Evaluation of the Radiance FN Soft Tissue Filler for Facial Soft Tissue Augmentation

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Objective: To evaluate the clinical efficacy and patient satisfaction of Radiance FN (fine needle) (BioForm Inc, Franksville, Wis), a highly biocompatible, calcium hydroxyapatite–based implant, when used for facial soft tissue augmentation.

Methods: Ninety patients aged between 25 and 85 years underwent subdermal injection with Radiance FN. The primary areas treated were lips, nasolabial folds, glabellar rhytids, marionette lines, prejowl depressions, acne scars, and surgical soft tissue defects. Patients were surveyed after treatment and for up to 6 months for pain, ecchymosis, skin erythema, nodules, softness, appearance, and satisfaction.

Results: In terms of efficacy, at 6 months, appearance, softness, and overall patient satisfaction were rated good or excellent in 74%, 80%, and 88% of patients, respectively. Moderate or severe pain occurred with injection in 59% of patients but disappeared 2 to 5 minutes after injection. Erythema, edema, and ecchymosis were common immediately after treatment but resolved in all patients within 2 weeks. Seven patients had persistent visible mucosal lip nodules, 4 of whom required intervention.

Conclusions: Radiance FN is highly effective and well tolerated when used for facial soft tissue augmentation. Additional experience with longer follow-up will help determine the most appropriate use and long-term safety for the implant.

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OFT TISSUE AUGMENTATION has been used since free-fat grafting was introduced in 1893, but it became a common procedure only with the development of injectable bovine collagen in the late 1970s. Presently, clinical indications for soft tissue augmentation include plastic and reconstructive surgery, laryngology, urinary incontinence, vesicourethral reflux, gastroesophageal reflux, and fecal incontinence.

The ideal agent for soft tissue augmentation is one that

- Is readily injected with minimal extravasation, burning, or stinging
- Does not require sensitivity testing
- Is nonantigenic, nontoxic, nonpyrogenic, nonmutagenic, and nonteratogenic
- Causes only minimal pain, edema, ecchymosis, erythema, or inflammation immediately after treatment
- Is not visible or palpable
- Is persistent and durable with a long-lasting, but not permanent, effect in the long term
- Does not migrate or harden
- Has a physical consistency similar to normal tissue texture.

Until recently, this agent did not exist.

Literally dozens of different materials have been developed for soft tissue augmentation. They include biologically derived products such as bovine (and human) collagen, autologous fat, and hyaluronic acid. Synthetic fillers include silicone and expanded polytetrafluoroethylene (e-PTFE). Despite the wide variety of materials available, they all have significant limitations that compromise their use: the biologic materials provide transient correction because of rapid resorption or biodegradation; e-PTFE may constrict within the tissue, become visible, or extrude through the skin; bovine collagen often has undesirable immunological reactivity, requiring sensitization testing and delayed treatment; and silicone may cause chronic inflammation, persistent foreign body reaction, or granulomas.

Radiance (BioForm Inc, Franksville, Wis) is a new product developed for
soft tissue augmentation. The formulation contains 35% spherical particles of synthetic calcium hydroxylapatite (CaHA), which is identical in chemical composition to the inorganic constituent of teeth and bone, blended in a gel that contains water, glycerin, and sodium carboxymethylcellulose. In standard Radiance, the CaHA particles are produced in a narrow size range of approximately 75 to 125 µm in diameter. In Radiance FN (fine needle) the particles range from approximately 25 to 45 µm to facilitate ease of injection.

All of the components in Radiance have been extensively used in implants and drug delivery systems. Synthetic CaHA is a standard biomaterial (American Society for Testing and Materials F1185) that has been used extensively in many medical devices for laryngeal, otologic, dental, and orthopedic applications. The gel ingredients are USP grade pharmaceutical excipients that are classified “Generally Recognized as Safe” (21 CFR §182) by the US Food and Drug Administration (FDA). The gel carrier suspends the particles and allows them to be readily delivered by injection needle, and the spherical particles of CaHA provide a durable matrix for tissue infiltration.

The biocompatibility of Radiance has been tested extensively in preclinical studies. In vitro testing, it was nontoxic, hemocompatible, and caused no mutagenic response (Hubbard W. 36-Month biocompatibility study of calcium hydroxylapatite microspheres in 24 female dogs [unpublished report]. Bioform Inc; 2000 [hereafter “Hubbard report”]). In in vivo testing it was nonantigenic, nonirritating, and nontoxic (Hubbard report). And in a 36-month biocompatibility study in 24 female dogs, macrophage activity associated with injection subsided with time and cleared by 12 months from the injection sites. The CaHA particles were fixed in place with thin connective tissue, without reaction in surrounding tissue, evidence of migration, or evidence of heterotopic bone growth when the particles were placed in soft tissue (Hubbard report). There was some degradation of the microspheres at 18 months and beyond into metabolites consisting of calcium and phosphate ions (Hubbard report).

