antiseptic solutions have been used to prepare the skin.

The material has been placed into the mid dermis using 27 or 30 gauge needles 13-20 mm long, bevel up, injecting longitudinally to the wrinkle with a 33° angle to the plane of the skin. Our technique consisted of serial injections creating a continuous row of observable swellings without blanching, the delivering of the material being done in withdrawing the needle. An immediate moulding with finger pressure of the

Table 4. Response to Hyaluronic Acid Gel Implant: Lips

Lips (n 78) Evaluation	Time 0			Month 1			Month 2			Month 4			Month 8		
	Ps	Pt	Ph	Ps	Pt	Ph	Ps	Pt	Ph	Ps	Pt	Ph	Ps	Pt	Ph
No improvement	0	0	0	0	2	0	0	4	0	2	7	2	5	11	3
Slight improvement	0	0	0	1	4	0	7	7	4	12	11	9	7	12	9
Moderate improvement	0	1	0	15	11	14	21	15	20	30	23	28	43	31	46
Marked improvement	69	66	72	62	61	64	50	52	54	34	37	39	23	24	20
Overcorrection	9	11	6	0	0	0	0	0	0	0	0	0	0	0	0

Abbreviations as in Table 1.

lasted less than three days and resolved spontaneously; in one case erythema and swelling lasted 5 days. Thirteen patients complained, particularly after lip augmentation, of an intermittent swelling of the implanted material. This swelling was more relevant in the first post-operative week, but was present all through the period of the study. This event was, in some cases, stimulated by exercise, sun exposure and menstruation and was probably due to the hydrophilic properties of hyaluronic acid, but may have also been due to a possible fermentation contamination or to immunologic phenomena, as reported with collagen and hyaluronic acid gel itself.¹² There have been no sequelae to these events. There was no clinical evidence of major systemic side effects nor of acute or chronic hypersensitivity. No blood chemistry data are available.

Figure 1. Hyaluronic acid gel implant: glabella. Mean among the three evaluation methods.

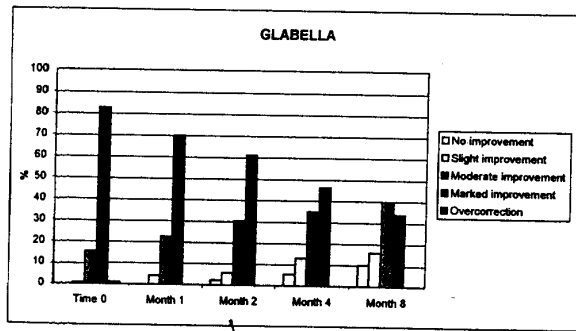
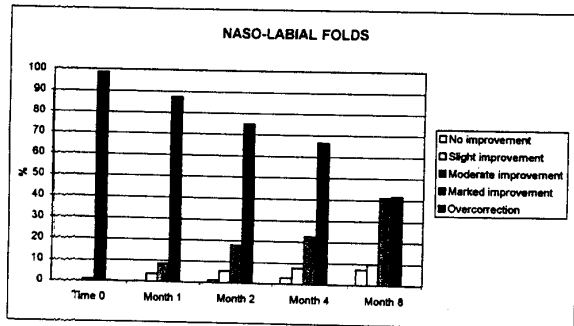


Figure 2. Hyaluronic acid gel implant: naso-labial folds. Mean among the three evaluation methods.



Histological Study

Patients and Study Design

Five female volunteers aged 26 to 54 were recruited. Prior to inclusion in the study they were examined for skin diseases and double tested for possible sensitivity to hyaluronic acid gel and collagen (Zyplast, Collagen Corp., USA). The treatment consisted of spot injections of 0.05 ml of each product at four sites alternating between the products on the volar surface of the left and right forearm; each person received a total of eight implants.

Observations and Histochemical Technique

Each person received four Restylane and four Zyplast injections at time 0. Each couple of implants was intended to be

Figure 3. Hyaluronic acid gel implant: oral commissure folds. Mean among the three evaluation methods.

