INJECTABLE IMPLANT
INSTRUCTIONS FOR USE

℞ ONLY

DEVICE DESCRIPTION

RADIESSE injectable implant is a sterile, non-pyrogenic, semi-solid, cohesive implant, whose principle component is synthetic calcium hydroxylapatite suspended in a gel carrier of sterile water for injection, glycerin and sodium carboxymethylcellulose. RADIESSE injectable implant 1.5cc, RADIESSE injectable implant 1.3 cc, RADIESSE injectable implant 0.8cc, and RADIESSE injectable implant 0.3 cc have a CaHA particle size range of 25–45 microns and should be injected with a 25 to 27 gauge Inner Diameter (I.D.) needle.

INTENDED USE / INDICATIONS

RADIESSE injectable implant is indicated for subdermal implantation for the correction of moderate to severe facial wrinkles and folds, such as nasolabial folds and it is also intended for restoration and/or correction of the signs of facial fat loss (lipoatrophy) in people with human immunodeficiency virus.

CONTRAINDICATIONS

- Contraindicated for patients with severe allergies manifested by a history of anaphylaxis, or history or presence of multiple severe allergies.
- Not intended to be used in patients with known hypersensitivity to any of the components.

WARNINGS

- Use of RADIESSE injectable implant in any person with active skin inflammation or infection in or near the treatment area should be deferred until the inflammatory or infectious process has been controlled.
- Injection procedure reactions have been observed consisting mainly of short-term (i.e., < 7 days) bruising, redness and swelling. Refer to adverse events sections for details.
- Special care should be taken to avoid injection into the blood vessels. An introduction into the vasculature may occlude the vessels and could cause infarction or embolism.
- Do not overcorrect (overfill) a contour deficiency because the depression should gradually improve within several weeks as the treatment effect of RADIESSE injectable implant occurs (see Patient Treatment).
- The safety and effectiveness for use in the lips has not been established. There have been published reports of nodules associated with the use of RADIESSE injectable implant injected into the lips.

PRECAUTIONS

- The calcium hydroxylapatite (CaHA) particles of RADIESSE injectable implant are radiopaque and are clearly visible on CT Scans and may be visible in standard, plain radiography. In a radiographic study of 58 patients, there was no indication that RADIESSE injectable implant potentially masked abnormal tissues or being interpreted as tumors in CT Scans. Patients need to be informed of the radiopaque nature of RADIESSE injectable implant, so that they can inform their primary care health professionals as well as radiologists.
- Should only be used by health care providers with expertise in the correction of volume deficiencies in patients with human immunodeficiency virus after fully familiarizing themselves with the product, the product educational materials and the entire package insert.
- Packaged for single patient use. Do not resterilize. Do not use if package is opened or damaged. Do not use if the syringe end cap or syringe plunger is not in place.
- Long-term safety and effectiveness of RADIESSE injectable implant beyond one year have not been investigated in clinical trials.

- The safety of RADIESSE injectable implant in patients with increased susceptibility to keloid formation and hypertrophic scarring has not been studied.
- As with all transcutaneous procedures, RADIESSE injectable implant injection carries a risk of infection. Standard precautions associated with injectable materials should be followed.
- Safety of RADIESSE injectable implant for use during pregnancy, in breastfeeding females or in patients under 18 years has not been established.
- Patients who are using medications that can prolong bleeding, such as aspirin or warfarin, may, as with any injection, experience increased bruising or bleeding at the injection site.
- Universal precautions must be observed when there is a potential for contact with patient body fluids. The injection session must be conducted with aseptic technique.
- After use, treatment syringes and needles may be potential biohazards. Handle accordingly and dispose of in accordance with accepted medical practice and applicable local, state and federal requirements.
- The patient should be informed that he or she should minimize exposure of the treated area to extensive sun or heat exposure for approximately 24 hours after treatment or until any initial swelling and redness has resolved.
- Safety and effectiveness in the periorbital area has not been established.
- No studies of interactions of RADIESSE injectable implant with drugs or other substances or implants have been conducted.
- To help avoid needle breakage, do not attempt to straighten a bent needle. Discard it and complete the procedure with a replacement needle.
- Do not reshield used needles. Recapping by hand is a hazardous practice and should be avoided.

