Injective treatment with soft-tissue filler is the second most frequently performed aesthetic procedure (after botulinum toxin type A) in the United States. Although resorbable materials (e.g., hyaluronic acid) are most frequently used, a number of permanent materials are injected to enhance soft-tissue volumes and fill subcutaneous defects. Furthermore, even discontinued nonresorbable substances remain for decades in the tissues and can potentially cause inflammation at any time.

Regulatory bodies do not easily approve the use of such permanent substances. However, these limitations are often bypassed by patients that seek cosmetic treatment abroad and are eventually injected with unapproved fillers.

According to our experience, the most commonly encountered complaints in case of complications after such procedures are tedious long-lasting inflammatory reactions of different grades. In case of nonresorbable materials, these complications are rarely self-resolving. Most treatment options used until now have focused on nonspecific antiinflammatory treatments because
of the possible presence of an ill-defined immune reaction to the alloplastic substances.\textsuperscript{5–15} Inflammatory complications after nonresorbable filler injections are often called granulomas.\textsuperscript{16–19}

Foreign body granulomas are defined as lesions appearing as lumps or nodules after injection of different materials, showing (microscopically) a foreign body reaction consisting of protein absorption, macrophages, multinucleated foreign body giant cells (macrophage fusion), fibroblasts, and angiogenesis.\textsuperscript{14,20,21} It is unclear why the term “granuloma” is often used without the support of such histologic diagnosis. We therefore suggest the use of the term “inflammatory nodules” in the absence of histologic confirmation.

Some authors believe that these adverse reactions are caused by a bacterial low-grade infection surrounding the foreign material. The physical properties and inherent characteristics of the implant determine the development of associated fibrosis.\textsuperscript{14}

Materials made of microspheres with a smooth surface [e.g., Artecoll (Canderm Pharma Inc., Montreal, Quebec, Canada), New-Fill (Valcanc US, Sinclair Pharma Paris, France), and Evolution (Pro-Cytech SA, Bordeaux, France)] have been reported to be less prone to inflammation than the ones made of particles with an irregular surface [e.g., Bioplastique (Uroplasty Ltd., Reading, United Kingdom), Dermalive (Dermatech, Paris, France)].\textsuperscript{22} The incidence of granulomas is reported to be between 0.01 and 1.0 percent of such procedures.

Although the overall incidence seems low, the number of patients undergoing nonresorbable filler injection\textsuperscript{23} makes its clinical impact considerable. The prevalence of complications seems to be growing as expected\textsuperscript{3} and as shown by the numerous reports in the literature.\textsuperscript{16}

This complication, like many others, is probably underreported. In the practice of plastic surgeons, it is not unusual to have to deal with patients seeking treatment of subcutaneous dermal nodules because of disfigurement, pain, or recurrent inflammatory episodes.

These lesions are challenging to treat. Among described therapeutic approaches are systemic antibiotics and antiinflammatory drugs, intraleisional corticosteroid and 5-fluorouracil injection, needle aspiration, surgical drainage, and excision.\textsuperscript{15}

A more recent alternative treatment modality for infectious or granulomatous lesions caused by foreign material injections is the minimally invasive laser technique. A preliminary report showed our initial experience (2006 to 2009),\textsuperscript{24} on the basis of which a dedicated regional center was established in 2009 at the University Hospital of Modena (regional referral center for the treatment of filler complications of the face). This treatment modality is capable of removing the foreign substance together with the inflammatory reaction in a microinvasive manner. This article includes our problem-oriented systematic approach to inflammatory complications from permanent fillers and describes the comprehensive results we have obtained in the above-mentioned period with this technique.