Standard Radiance has received FDA approval for laryngeal augmentation, radiological soft tissue marking, and filling and/or augmentation of dental intraosseous and oral/maxillofacial defects including craniofacial augmentation. The present study was designed to evaluate the biological behavior, clinical efficacy, and tolerability of Radiance FN for soft tissue augmentation of the face.

<table>
<thead>
<tr>
<th>Table 1. Areas Treated</th>
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<tbody>
<tr>
<td>Area</td>
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</tr>
<tr>
<td>Nasolabial folds</td>
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<td>Upper and lower lip</td>
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<td>Glabella region</td>
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<td>Prejowl areas</td>
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<td>Marionette lines</td>
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<td>Malar area</td>
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<tr>
<td>Philtrum</td>
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<tr>
<td>Acne scarring</td>
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<td>Upper lip only</td>
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<td>Cheeks</td>
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<td>Chin lines</td>
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<tr>
<td>Depressions</td>
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<tr>
<td>Lip lines</td>
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<tr>
<td>Infraorbital area</td>
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<td>Latero-orbital area</td>
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<tr>
<td>Chin</td>
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<td>Nose</td>
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or infection were not eligible to participate. The patients were specifically counseled as to the benefits and risks of the experimental, off-label treatment, and only those who provided informed consent were enrolled.

TREATMENT

Radiance FN was provided in sterile, premixed, prefilled, 1-mL syringes by BioForm Inc. For the 90 patients, a total of 142 syrings were used in 103 treatment sessions. Before injection, the skin was cleaned with alcohol wipes and marked. Xylocaigne (2%) was injected locally as a nerve block to reduce treatment pain, but no anesthetic was placed in the areas of desired augmentation to avoid distortion of the tissue. The primary areas treated were the lips, nasolabial folds, glabellar rhytids, marionette lines, prejowl depressions, acne scars, and surgical soft tissue defects (Table 1).

Standard Radiance can be injected using a 27-gauge needle, but most patients were injected with a special 30-gauge needle with a larger inner diameter (RJMaxflo, RJ Development Corp, Peabody, Mass). Radiance FN was injected subdermally between the dermis and the subcutaneous fat. In all injections except for the lips, a fanning method with minimal smooth linear tracts of material was used. Radiance FN was injected only on withdrawal of the needle. After injection, the material was manually compressed to mold within the tissue, and ice was applied to reduce discomfort.

For lip augmentation, Radiance FN was injected with a long 27-gauge needle in a plane superficial to the orbicularis muscle. The material was injected from the oral commissure to the midpoint of the upper and lower lip. Approximately 0.2 mL of material was used in each half of the upper and lower lip, and the remaining 0.2 mL was usually used to treat vertical lip rhytids and oral commissure depressions. As a precaution after injection, steri-strips were placed in the area of injection and around the lips. Each patient treated in the lips was instructed to avoid excessive lip motion for 24 hours.

DOCUMENTATION

Immediately after treatment and at each follow-up visit, the patient’s condition and level of overall satisfaction were surveyed. Efficacy measurements included appearance, softness, and patient satisfaction. Adverse event measurements included pain, ecchymosis, erythema, and nodules.
Photography (35 mm) was performed on each patient immediately before and after treatment and at each follow-up visit. The photographs were standardized with respect to camera (Nikon N8008; Nikon Corp, Tokyo, Japan), lens (105 mm), film (Fujicolor ASA 200; Fuji Photo Film Co, Tokyo), lighting, and angles.

Computed tomographic imaging was performed for 1 patient 7 months after treatment, who had received augmentation with Radiance FN in the lips. Continuous axial and coronal imaging (2-mm thick) was performed (without intravenous contrast) through the lips to assess calcium deposition and possible migration of the implant. Dental x-ray films of the same patient were taken by standard techniques to assess whether the calcific density in the lips caused any noticeable interference in the images.

### RESULTS

#### CLINICAL RESULTS

Postimplantation follow-up with this group of patients is ongoing. Ninety patients originally enrolled and completed the 6-month patient survey. Appearance, softness, and patient satisfaction were evaluated on a 4-point scale (ie, excellent, good, fair, and poor). At 6 months, appearance and softness were rated good or excellent in 74% and 80% of patients, respectively (Table 2). Patient satisfaction with treatment was uniformly high: 47% of patients rated their satisfaction as excellent; 41% rated their satisfaction as good. Only 2% reported poor overall satisfaction (Table 2).

Pain, erythema, and ecchymosis were common immediately after treatment (Table 3). Within 2 weeks, however, ecchymosis had completely resolved in all patients and only very minimal residual edema was present in most patients. Complete resolution of edema may require months. Two patients had mild erythema that persisted for up to 4 weeks that responded to topical corticosteroid treatment. Additionally, by 2 weeks after treatment, no induration, tenderness, chronic pain, or inflammation was present in any patient.

Postinjection mucosal lip nodules occurred in several patients (Table 3). While most nodules were of minimal severity and resolved within 4 to 6 weeks, 7 patients experienced visible, persistent nodules, 4 of whom required intervention.