ADVERSE EVENTS

A. NASOLABIAL FOLDS

Tables 1-4 contains the adverse events for 117 patients in a randomized, controlled study at 4 US investigational sites. Patients in the study received RADIESSE injectable implant in one side of the face and a collagen dermal implant as the Control in the other side of the face. Adverse events reported in patient diaries during the 14 days after treatment are listed in Tables 1 and 2. Physician reported adverse events are those reported by Investigators and patients any time outside the 2 week diaries. Those adverse events are presented in Tables 3 and 4.

Table 1. **ADVERSE EVENTS**

Reported Through Patient Diaries Number of Patients With at Least One Adverse Event

By Adverse Event Type N = 117

ADVERSE EVENT TYPE	RADIESSE® Total Reporting Symptoms N(%)	CONTROL Total Reporting Symptoms N(%)
Ecchymosis	74 (63.2%)	50 (42.7%)
Edema	81 (69.2%)	62 (53.0%)
Erythema	78 (66.7%)	84 (71.8%)
Granuloma	0 (0.0%)	0 (0.0%)
Needle Jamming	0 (0.0%)	0 (0.0%)
Nodule	1 (0.9%)	1 (0.9%)
Pain	33 (28.2%)	26 (22.2%)
Pruritis	21 (18.0%)	24 (20.5%)
Other*	35 (29.9%)	26 (22.2%)

* "Other" adverse events for both RADIESSE injectable implant and Control include soreness, numbness, contour irregularity, tenderness, and irritation. None of the reports of contour irregularities was determined to be nodules or granulomas.

There were 12 systemic adverse events reported for 9 patients. None of these systemic adverse events were related to either RADIESSE injectable implant or Control and included emergency gallbladder surgery, breast pain, infected and exposed breast implant, gastroenteritis, uterine fibroids, headache, burning and numbness in tongue and lips, tongue ulceration and fatigue.

Table 2. **PATIENT REPORTED ADVERSE EVENTS**

By Adverse Event Type

ADVERSE EVENT TYPE	RADIESSE® Total Reporting Symptoms N(%)	CONTROL Total Reporting Symptoms N(%)	RADIESSE® Number of Days				CONTROL Number of Days			
			1-3 N(%)	4-7 N(%)	8-14 N(%)	>14 N(%)	1-3 N(%)	4-7 N(%)	8-14 N(%)	>14 N(%)
Ecchymosis	91 (60.3%)	60 (39.7%)	16 (10.6%)	37 (24.5%)	33 (21.9%)	5 (3.3%)	15 (9.9%%)	29 (19.2%)	12 (7.9%)	4 (2.6%)
Edema	104 (54.5%)	87 (45.5%)	34 (17.8%)	43 (22.5%)	17 (8.9%)	10 (5.2%)	34 (17.8%)	39 (20.4%)	10 (5.2%)	4 (2.1%)
Erythema	105 (45.1%)	128 (54.9%)	39 (16.7%)	26 (11.2%)	19 (8.2%)	21 (9.0%)	45 (19.3%)	35 (15.0%)	16 (6.9%)	32 (13.7%)
Granuloma	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Needle Jamming	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nodule	1 (50.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (50.0%)
Pain	40 (54.8%)	33 (45.2%)	22 (30.1%)	13 (17.8%)	4 (5.5%)	1 (1.4%)	20 (27.4%)	10 (13.7%)	2 (2.7%)	1 (1.4%)
Pruritis	24 (47.1%)	27 (52.9%)	15 (29.4%)	5 (9.8%)	3 (5.9%)	1 (2.0%)	11 (21.6%)	10 (19.6%)	3 (5.9%)	3 (5.9%)
Other*	52 (56.5%)	40 (43.5%)	15 (16.3%)	7 (18.5%)	8 (8.7%)	12 (13.0%)	8 (8.7%)	10 (10.9%)	11 (12.0%)	11 (12.0%)