**PATIENTS AND METHODS**

Two hundred nineteen consecutive patients referred from September of 2006 until June of 2013 for inflammatory reactions to permanent fillers and treated with the 808-nm diode laser (LASEMaR 800; Eufoton, Trieste, Italy) at our institution with a minimum follow-up of 6 months from the end of the treatment were included in the study. Medical history, ongoing medications, and concomitant medical conditions were recorded. Most patients were referred to our center after being treated elsewhere with local or systemic corticosteroids and antibiotics with limited and temporary improvement, if any. All patients were screened with an ultrasound soft-tissue examination performed by an experienced operator, obtaining precise information about the volume, nature, and position of the injected material.\textsuperscript{25–31}

The most important information is whether its distribution in the tissues is “cystic,” as in bolus injections, or “infiltrating,” as in crisscross retrograde injection. This will guide our decision of which type of laser-assisted evacuation we shall choose for each case. Infiltrating patterns were treated with intralesional laser treatment alone, whereas cystic distribution cases were also drained through stab wound incisions. Practically, patients were divided into two treatment groups according to their ultrasonographic image (Fig. 1).

The mean age of the patients was 49 years (range, 23 to 72 years); 204 were female and 15 were male. All patients presented with facial lesions (specific locations in Fig. 2) except for three cases where fillers were also located in the pectoral, bicipital, and calf areas.

**Infiltrating**

Usually, injectables such as silicone oil and poly(methyl methacrylate) [e.g., Artecoll, Artefill (Suneva Medical, Inc., San Diego, Calif.), and Bioplastique] form an acoustic barrier that does not allow precise ultrasonographic mapping.

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Therefore, we must rely on only their contour to mentally visualize their distribution in the tissues. Furthermore, their recommended means of injection is in microdroplets. For these reasons, we have never encountered a cystic lesion caused by these materials, and we have treated them only with intralosional laser.

However, it is possible that silicone oil can be injected not according to the standard technique. Therefore, it can theoretically appear as a cystic deposit (e.g., if a large bolus is injected into a defined fat compartment).

Dermalive and Dermadeep

Dermalive and Dermadeep (Dermatech) are acrylic gels (hydroxyethylmethacrylate and ethylmethacrylate) (40 percent) mixed with hyaluronic acid (60 percent). After being implanted, the hyaluronic acid is absorbed progressively, leaving the sharp edges of the acrylic component microstructure exposed. This is believed to account for the numerous reports of inflammatory complications, most often untreatable, caused by these fillers.

These fillers have commonly been injected both for wrinkle reduction and for volumetric enhancement. Either way, after the resorbable gels are absorbed, they acquire a solid state that makes them nondrainable by a simple incision, thus necessitating intralosional laser treatment. Therefore, we include them in the infiltrating group for practical reasons.

Cystic

Polyacrylamides [Aquamid (Ferrosan A/S, Contura International, Soeborg, Denmark),

Fig. 1. Typical ultrasonographic image of different permanent fillers. (Above) Polyacrylamide gel nasolabial implant. The material is hypoechoic. A pseudocapsule is visible. (Below) Silicone oil infiltration of the nasolabial fold. The ultrasonographic typical “barrier” is visible as a white wall hiding the underlying structures.

Fig. 2. Graph showing the different locations of the facial lesions: nasolabial folds, 60 percent; lips, 53 percent; malar area, 41 percent; periocular, 27 percent; and frontal, 8 percent.
Evolution, Argiform (Bioform, Moscow, Russia), Formacryl (Bioform), Amazingel (NanFeng Medical Science & Technology Development Co., Shijiazhuang, People’s Republic of China), Outline (ProCytech, Bordeaux, France) and polyalkylimide (Bio-Alcamid; Polymekon, Milan, Italy) gels are recommended to be injected in well-defined implants to form an endoprosthesis.35–39

Operative Procedures
Intralesional Laser Treatment. An 808-nm diode laser (LASEmaR 800) was used. The intralesional laser treatment procedure consists of percutaneously inserting a 200-μm fiberoptic laser into the lesions, drilling several small holes. Typically, no anesthesia is used. Because the presence of bacteria is hard to rule out, even with negative cultures, local infiltration in this inflamed and contaminated area could be ineffective or even spread the infection farther around. Moreover, all polymers are obviously lacking any perception of pain and temperature, and so are the giant cells that usually surround them.14 In contrast, the native host facial tissue is exquisitely sensitive to pain and temperature, especially when subjected to acute, subacute, or chronic inflammation.