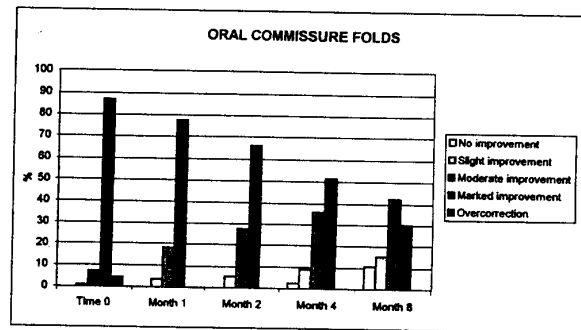


Figure 4. Hyaluronic acid gel implant: lips. Mean among the three evaluation methods.

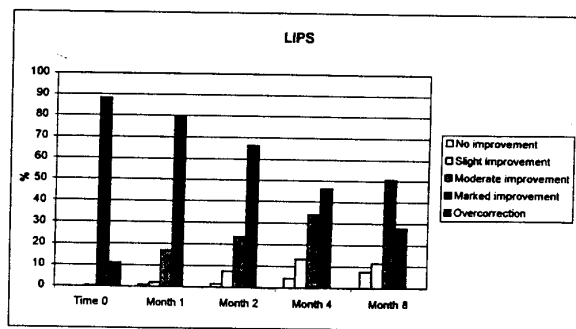




Figure 5. Naso-labial folds, before treatment.

taken as biopsy specimens at 4th, 12th, 24th and 52nd week for histological examination. In addition, all the implants were visually evaluated, if recognizable, at all time-points provided that they were not previously biopsied.

The visual score used for evaluating the implants was as follows: 0: visible implant with normal skin, 1: bulking with normal skin, and 2: inflammatory reaction.

Skin biopsies were fixed in formaldehyde and processed



Figure 8. Oral commissure folds, after treatment.

for routine histology. Thin sections (5μ) were prepared and stained with hematoxyline-eosin, Picro-Sirius (for collagen) and Toluidine blue (for hyaluronic acid). The slides were blindly evaluated by two experienced pathologists and discussed until consensus was reached by them. The pathologists did not know the nature of the samples and were asked to evaluate the tissue with respect to inflammation, foreign body reaction and fibrosis. In addition, they were asked to describe

Figure 6. Naso-labial folds, after treatment.



Figure 7. Oral commissure folds, before treatment.



Figure 9. Lips, before treatment.



Figure 10. Lips, after treatment.



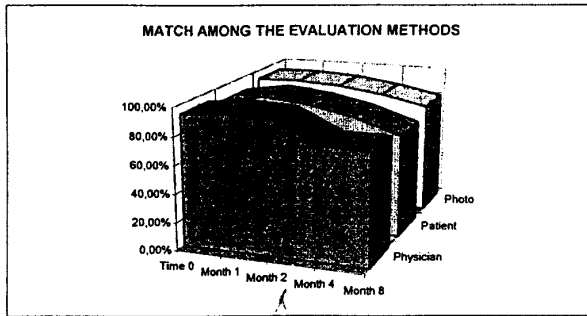


Figure 11. Hyaluronic acid gel implant: match among the three evaluation methods independently of the treated area.

the presence and nature of the implant in the biopsy specimen.