Table 3. **PHYSICIAN REPORTED ADVERSE EVENTS**

Number of Patients With at Least One Adverse Event

By Adverse Event Type N = 117

ADVERSE EVENT TYPE	RADIESSE® Total Reporting Symptoms N(%)	CONTROL Total Reporting Symptoms N(%)
Ecchymosis	0 (0.0%)	2 (1.7%)
Edema	5 (4.3%)	4 (3.4%)
Erythema	6 (5.1%)	9 (7.7%)
Granuloma	0 (0.0%)	0 (0.0%)
Needle Jamming	1 (0.9%)	0 (0.0%)
Nodule	0 (0.0%)	2 (1.7%)
Pain	2 (1.7%)	1 (0.9%)
Pruritis	1 (0.9%)	2 (1.7%)
Other*	3 (2.6%)	3 (2.6%)

* "Other" adverse events for both RADIESSE injectable implant and Control include soreness, numbness, contour irregularity tenderness and irritation. None of the reports of contour irregularities was determined to be nodules or granulomas.

Table 4. **PHYSICIAN REPORTED ADVERSE EVENTS**

By Adverse Event Type N = 117

ADVERSE EVENT TYPE	RADIESSE® Total Reporting Symptoms N(%)	CONTROL Total Reporting Symptoms N(%)	RADIESSE® Number of Days				CONTROL Number of Days			
			1-3 N(%)	4-7 N(%)	8-14 N(%)	>14 N(%)	1-3 N(%)	4-7 N(%)	8-14 N(%)	>14 N(%)
Ecchymosis	0 (0.0%)	2 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (50.0%)	1 (5.0%)	0 (0.0%)
Edema	5 (41.7%)	7 (58.3%)	5 (41.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (41.7%)	0 (0.0%)	0 (0.0%)	2 (16.7%)
Erythema	9 (42.9%)	12 (57.1%)	4 (19.0%)	2 (9.5%)	2 (9.5%)	1 (4.8%)	2 (9.5%)	3 (14.3%)	4 (19.0%)	3 (14.3%)
Granuloma	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Needle Jamming	1 (100.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nodule	0 (0.0%)	3 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (33.3%)	2 (66.7%)
Pain	3 (75.0%)	1 (25.0%)	1 (25.0%)	1 (25.0%)	0 (0.0%)	1 (25.0%)	1 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pruritis	1 (33.3%)	2 (66.7%)	0 (0.0%)	0 (0.0%)	1 (33.3%)	0 (0.0%)	1 (33.3%)	0 (0.0%)	1 (33.3%)	0 (0.0%)
Other*	4 (50.0%)	4 (50.0%)	1 (12.5%)	0 (0.0%)	2 (25.0%)	1 (12.5%)	1 (12.5%)	1 (12.5%)	0 (0.0%)	2 (25.0%)

B. HIV-ASSOCIATED FACIAL LIPOATROPHY

In a prospective, open label study of 100 patients at three U.S. sites, adverse events reported after RADIESSE injectable implant treatments are provided in Tables 8-11. Adverse events reported in patient diaries during the 14 days after treatment are listed in Tables 5 and 6. Physician reported adverse events are those reported by Investigators and patients any time outside the 2 week diaries. Those adverse events are presented in Tables 7 and 8.

Table 5. **NUMBER OF PATIENTS WITH MAXIMAL SEVERITY OF LOCAL ADVERSE EVENTS**

Reported Through Patient Diaries N = 100

ADVERSE EVENT TYPE	PATIENTS REPORTING SYMPTOMS	MILD N(%)	MODERATE N(%)	SEVERE N(%)
Ecchymosis	64	34/64 (53.1%)	25/64 (39.1%)	5/64 (7.8%)
Edema	99	46/99 (46.5%)	49/99 (49.5%)	4/99 (4.0%)
Erythema	55	32/55 (58.2%)	23/55 (41.8%)	0/55 (0.0%)
Granuloma	0	0/0 (0.0%)	0/0 (0.0%)	0/0 (0.0%)
Nodule	0	0/0 (0.0%)	0/0 (0.0%)	0/0 (0.0%)
Pain	37	24/37 (64.9%)	13/37 (35.1%)	0/37 (0.0%)
Pruritis	21	18/21 (85.7%)	3/21 (14.3%)	0/21 (0.0%)
Other*	43	27/43 (62.8%)	15/43 (34.9%)	1/43 (2.3%)

* "Other" adverse events were those reported that did not fit into the categories detailed the tables above. The most common "Other" adverse event was contour irregularities. Additional "Other" adverse events included numbness, dryness, peeling, burning sensation, whiteheads and rash.