There is a thermal therapeutic margin between the lesion melting and the pain threshold elicited by excessive diffusion of heat into the surrounding tissues. The usual laser power setting is at 7 W in continuous wave mode, and the fiberoptic tip is inserted directly into the lesion. Energy delivery is modulated according to patient tolerance as follows: if the patient immediately shows excessive discomfort, power is reduced to 6 W and emission is switched from continuous wave to pulsed (500 msec on and 500 msec off).

Regarding the treatment pattern, the fiberoptic tip is inserted into the lesions (Fig. 3, left), attempting to uniformly heat up the mass. Manual palpation usually reveals a softening of the deposits as the immediate clinical endpoint, caused by the polymer increased fluidity. If the operator inadvertently overheats the lesion, the heat excess will diffuse into the surrounding tissues, and the discomfort will gradually become unbearable. Patients are previously instructed to alert the operator in this case to prevent untoward tissue damage. Therefore, the total amount of energy applied to each lesion depends on its dimensions and cannot be calculated a priori.

At this point, the heat-liquefied materials are evacuated (squeezed out) (Fig. 3, right) by gentle finger compression through the skin entrance points of the probe. If the access is through mucosa, the fear for permanent scarring at the laser entry points is minimal, and therefore the openings are made wider (up to 1 mm) to keep them patent and facilitate drainage for a longer period. Particular care is needed when the lesion is intradermal and longstanding. In this case, soft-tissue atrophy is common because of the chronic inflammatory process and the repeated steroid injections usually administered before referral to our centers. This makes the skin thinner and less resistant to thermal injury. For this reason, before proceeding, patients are informed that small, acne-like scarring may occur, and they are asked permission...
to continue the treatment (in no case has the patient refused). When patients have undergone attempts at surgical excision of the lesions before referral, advancing the laser fiber is made more difficult by fibrotic scarring, and care must be taken not to break the delicate fiberoptic against the rock-hard tissue. Advancing the laser fiber parallel to the scar lines is preferable to trying to pierce through them. This treatment modality is applied to all infiltrating cases.

**Stab Wound Incision.** If the clinical and ultrasonographic picture is consistent with a cystic implant, a stab incision (no. 11 blade) is performed according to the relaxed skin tension lines. Usually, implants subject to longstanding inflammatory processes have changed their characteristics. Instead of the light transparent and aqueous gel that was injected at first, a much thicker, fat-like substance is extracted (Fig. 4, above).

In some cases, the substance is almost solidified because of the gradually growing scaffold of thin connective tissue fibers within it. In these cases, the fiberoptic is introduced through the stab wound incision and the implant is irradiated uniformly with the laser using the above-mentioned parameters and modality, to disrupt the fibrous scaffold and allow easy evacuation of the liquefied substance.

The empty cavity is irrigated with saline solution to rinse out small residuals adhering to the pseudocapsule. The stab wound is left open for drainage and heals spontaneously in a few days.

**Postoperative Treatment.** Patients are instructed to apply frequent lukewarm saline compresses. Frequent gentle squeezing of the treated area is recommended to ensure continuous drainage of the liquefied foreign material and necrotic inflammatory tissue. Oral macrolide antibiotic treatment is recommended in patients at risk of postoperative infection, such as those with incompletely evacuated cystic lesions, those under corticosteroid treatment, and immunocompromised patients (e.g., human immunodeficiency virus, diabetes).

The typical healing time from the combined mechanical and thermal trauma caused by the treatment depends on the treated area site and size. A period of up to 6 months is usually necessary to fully appreciate the resolution of the lump together with the healing of the surrounding inflammation often extended far beyond the original implant. Thus, the need for eventual further treatment is evaluated at 6 months. Treatment is considered successful in the following cases:

- All symptoms are completely cured or judged tolerable by the patient.
- Lump visibility is reduced to a degree judged tolerable by the patient.
- Interrupting the steroid therapy without recurrence is possible.
Patients were photographed at first consultation, before each treatment session, and at 6 months. Cosmetic and functional results, adverse events episodes, and patient satisfaction were evaluated by two board-certified plastic surgeons at 6 months after the end of treatment. Results have been classified into three categories (i.e., improved, not improved, or resolved) evaluating three parameters: inflammation (i.e., rubor, calor, dolor, and loss of function), nodules, and paresthesia.