The histologic score used for evaluating the biopsies was defined as the level of foreign body reaction: 0: no visible reaction, 1: slight reaction with a few inflammatory cells, 2: clear inflammatory reaction with one or two giant cells, 3: fibrous tissue with inflammatory cells, lymphocytes and giant

Table 5. Immediate Implant Related Adverse Events

Adverse Events	N of Cases
Intermittent swelling	13
Erythema	7
Edema	5
Discomfort	5
Tenderness	3
Bruising	3
Itching	1
Pain	1

Table 6. Histologic and Visual Observations of 4th Week Site and Visual Observations of All Remnant Implant Sites

ID	4th week site Histologic Score Zyplast/Restylane	4th week site Visual Score Zyplast/Restylane	12th week site Visual Score Zyplast/Restylane	24th week site Visual Score Zyplast/Restylane	52nd week site Visual Score Zyplast/Restylane
Subj. 1	1/0	0/0	0/0	0/0	0/0
Subj. 2	0/0	0/0	0/0	0/0	0/0
Subj. 3	0/1	0/1	0/1	0/0	0/0
Subj. 4	0/1	0/1	0/1	0/1	0/1
Subj. 5	0/0	0/0	0/0	0/0	0/0

0: visible implant with normal skin, 1: bulking with normal skin, 2: inflammatory reaction.

Table 7. Histologic and Visual Observations of 12th Week Site and Visual Observations of All Remnant Implant Sites

ID	12th week site Histologic Score Zyplast/Restylane	12th week site Visual Score Zyplast/Restylane	24th week site Visual Score Zyplast/Restylane	52nd week site Visual Score Zyplast/Restylane
Subj. 1	-/1	0/0	0/0	0/0
Subj. 2	0/0	0/0	0/0	0/0
Subj. 3	1/1	0/0	0/0	0/0
Subj. 4	1/1	0/1	0/2	0/0
Subj. 5	0/1	0/0	0/0	0/0

—: no recognizable implant. 0: visible implant with normal skin, 1: bulking with normal skin, 2: inflammatory reaction.

Table 8. Histologic and Visual Observations of 24th Week Site and Visual Observations of All Remnant Implant Sites

ID	24th week site Histologic Score Zyplast/Restylane	24th week site Visual Score Zyplast/Restylane	52nd week site Visual Score Zyplast/Restylane
Subj. 1	-/0	-/0	-/0
Subj. 2	-/0	-/0	-/0
Subj. 3	-/1	0/0	0/0
Subj. 4	-/2	-/1	-/0
Subj. 5	-/0	-/0	-/0

No recognizable implant. 0: visible implant with normal skin, 1: bulking with normal skin, 2: inflammatory reaction.

cells, and 4: granuloma with encapsulated implant-clear foreign body reaction.

Results

All implant sites had a redness reaction at the time of injection that completely recovered within one day. All implant sites showed a visual presence of the same magnitude at the start of the test. In the course of the observation period, no single spot showed any reaction or sign of important inflammation. In two occasions a slight redness was observed in all remnant implants on two individuals; this observation was associated with a systemic viral infection and was probably caused by immunologic phenomena related to that situation.

Tables 6-9 summarize the results. Each table details the histologic and visual score of the couple of implants biopsied at that time-point and the visual score of all other remnant implant sites. The Zyplast implants presented a gradual shrinkage of the implant between the

Table 9. Histologic and Visual Observations of 52nd Week Site.

ID	52nd week site Histologic Score Zyplast/Restylane	52nd week site Visual Score Zyplast/Restylane
Subj. 1	-/-	-/-
Subj. 2	-/0	-/0
Subj. 3	-/0	-/0
Subj. 4	-/*	-/0
Subj. 5	-/*	-/0

—: no recognizable implant. 0: visible implant with normal skin, 1: bulking with normal skin, 2: inflammatory reaction.

* These histological blocks were lost due to a technical problem.

12th and the 24th week; at week 24 only two implant sites out of ten were visually recognizable. These two sites had a pigmented area over the reabsorbed spot although histological examination showed normal skin. At week 52 no implant was present (Figure 12). The Restylane implants maintained their spot size between the 12th and the 24th week; at week 52 four of the implants were still clearly visible under the skin. Staining for hyaluronic acid revealed the presence of such material but with a significantly more watery appearance than at earlier biopsies (Figure 13). This feature of hyaluronic acid gel, called isovolemic degradation,⁴ allows the product to hold more water the less concentrated it is.