Table 6. **DURATION OF ADVERSE EVENTS AS REPORTED THROUGH PATIENT DIARIES**

ADVERSE EVENT TYPE	TOTAL REPORTING SYMPTOMS	NUMBER OF DAYS			
		1-3 N(%)	4-7 N(%)	8-14 N(%)	>14 N(%)
Ecchymosis	142	29/142 (20.4%)	51/142 (35.9%)	50/142 (35.2%)	12/142 (8.5%)
Edema	430	205/430 (47.7%)	153/430 (35.6%)	52/430 (12.1%)	20/430 (4.7%)
Erythema	210	114/210 (54.3%)	69/210 (32.9%)	22/210 (10.5%)	5/210 (2.4%)
Pain	110	54/110 (49.1%)	32/110 (29.1%)	18/110 (16.4%)	6/110 (5.5%)
Pruritis	54	28/54 (51.9%)	9/54 (16.7%)	6/54 (11.1%)	11/54 (20.4%)
Other	112	40/112 (35.7%)	19/112 (17.0%)	18/112 (16.1%)	35/112 (31.3%)

Table 7. **MAXIMAL SEVERITY OF LOCAL ADVERSE EVENTS**
Physician Reported Adverse Events N = 100

ADVERSE EVENT TYPE	PATIENTS REPORTING SYMPTOMS	MILD N(%)	MODERATE N(%)	SEVERE N(%)
Ecchymosis	3	2/3 (66.7%)	1/3 (33.3%)	0/3 (0.0%)
Edema	8	8/8 (100.0%)	0/8 (0.0%)	0/8 (0.0%)
Erythema	3	3/3 (100.0%)	0/3 (0.0%)	0/3 (0.0%)
Granuloma	0	0/0 (0.0%)	0/0 (0.0%)	0/0 (0.0%)
Nodule	0	0/0 (0.0%)	0/0 (0.0%)	0/0 (0.0%)
Pain	2	1/2 (50.0%)	0/0 (0.0%)	1/2 (50.0%)
Pruritis	0	0/0 (0.0%)	0/0 (0.0%)	0/0 (0.0%)
Other*	26	20/26 (76.9%)	6/26 (23.1%)	0/26 (0.0%)

* "Other" adverse events were those reported that did not fit into the categories detailed the tables above. The most common "Other" adverse event was contour irregularities. Additional "Other" adverse events included numbness, dryness, peeling, burning sensation, whiteheads and rash.

Table 8. **DURATION OF ADVERSE EVENTS**
Physician Reported Adverse Events

ADVERSE EVENT TYPE	TOTAL REPORTING SYMPTOMS	NUMBER OF DAYS			
		1-3 N(%)	4-7 N(%)	8-14 N(%)	>14 N(%)
Ecchymosis	5	3/5 (60.0%)	0/5 (0.0%)	2/5 (40.0%)	0/5 (0.0%)
Edema	13	10/13 (76.9%)	1/13 (7.7%)	1/13 (7.7%)	1/13 (7.7%)
Erythema	4	1/4 (25.0%)	2/4 (50.0%)	0/0 (0.0%)	1/4 (25.0%)
Pain	4	2/4 (50.0%)	0/4 (0.0%)	2/4 (50.0%)	0/4 (0.0%)
Pruritis	0	0/0 (0/0%)	0/0 (0.0%)	0/0 (0.0%)	0/0 (0.0%)
Other	62	27/62 (43.5%)	0/62 (0.0%)	1/62 (1.6%)	34/62 (54.8%)

CLINICAL STUDIES

A. NASOLABIAL FOLD CLINICAL DATA

Study design

The safety and effectiveness of RADIESSE injectable implant for the treatment of nasolabial folds (NLFs) was evaluated in a multi-center, prospective, randomized clinical trial. Patients were randomized to receive RADIESSE injectable implant in one fold and a commercially available collagen implant in the contralateral fold.