**RESULTS**

Different materials have been removed (Fig. 5) according to the characteristics of the lesions (Tables 1 and 2). The average number of treatment sessions per lesion was 1.7. Partial improvement (with >50 percent reduction) was obtained in 30 percent of cases. Eight percent of patients discontinued the treatment because of a lack of satisfaction. Complete disappearance of lesions (lumps and inflammation) was obtained in 62 percent of cases.

Of the 219 patients, 20 were referred to us while on chronic oral steroid therapy. Even though we do not advocate systemic steroid treatment because of possible side effects, high recurrence rates, and rebound effects, we cannot stop steroid administration because of the risk of immediate flare-up of their condition and therefore we

![Graph showing the different materials that have been removed: Dermalive, 30 percent; silicone oil, 20 percent; Artecoll, 13 percent; Bio-Alcamid, 12 percent; Aquamid, 11 percent; and unidentified, 14 percent.](image)

**Table 1. Different Filler Materials, Distribution Pattern, and Behavior**

| Type  | Description | Polyacrylamide | Polyalkylimide Gel | Methacrylate | Silicone |
|-------|-------------|----------------|-------------------|--------------|----------|
| Brand names | Evolution, Argiform, Bio-Formacryl, Aquamid, Amazigel | Bio-Alcamid | Dermalive, Dermadep, Artecoll, Artefill, PMMA (Arteplast) | Infiltrating | Silicone oil, Bioplastic |

PMMA, poly(methyl methacrylate); ILT, intralesional laser treatment.
suggest beginning tapering of the drug only 1 month after the first treatment.

This attempt was successful in 16 of 20 patients (80 percent). Only four of 20 patients needed more (up to five) laser sessions before it was possible to successfully treat them. Not surprisingly, these patients had diffused, multifocal, almost panfacial disseminated involvement.

The vast majority of complications were transient and caused by the inflammatory response to the laser procedure and recurrent squeezing. In 22 cases (10 percent), the skin was focally atrophic because of unsuccessful attempts at intradermal steroid infiltration performed elsewhere before referral. The inflammatory nodule basically had replaced the dermis as a support to the epidermis.

Eliminating the polymer left a visible depression similar to a deep acne scar. Similar to other laser procedures, another potential complication is scarring caused by excessive heating of the surrounding tissues by the inexperienced operator. The other complications are shown in Figure 6, and clinical cases are shown in Figures 7 through 12.

**DISCUSSION**

Current review of the literature shows that many different treatments are advocated for inflammatory complications from nonresorbable fillers. However, many of these treatments are administered regardless of the possible cause of the complication, without considering the possible risks and the incidence of relapse.

The “inflammatory response” to the foreign body is often seen as the treatment target, although it could also be just an epiphenomenon. Limiting treatment to this (e.g., steroids that depress the immune system and antibiotics to help defenses) inevitably results in an unacceptable recurrence rate.

Complications from nonresorbable fillers are either inflammatory or noninflammatory. The term granuloma has been indiscriminately applied to both inflammatory and noninflammatory cases for years, whereas some authors postulate that hyaluronic acid implants cannot result in granulomatous reactions. Granuloma is a histologic diagnosis, not a clinical one; therefore, we suggest avoiding this term unless biopsy proven, and to use instead a problem-oriented clinical classification that does not include improper use of unproven histologic terms.

This clinical approach is the result of several considerations. The nature of the injected material, its pattern of injection, and the clinical manifestations of the complication guide us in choosing the safest and most effective means for its removal. Extracting the ill-tolerated substance eliminates the cause of the problem. We advocate minimally invasive laser-assisted drainage through a stab wound for cystic implants, whereas infiltrative patterns of injection are treated by intralosional laser.