All of the specimens were free from fibrosis and severe foreign body reaction but often presented a slight inflammatory reaction. There were no differences in the presence of cells around each of the implants over time throughout the 52 weeks of observation.

Discussion

Our study shows that hyaluronic acid gel (Restylane) is well tolerated and effective in augmentation therapy of soft tissues of the face.

Hyaluronic acid revealed several advantages in comparison to previously used injectable biomaterials. Its high biocompatibility allowed us to eliminate the preliminary skin test without any local or systemic immunologic reaction; for this reason it should become the material of choice in those patients hypersensitive to bovine collagen and should be indicated in case of "urgent" implant. Being produced by biotechnology, it carries very little risk of transmissible infectious bacterial or viral diseases (BSE). Not undergoing immediate reabsorption, it produces an instant result.

Hyaluronic acid gel is versatile enough to be injected through 27 or 30 gauge needles, and requires a full correction of the defect; the material is however forgiving for the physician in case of slight overcorrection (about 20% in our experience). After the injection, the material should be lightly massaged to conform to the



A



B



C

Figure 12. Zyplast: histological sections from three different time points. The implant is clearly visible at weeks 1 and 12 but not at week 24. This later site had no bulking but was identified by the presence of a slight hyperpigmentation (H&E plus Picro-Sirius, original magnification $\times 200$).