Patients were eligible to receive up to three injections during the initial treatment phase (week 0, week 2 and week 4). At 2 weeks after each treatment, the level of correction was determined and if correction was less than optimal, the Investigator re-treated the nasolabial fold using the same respective treatment materials as in the initial treatment. A safety follow-up was conducted 1 month after any injection and at 3 and 6 months after the last injection. Effectiveness evaluations were conducted at 3 and 6 months after the last injection. Three blinded reviewers independently evaluated the severity of the subject's nasolabial folds using a validated 6-point wrinkle severity scale.

Study Endpoints

The primary effectiveness endpoint of the study was the blinded reviewers' Lemperle Rating Scale (LRS) score of wrinkle severity at 3 months after the last touch-up (at which optimal correction was achieved). In this assessment, LRS scores were determined, (using this validated 6-point scale), via blinded, photographic assessments by 3 board certified physicians. A change in LRS of 1 was considered to be clinically significant. Secondary effectiveness endpoints included the blinded reviewers' assessment of wrinkle severity at 6 months after treatment, and the volume of material injected.

Study Population

A total of 117 subjects (31-76 years of age) were randomized and treated and 115 (98.3%) completed the 3 month primary effectiveness evaluation and 113 (96.6%) completed the 6 month follow-up visit. The baseline demographics of the study population are presented in Table 9.

Table 9. **PATIENT DEMOGRAPHICS, NASOLABIAL FOLDS**
N = 117

AGE (YEARS)	
Mean	**54.7**
Standard Deviation	**8.9**
Minimum	**31.0**
Maximum	**76.0**
GENDER	
Female	**105** (89.7%)
Male	**12** (10.3%)
RACE	
American Indian	**0** (0.0%)
Asian	**0** (0.0%
Black	**2** (1.7%)
Caucasian	**102** (87.2%)
Hispanic	**11** (9.4%)
Other	**2** (1.7%)
SMOKING HISTORY	
Quit Smoking	**26** (22.2%)
Never Smoked	**83** (70.0%)
Smokes	**8** (6.8%)

As indicated in Table 9, the study enrolled a population of predominantly female, Caucasian non-smokers.

Treatment Material Delivered

Volumes injected during the initial treatment phase are detailed in Table 10 below. The total mean volume for RADIESSE injectable implant was 1.2mL and 2.4mL for the Control.

Table 10. **TOTAL VOLUME OF MATERIAL INJECTED (ML),**
Nasolabial Folds N = 117

	RADIESSE®	CONTROL
Mean	1.2	2.4
Median	1.1	2.2
Standard Deviation	0.5	0.9
Minimum	0.3	0.8
Maximum	2.7	4.7

Effectiveness Results:

Table 11 contains the mean LRS at baseline, 3 months and 6 months for the RADIESSE injectable implant treated nasolabial folds and the Control treated nasolabial folds with the difference between the means. Baseline scores for the RADIESSE injectable implant and Control groups were not statistically different.

Table 11. **COMPARISON OF MEAN LRS SCORES* FOR RADIESSE INJECTABLE IMPLANT AND CONTROL**
Nasolabial Folds - Baseline, 3 and 6 Months

	RADIESSE®	CONTROL	DIFFERENCE
Baseline	3.4	3.4	0.0
3 Months	1.9	3.5	1.6
6 Months	2.1	3.4	1.3

* Grading Scale: 0 = No wrinkles, 1 = Just perceptible wrinkle, 2 = Shallow wrinkle, 3 = Moderately deep wrinkle, 4 = Deep wrinkle, well-defined edges, 5 = Very deep wrinkle, redundant fold

Primary Effectiveness Endpoint

The primary effectiveness endpoint was to use mean LRS scores to evaluate whether RADIESSE injectable implant was non-inferior to Control for the correction of nasolabial folds 3 months after final treatment. At 3 months, 84.6% of the RADIESSE injectable implant treated nasolabial folds were scored at least 1-point higher than the Control, 12.8% were scored equally, and 2.6% were scored at least 1-point lower than the Control. RADIESSE injectable implant met the statistical criteria for non-inferiority to Control at 3 months ($p<0.0001$), however, the Control scored no effectiveness at 3 months.