#### PHOTOGRAPHY

Photography was used before and immediately after treatment, as well as at each follow-up visit, to document improvements in appearance and the resolution of injection-related adverse events. The photographs show the dramatic improvement possible after Radiance FN injection in the nasolabial folds (Figure 1 and Figure 2), lips and oral commissure (Figure 3), marionette lines (Figure 4), and nasolabial folds and lips (Figure 5).
One patient who had received lip augmentation with Radiance FN was evaluated by computed tomography 7 months after treatment to assess calcium deposition and possible migration of the implant. The images showed calcific density throughout the expected course of the upper and lower lips, while the surrounding soft tissue was clear. No adenopathy was observed in the face or neck, and no evidence of remote calcium deposition was identified (Figure 6). Dental x-ray films of the same patient showed that Radiance FN implants are not opaque and caused no discernible interference in standard radiography (Figure 7).

The results of this study show that Radiance FN is effective and well tolerated when used for facial soft tissue augmentation. Radiance FN is premixed, prefilled, and ready to use, with no special storage or handling requirements. It is formulated from pharmaceutical components with extensive use and safety profiles and is readily injectable. Because CaHA is identical in chemical composition to the mineral component of bone and teeth, Radiance FN is nonantigenic and biocompatible and does not require sensitivity testing that can delay the initiation of treatment. The CaHA particles allow the fibroblasts from the injection site to grow directly on their surface, anchor-
ing the implant in place, resulting in an injection site similar in physical characteristics to the surrounding tissue. As a result, the material naturally conforms to the body without reaction, extrusion, or migration.12-14

Animal and clinical studies confirm that Radiance is persistent, yet it is biodegradable in the long-term, resulting in lasting correction of soft tissue deficiencies and long-term patient satisfaction. The small, smooth, rounded profile of the CaHA particles allows easy injection through small-gauge needles (eg, 30-gauge RJMaxflo). The small needle size reduces injection site pain and allows for more accurate injection of the material.

Radiance FN has been an ideal filler for deeper rhytids, the oral commissure, marionette lines, and nasolabial folds. Generally, more than 1 syringe is required to treat the perioral region, and the injections can be performed in 1 or more stages.

No serious adverse effects have been reported with Radiance, but as with all soft tissue fillers, it should not be used in the presence of foreign body reaction, inflammation, or infection. It should not be injected into blood vessels, and scar tissue and compromised tissue may not accept the injection appropriately. As with all durable soft tissue fillers, it is important to use precise injection technique and avoid overcorrection during treatment. The risk of overcorrection is reduced by adopting a conservative approach and by injecting in stages at least 1 month apart. If necessary, however, a misplaced or overcorrected implant of Radiance FN can be removed surgically.

When treating the lip, the injection must be superficial to the orbicularis oris muscle and no more than 1 mL should be injected at any one treatment to minimize the risk of nodule development. A 27-gauge, 1.25-in
(3.18-cm) needle is inserted from the corner of the lip to the midline, and Radiance FN is injected on withdrawal of the needle. Small linear threads of material are injected in multiple passes starting at the vermilion border and progressing into the body of the lip. Generally, no more than 0.2 mL is injected into each half of the lip. Caution should be exercised when injecting vertical lip rhytids. Since Radiance is injected subdermally, full correction is not possible and overcorrection will result in an unwanted cosmetic result that will take months to resolve.

Ecchymosis and injection pain are common during and after injection, especially when treating the lips. The pain usually resolves within 2 to 3 minutes after injection but can be minimized by using a pretreatment nerve block and posttreatment ice. The injection of a minimal amount of lidocaine hydrochloride containing epinephrine (1:100,000) into the lips prior to injection of Radiance FN has markedly decreased the discomfort of lip augmentation. This local anesthetic technique has become the current standard and was incorporated subsequent to this initial study. Ecchymosis resolves completely within 2 weeks of treatment.

Precise technique is also required with lip augmentation to reduce the risk of submucosal nodules. Even in experienced hands, approximately 10% of patients treated in the lips will develop nodules. Most often the nodules are not visible and resolve without intervention. Rarely, they may be visible and require treatment. Oral corticosteroids have been slightly effective, but the most effective treatment has been anesthetizing the area, disrupting the nodule with a 22-gauge needle, and manually compressing the area to disperse the material.

In this study, we evaluated the clinical results and patient satisfaction with the use of Radiance FN for the treatment of facial soft tissue augmentation. We found that Radiance FN is effective and well tolerated, and patient satisfaction with treatment is uniformly high.

Radiance has been used for facial plastic surgery in more than 5000 patients in the United States, Argentina, and Italy, but the follow-up to date has been approximately only 3 years. As such, several questions remain regarding its use. Are there long-term adverse reactions associated with treatment? Does the implant stay soft in the face in the long term? How predictable is its use in mobile regions of the face? As we gain additional experience with this promising new material, we will be better able to determine its most appropriate use and long-term safety profile.

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REFERENCES