Although medical history and physical examination can provide enough information for treatment in selected cases, the distinction between

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**Table 2. Characteristics of the Lesions in the Study Population**

| Type of Lesion   | Incidence (%) |
|-----------------|---------------|
| Cystic          | 23            |
| Infiltrating    | 65            |
| Inflammatory    | 70            |
| Noninflammatory | 30            |

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**Fig. 6.** Complications are shown in the graph: swelling, 100 percent; hematoma, five cases; secondary sterile abscess, 21 cases; and scarring (smallpox like), 22 cases.
these two categories is best made by a dedicated ultrasound examination. An experienced radiologist using the appropriate ultrasound frequency and probe can add precious information about each case, such as shape, dimensions, and depth of each deposit. Different materials are often injected into the same area: the different densities can be detected and related to the different substances. Sometimes, the same material can show different densities according to the time lapse since injection. Many gels are slowly infiltrated by collagen fibers and microscopic blood vessels so that, after years, they appear on ultrasound as a low-density tissue, often lobulated and with focal calcifications.29–31

Implant density is of utmost importance for the choice of the right extraction technique. Although recently injected gels maintain their structure and rheologic proprieties and are easily squeezed out, older implants can be extruded only through a 3-mm stab-wound incision after their density is reduced by an increase in temperature provided by the intralesional laser treatment (Fig. 4). These principles are summarized as an algorithm flowchart (Fig. 13).

Different Filler Material Behavior at Laser
Silicone Oil
Among the hydrophobic polymers, this is the only one present naturally as a liquid substance. The others (methacrylates) are solid particles suspended in a solution. To allow easy extrusion of the silicone through the microscopic holes made by the fiberoptic laser, it is enough to increase its fluidity by raising its temperature to 50°C at most.

Methacrylates are made of solid particles, with a much higher theoretical melting temperature. A higher energy dose is usually needed to liquefy them together with the surrounding inflammatory tissue. However, the heating process must be slow and gradual to avoid carbonization of the polymer tissue compound. Polyacrylamides (e.g., Aquamid) and polyalkylimides do not contain solid particles.23,46

The subcutaneous deposits caused by these gels are in reality cystic lesions. The gel maintains its state and form according to its original placement, with an ingrowth of vessels and connective tissue. In later years, we have observed that it does not maintain its original transparent colorless aspect but turns yellowish (similar to fat) (Fig. 4, above). Therefore, the timing of onset of complications and eventual need for removal is critical for the treatment choice. In a recently injected case, it is possible to extract the material through a puncture or a stab incision. When the lesion is inflamed, intralesional laser treatment is administered to decrease or eradicate the material load/biofilm eventually present. The heat is administered to the tissues through the laser fiber to achieve other beneficial effects such as
shrinking of the pseudocapsule and obliteration of the cavity. In these cases, a stab incision may be performed after the intralesional laser treatment. Particular care needs to be taken to avoid excessive heating of the product to maintain the integrity of the polymer chains. Claims have been made that monomers of polyacrylamide gels are potentially toxic/carcinogenic. Therefore, we refrain from overheating these products as with silicone oil.

**Technical Aspects**

Our objective is not overheating the polymer to avoid the presence of carbonized residuals in tissues. That increase in temperature is empirically
determined until the clinical endpoint of nodule softening is achieved. In our experience, this corresponds to a degree of fluidity sufficient to allow for polymer extrusion by gentle squeezing. When using a 200-μm optic fiber, we typically start at 4 W, with 100-msec on time and 100-msec off time.

Unlike for dermatologic cosmetic treatments, here, the laser is used as a surgical tool. As in other intralesional treatments, we look for the clinical endpoint of nodule softening and content extrusion. Number of passes, delivered energy, duration, and temperature measurements are not considered reliable parameters because the treated lesions differ extremely from one another. Temperature is not measured, as treatments are performed without anesthesia. Pain arises before real tissue damage is caused; thus, temperature monitoring is clinically unnecessary. It could be scientifically interesting but is far beyond the scope of our therapeutic work.

This chosen laser wavelength (810 nm) was preferred, as it resulted in less pain than other infrared diodes. The other laser wavelengths tried by the author (i.e., 940, 980, 1064, 1320, and 1470 nm) were not as well tolerated by patients, probably because of their higher absorption by water and fat.