Secondary Effectiveness Endpoint

The pre-specified secondary superiority analyses at 6 months required a mean 1-point LRS difference between the improvements for the RADIESSE injectable implant treated nasolabial fold versus improvement on the Control treated nasolabial fold and that in at least 50% of patients, the RADIESSE injectable implant treated nasolabial fold be superior to the Control treated nasolabial fold. At 6 months after optimal correction was achieved, 78.6% of the RADIESSE injectable implant treated nasolabial folds were scored at least 1-point higher than the Control-treated folds ,16.2% were scored equally, and 5.1% were scored at least 1-point lower than the Control. The mean LRS for the RADIESSE injectable implant treated nasolabial folds demonstrated superiority when compared to the mean LRS for the Control-treated nasolabial folds at 6 months ($p<0.0001$).

B. HIV-ASSOCIATED FACIAL LIPOATROPHY CLINICAL DATA

Study design

The safety and effectiveness of RADIESSE injectable implant for the treatment of facial lipoatrophy was evaluated in a prospective, open-label, multi-center study of 100 patients with facial lipoatrophy with human immunodeficiency virus. Patients received an initial treatment (initial injection and an additional injection at 1 month as needed). Six months later, all patients were assessed for the need for a touch up injection. Effectiveness was assessed at 3, 6 and 12 months from initial treatment by means of a Global Aesthetic Improvement Scale (GAIS) rating, cheek skin thickness measurements, and patient satisfaction assessment. Safety was assessed by the recording of adverse events through 12 months.

Study Endpoints

The primary endpoint of the study was to evaluate the correction of lipoatrophy 3 months after treatment by comparing changes from baseline on the GAIS. The GAIS is a 5-category scale (Very much improved, much improved, improved, no change and worse). The secondary endpoints of the study were to evaluate the correction of facial lipoatrophy 6 months after treatment by comparing changes from baseline on the GAIS, and 3 and 6 months after treatment by comparing changes from baseline in cheek skin thickness measurements.

Study Population

The inclusion criteria for the clinical study were that the patient was to be HIV positive, had a CD4 count ≥ 250 /mm3 and viral load ≤ 5000 copies/mL, had been receiving HAART therapy for a minimum of 3 years, had HIV-associated facial lipoatrophy that was a grade 2, 3, or 4 on the Facial Lipoatrophy Severity Scale, was at least 18 years of age, signed a written informed consent, understood and accepted the obligation not to receive any other facial procedures or treatment affecting facial lipoatrophy through 12 month follow-up and understood and accepted the obligation and was logistically able to present for all scheduled follow-up visits.

The exclusion criteria for the clinical study were patients that had a known bleeding disorder (e.g., thrombocytopenia, thrombasthenia, or von Willebrand's disease), had received or was anticipated to receive antiplatelets, anticoagulants, thrombolytics, vitamin E, anti-inflammatories, interferon, or prednisone from 1 week pre- to 1 month post-injection, was receiving systemic or topical corticosteroids or anabolic steroids, had another medical condition that would preclude study participation or suggested an AIDS diagnosis (e.g., Kaposi sarcoma, recurrent infection, recurrent pneumonia), had received silicone injections, facial tissue augmentation other than collagen, grafting, or any other surgery in the cheek area, had received collagen in the cheek area within the past 6 months, had received over-the-counter wrinkle products (e.g., alpha-hydroxy acids) or prescription treatments (e.g., Renova, Retin-A, microdermabrasion, chemical peels) within 4 weeks prior to study or intended to receive these products and/or treatments during the study, had facial hair that would preclude ability to assess facial lipoatrophy, had a history of keloid formation, was pregnant or lactating or not using a reliable form of birth control, if female of child bearing potential and was enrolled in an interfering study.