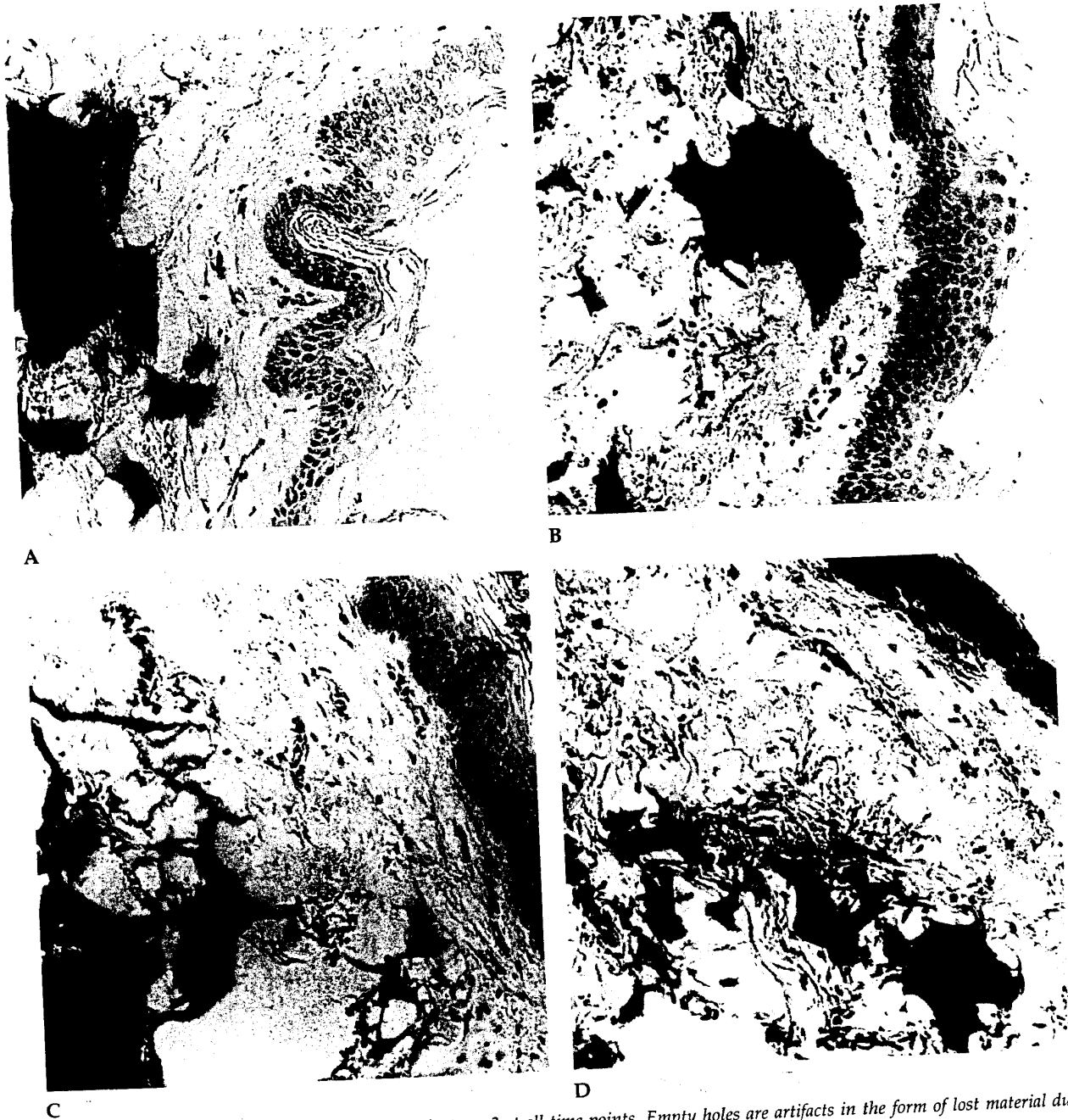


Figure 13. Restylane: histological section from patient no. 3 at all time points. Empty holes are artifacts in the form of lost material due to the washing and staining procedure (H&E plus Toluidine Blue, original magnification $\times 200$).

contour of the surrounding tissues. After the first treatment, an additional implantation may be necessary to achieve the desired level of correction.

Hyaluronic acid gel has physical properties that are typical of thixotropic fluids and make its implant easy and durable; in fact, its low viscosity at high shear rates (when forced through a needle) facilitate its injection,

whereas its high viscosity at low shear rates (when stationary) allows a long residence in the tissues.^{4,12} The physical characteristics of the gel also depend on temperature; we learned from our clinical experience that at higher temperatures the gel flows more easily. For these reasons, the use of narrow needles (30 g) may cause a possible difficulty in the injection of the product at the

beginning of the procedure or a discontinuity of delivering of the product after a stop; it is sufficient to warm the syringe in the hand before implantation to avoid this problem.

Like any other filler material, hyaluronic acid gel gives best results in those defects of the face whose etiology is not muscular or gravitational in origin and a "real" volumetric augmentation is needed; in our experience, Restylane turned out to be particularly suitable for lip augmentation and recontouring, with a satisfactory volumetric augmentation and no nodule sensation by the patient.

The disadvantages include a greater discomfort at the injection site since the material lacks anesthetics, and an immediate longer lasting (1-2 days) erythema and swelling. Edema is to be expected particularly after treatment of the lips, where in some cases it can cause an immediate slight asymmetry between the right and left part of the vermillion; it is necessary to refrain from correcting it and wait some hours because it resolves spontaneously.

Histologically, our study demonstrated a long duration in the tissue of hyaluronic acid gel when injected into the dermis, even if the timing of the biopsy check up could probably be improved since not much additional information is obtained throughout the degradation period. The slow digestion of this gel shows that stabilization of the material through cross-linkage is able to increase its longevity several hundred folds compared to the natural polymer, without decreased biocompatibility. The isovolemic pattern of degradation keeps the gel always in balance with water in the tissue, and this increased capacity to bind water of a less concentrated hyaluronan network allows to maintain the correction even in low presence of the material, but it also eventually determines a quite sudden disappearance of it.

The intrinsic properties of the molecule of hyaluronic acid, like its ability to bind to water and to peptide growth factors, and its high, almost plastic, viscosity when stationary^{4,12} make this substance a sort of etio-

logic therapy of the aging face. Its persistence in the tissue^{12,14} and its possible association with collagen¹⁵ make it possible to expand the therapeutic armamentarium of the cutaneous surgeon in the field of soft tissue augmentation.

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