An experienced operator can choose to operate in continuous wave mode. The pattern of tunneling is designed according to nodule shape, depth, and position, but generally the fiber is inserted from the most dependent entry point to favor drainage when patients stand/sit up after treatment. Patients’ diligent compliance in gently squeezing out the material during the first postoperative days is of utmost importance for a successful outcome. When patients refrain from doing this, a much larger number of treatments might be needed. The squeezing should be very gentle to avoid mechanical occlusion of the tiny drainage points. This aspect requires good manual ability by the operator and by the patient.

All of the patients in our study that were affected by recurrent inflammatory episodes reported an improvement in both the frequency and the intensity of those events. Possible explanations could be the reduced residuals in the subcutaneous tissue and, possibly, the changes in the inflammatory and contaminated component of the fibrotic tissue of the lesion induced by the laser.45

Steroids and Other Infiltrative Treatments

Intralesional steroids and 5-fluorouracil may provide temporary improvement but do not address the root of the problem. The risk of rebound effects, skin atrophy, and telangiectasias have discouraged us from using them.

The idea of injecting intralesional steroids into inflammatory complications caused by fillers originates in common dermatologic practice, where annular granuloma is routinely treated with steroids with good results. The term granuloma is often applied without justification to many of the complications we are dealing with, because histologic evaluation is not performed. Nevertheless, the same treatment has been projected by analogy without a clinical rationale.45

Fig. 12. A 65-year-old patient with longstanding panfacial silicone-induced inflammatory reaction. There is an inflammatory silicone nodule in the left lateral canthal area. (Left) Before treatment. (Center) Extrusion of silicone after intralesional laser treatment. (Right) Four years after treatment.
When silicone oil is injected into fine lines, its microdroplets stimulate the formation of fibrotic tissues around them. Over years, this might lead to overcorrection, even without clinical signs of inflammation, because there is no way to regulate the amount of reactive tissue.

Historically, triamcinolone has been used to diminish the fibrotic reaction around the silicone oil microdroplets. In selected cases of overproduction of fibrotic tissues without clinical inflammation, cautious intraliesional injections of corticosteroids can be successful and acceptable (e.g., silicone oil) because of their selective inhibition of collagen production by fibroblasts. In inflamed cases, the intraliesional injections of corticosteroids should be avoided because of the possible rebound effect after the initial improvement caused by the immunosuppressive effect on the possible bacterial contamination.

It should be noted that our patient population is selected. The majority of our patients are referred to our center after previous treatment attempts, such as intraliesional injections of corticosteroids or other substances (e.g., 5-fluorouracil, systemic steroids). Some are only partially treated with antibiotics.

Safety studies for fillers have been published with a follow-up of up to 5 years. In our series, the typical average onset of inflammatory complications is 6 to 7 years (range, 1 day to 12 years). Therefore, we find that the 5-year safety data do not reflect absolute immunity from long-term complications.

The satisfaction rate was less than complete in a few of the treated subjects. Even though all

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*Fig. 13. Flowchart summarizing the principles of treatment of inflammatory complications after nonresorbable filler injections. The distinction between cystic implants and infiltrative pattern of injection is best made by a dedicated ultrasound (US) examination. Cystic implants are treated by minimally invasive laser-assisted drainage through a stab wound, whereas infiltrative lesions are treated by intraliesional laser treatment (ILT) only. See text for details. *Before any future invasive procedure; #azithromycin administered orally, 500 mg/day.
patients are correctly informed before the procedure about the possible outcome, too many of them do not fully realize that they are being treated for a pathologic condition. Instead, they are probably still considering it a continuation of the initial filler treatment that was supposed to make them “permanently more beautiful” in their perception. Their unconfessed desire is for their pristine aspect to be restored, which is obviously impossible to achieve after many years of aging and the unwanted effects of chronic inflammation and steroids on their faces.

CONCLUSIONS

In the literature, there is no consensus on treatment of permanent filler complications. Traditional medical and surgical treatment modalities have not been satisfactory. A minimally invasive approach, combining laser-assisted implant removal and eradication of the eventual bacterial contamination, is proposed in a large series of consecutive patients, in which the longstanding improvement rate was 92 percent. Although the learning curve for this type of intralesional treatment is not negligible, we believe this might be a breakthrough for this difficult group of patients.

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