Study Results

Demographics / Injection Information:

The study enrolled a population of predominantly multi-ethnic, non-smoking males (94% male) with a mean age of 48 years. Forty-four (44) percent of patients were Black, Hispanic or Asian. Fifty-six (56) percent were Caucasian. Fifty-one (51) percent of patients had a Fitzpatrick Skin score of IV, V or VI. All treatments were performed with a 25 gauge, 1½ inch needle. Mean initial treatment volumes were 4.8mL for the initial treatment and 1.8mL at 1 month if necessary (85% of patients were treated at 1 month). At 6 months, the mean touch up volume was 2.4mL (89% of patients). Four (4) percent of patients received only one treatment, 18% of patients received a total of two treatments and 78% of patients received a total of three treatments. No patient received more than three treatments.

Effectiveness Results:

A live GAIS rating was determined at 3 and 6 months (see Table 12).

Table 12. **GAIS RATINGS**

% OF PATIENTS	3 MONTH N = 100	6 MONTH N = 98
Very Much Improved	26%	7%
Much Improved	72%	86%
Improved	2%	7%
No Change	0%	0%
Worse	0%	0%
TOTAL	100%	100%

Cheek thickness measurements of patients left and right cheeks were performed at baseline, 3 and 6 months (see Table 13).

Table 13. **CHEEK THICKNESS MEASUREMENTS**

	BASELINE	3 MONTH			6 MONTH		
	Mean (N=100)	Mean (N=100)	Δ From Baseline	P-Value	Mean (N=97)	Δ From Baseline	P-Value
Left Cheek	4.7mm	7.3mm	2.6mm	<0.0001	7.1mm	2.4mm	<0.0001
Right Cheek	4.9mm	8.0mm	2.1mm	<0.0001	7.5mm	2.7mm	<0.0001

Patients provided responses to a 5-question patient satisfaction questionnaire at 3 and 6 months (see Table 14).

Table 14**. PATIENT SATISFACTION ASSESSMENT**

	3 Month N=100	6 MONTH N=98
	YES	YES
Would you recommend RADIESSE treatment?	99%	99%
Has the RADIESSE treatment been beneficial to you?	100%	100%
Do you feel more attractive since receiving RADIESSE treatment?	98%	98%
Is your emotional wellbeing better since receiving RADIESSE®?	91%	96%
Do you have more confidence in your appearance since receiving RADIESSE®?	98%	98%

Short Term and Long Term Radiographic Evaluation of RADIESSE Injectable Implant

RADIESSE injectable implant contains calcium hydroxylapatite particles (25-45 microns) that are radiopaque and suspended in a water based gel. Therefore a radiographic study was conducted to assess the radiographic appearance of RADIESSE injectable implant in patients with both short-term and long-term follow-up after injection for HIV-associated facial lipoatrophy and treatment of nasolabial folds. The radiographic assessment consisted of standard, plain radiography and CT scanning. X-rays and CT Scans were assessed by two blinded, licensed radiologists. The inclusion of these patients allowed assessment of patients immediately after initial injection, at least 12 months after initial injection, and patients with varying volumes implanted.

A total of 58 patients in three patients groups were enrolled into the study. RADIESSE injectable implant was determined to be visualizable in the X-ray radiographs by both evaluators, but the X-ray readings were not conclusive for the presence of the implant, when in fact it was present. This may be due to the fact that the volume of RADIESSE injectable implant in some patients was small and the sensitivity of X-ray imaging may not be sufficient to detect small volumes of implant. RADIESSE injectable implant was more readily visualizable by CT Scan when compared to X-ray and the CT Scan results were read more consistently between two evaluators. RADIESSE injectable implant was easily seen when imaging was done soon after an injection and was also seen when imaging was done several months after injection (minimum of 12 months). As expected, the results for the CT Scan provided a superior image capability as compared to X-ray when visualizing RADIESSE injectable implant.

INDIVIDUALIZATION OF TREATMENT

Before treatment, the patient's suitability for the treatment and the patient's need for pain relief should be assessed. The outcome of treatment with RADIESSE injectable implant will vary between patients. In some instances, additional treatments may be necessary depending on the size of the defect and the needs of the patient.

DIRECTIONS FOR USE

General

The following is required for the percutaneous injection procedure:

- RADIESSE injectable implant syringe(s)
- 25-27 gauge ID needle(s) with Luer lock fittings

1. Prepare patient for percutaneous injection using standard methods. The treatment injection site should be marked and prepared with a suitable antiseptic. Local or topical anesthesia at the injection site should be used at the discretion of the physician.
2. Prepare the syringes of RADIESSE injectable implant and the injection needle(s) before the percutaneous injection. A new injection needle may be used for each syringe, or the same injection needle may be connected to each new syringe.
3. Remove foil pouch from the carton. Open the foil pouch by tearing at the notches (marked 1 and 2), and remove the syringe from the foil pouch. *There is a small amount of moisture normally present inside the foil pouch for sterilization purposes; this is **not** an indication of a defective product.*
4. Separate the needle packaging at the upper edge and peel apart to a point below hub. For use of needles other than the needle(s) provided with this package, follow the directions provided with the needle(s).
5. Remove the Luer syringe cap from the distal end of the syringe prior to attaching the needle. The syringe of RADIESSE injectable implant can then be twisted onto the Luer lock fitting of the needle taking care not to contaminate the needle. Discard needle package. **The needle must be tightened securely to the syringe and primed with RADIESSE injectable implant.** If excess implant is on the surface of the Luer lock fittings, it will need to be wiped clean with sterile gauze. Slowly push the syringe plunger until RADIESSE injectable implant extrudes from the end of the needle. If leakage is noted at the Luer fitting, it may be necessary to tighten the needle, or to remove the needle and clean the surfaces of the Luer fitting or, in extreme cases, replace both the syringe and the needle.
6. Locate the initial site for the implant. Scar tissue and cartilage may be difficult or impossible to treat. Avoid if possible, passing through these tissue types when advancing the injection needle.

7. The amount injected will vary depending on the site and extent of the restoration or augmentation desired. RADIESSE injectable implant should be injected subdermally.
8. Use a 1:1 correction factor. No overcorrection is needed.
9. Insert needle with bevel down at approximately a 30° angle to the skin. Needle should slide under the dermis to the point you wish to begin the injection. This should be easily palpable with the non-dominant hand.
10. If significant resistance is encountered when pushing the plunger, the injection needle may be moved slightly to allow easier placement of the material or it may be necessary to change the injection needle. One needle jam occurred in the nasolabial fold clinical study. Needle jams are more likely with use of needles smaller than 27gauge ID.
11. Advance the needle into the subdermis to the starting location. Carefully push the plunger of the RADIESSE injectable implant syringe to start the injection and slowly inject the implant material in linear threads while withdrawing the needle. Continue placing additional lines of material until the desired level of correction is achieved.
12. Apply slow continuous even pressure to the syringe plunger to inject the implant as you withdraw the needle. The implant material should be completely surrounded by soft tissue without leaving globular deposits. The injected area may be massaged as needed to achieve even distribution of the implant.
13. Use once and discard in accordance with local safety standards.

PATIENT COUNSELING INFORMATION

Refer to RADIESSE injectable implant Patient Information Guide.

STORAGE

RADIESSE injectable implant should be stored at a controlled room temperature between 15° C and 32° C (59° F and 90° F). The expiration date, when stored in these temperatures, is two years from date of manufacture. Do not use if the expiration date has been exceeded.

DISPOSAL

Used and partially used syringes and injection needles could be biohazardous and should be handled and disposed of in accordance with facility medical practices and local, state or federal regulations.

WARRANTY

BioForm Medical, Inc. warrants that reasonable care has been exercised in the design and manufacture of this product.

THIS WARRANTY IS IN LIEU OF AND EXCLUDES ALL OTHER WARRANTIES NOT EXPRESSLY SET FORTH HEREIN, WHETHER EXPRESSED OR IMPLIED BY OPERATION OF LAW OR OTHERWISE, INCLUDING BUT NOT LIMITED TO, ANY IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR ITS PARTICULAR PURPOSE.

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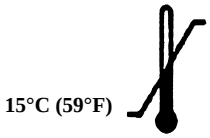
SYMBOLS

Do not resterilize



Store at a controlled room temperature between 15˚C and 32˚C (59˚F and 90˚ F)

Do not use if package is damaged

Latex free

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