



Editor's Note: Please help us bring Johns Hopkins eMedical Dermatology Review to our 2300+ subscribers for another year. The success of eMedical Dermatology Review depends on your valuable input for new topics and ideas.

Take our quick 9 question/5 minute survey (and be entered into a drawing for an iPod Shuffle.)

To access the survey, please visit here.



March 2010: VOLUME 2, NUMBER 4

Dermatologic Fillers

In this Issue...

To achieve natural looking facial rejuvenation, the physician must first assess the face as a whole and evaluate the texture and quality of the skin, dynamic rhytids, and the degree of volume loss that is present. Often, this leads to a treatment plan that utilizes multiple treatment modalities, such as laser or chemical resurfacing, neurotoxins, and replacement of lost volume with dermal fillers. In particular, since 2003, there has been a dramatic increase in the number of dermal fillers approved for use in the United States.

In this issue, we review selected studies which describe the safety and efficacy hyaluronic acid, calcium hydroxylapatite, and poly-L-lactic acid, and discuss recommendations for avoiding and managing potential complications that may arise from their use.

LEARNING OBJECTIVES

At the conclusion of this activity, participants should be able to:

- Identify the types of dermal fillers available in the United States,
- Describe the factors influencing the selection of a particular filler for a patient,
- Evaluate the safety and efficacy profiles of dermal fillers and how common complications can be avoided or managed.

IMPORTANT CME/CNE INFORMATION

▼ Program Begins Below

ACCREDITATION STATEMENTS

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of The Johns Hopkins University School of Medicine and The Institute for Johns Hopkins Nursing. The Johns Hopkins University School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

The Institute for Johns Hopkins Nursing is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

- **Bernard A. Cohen, MD**, has indicated he has received grants for studies from Novartis Pharmaceuticals and Astellas Pharma Inc.
- **Susan Matra Rabizadeh, MD, MBA** has disclosed no relationship with commercial supporters.
- **Mark Lebwohl, MD** has disclosed that he has received grants for clinical research, Advisory Board, speaker honorarium for/from Abbott, Amgen/Wyeth, Astellas, Centocor, Galderma, Genentech, Novartis, GlaxoSmithKline, Triax, Warner Chilcott. Serving as a consultant and receiving honorarium for/from Actelion, Cerexa, DermiPsor, Electro Optical Sciences, Helix BioMedix, Magen Biosciences, NeoStrata, Peplin, Sanofi-Aventis, Taro, Graceway and Pharmaderm. Advisory Board and receiving honorarium for/from Medicis, Nycomed and Pfizer. Speaker honorarium from Ranbaxy.

Program Information

CE Info
 Accreditation
 Credit Designations
 Intended Audience
 Learning Objectives
 Internet CME/CNE Policy
 Faculty Disclosure
 Disclaimer Statement

Length of Activity

1 hour
1 contact hour Nurses

Release Date

March 25, 2010

Expiration Date

March 24, 2012

Next Issue

May 18, 2010

TO COMPLETE THE POST-TEST

- Step 1.**
Please read the newsletter.
- Step 2.**
See the Post-test link at the end of the newsletter.
- Step 3.**
Follow the instructions to access the post-test.

CREDIT DESIGNATIONS Physicians

The Johns Hopkins University School of Medicine designates this educational activity for a maximum of 1.0 *AMA PRA Category 1 Credit(s)*[™]. Physicians should only claim credit commensurate with the extent of their participation in this activity.

Nurses

This 1 contact hour Educational Activity is provided by The Institute for Johns Hopkins Nursing. Each Newsletter carries a maximum of 1 contact hours.

POST-TEST

To take the post-test for eMedicalDermatology Review you will need to visit [The Johns Hopkins University School of Medicine's CME website](#) or [The Institute for Johns Hopkins Nursing](#). If you have already registered for another Hopkins CME program at these sites, simply enter the requested information when prompted. Otherwise, complete the registration form to begin the testing process. A passing grade of 70% or higher on the post test/evaluation is required to receive CME/CNE credit.

STATEMENT OF RESPONSIBILITY

The Johns Hopkins University School of Medicine and The Institute for Johns Hopkins Nursing take responsibility for the content, quality, and scientific integrity of this CME/CNE activity.

INTENDED AUDIENCE

This activity has been developed for the Dermatologist, Nurses, Dermasurgeon, Dermatopathologist, Pediatric Dermatologist, Immunodermatologist, Wound Care Specialist and Allied Healthcare providers.

FACULTY DISCLOSURE

As a provider accredited by the Accreditation Council for Continuing Medical Education (ACCME), it is the policy of Johns Hopkins University School of Medicine to require the disclosure of the existence of any relevant financial interest or any other relationship a faculty member or a provider has with the manufacturer(s) of any commercial product(s) discussed in an educational presentation. The Program Directors reported the following:

- **Elizabeth Sloand, PhD, CRNP** has disclosed no relationships with commercial supporters.

[Guest Author's Disclosures](#)

LAUNCH DATE

This program launched on September 22, 2009 and is published bi-monthly; activities expire 2 years from the date of publication, ending in May 2012.

INTERNET CME/CE POLICY

The Offices of Continuing Education (CE) at The Johns Hopkins University School of Medicine and The Institute for Johns Hopkins Nursing are committed to protect the privacy of its members and customers. The Johns Hopkins University maintains its Internet site as an information resource and service for physicians, other health professionals and the public.

The Johns Hopkins University School of Medicine and The Institute for Johns Hopkins Nursing will keep your personal and credit information confidential when you participate in a CE Internet based program. Your information will never be given to anyone outside The Johns Hopkins University program. CE collects only the information necessary to provide you with the service you request.

DISCLAIMER STATEMENT

The opinions and recommendations expressed by faculty and other experts whose input is included in this program are their own. This enduring material is produced for educational purposes only. Use of Johns Hopkins University School of Medicine name implies review of educational format design and approach. Please review the complete prescribing information of specific drugs or combination of drugs, including indications, contraindications, warnings and adverse effects before administering pharmacologic therapy to patients.

HARDWARE & SOFTWARE REQUIREMENTS

Pentium 800 processor or greater, Windows 98/NT/2000/XP or Mac OS 9/X, Microsoft Internet Explorer 5.5 or later, 56K Modem or better, Windows Media Player 9.0 or later, 128 MB of RAM
Monitor settings: High color at 800 x 600 pixels, Sound card and speakers, Adobe Acrobat Reader.

THIS ISSUE

- [COMMENTARY from our Guest Authors](#)
- [THE EFFICACY, DURABILITY, AND SAFETY OF HYALURONIC ACID FILLERS](#)
- [THE DURABILITY OF CROSS-LINKED HYALURONIC ACID GEL IN THE TREATMENT OF SEVERE NASOLABIAL FOLDS](#)
- [THE SAFETY AND EFFICACY OF CALCIUM HYDROXYLAPATITE](#)
- [CORRECTION OF HIV AND NON-HIV LIPOATROPHY WITH POLY-L-LACTIC ACID](#)
- [COMPLICATIONS OF DERMAL FILLERS](#)
- [THE INFLUENCE OF LASER, RADIOFREQUENCY, AND INTENSE PULSED LIGHT THERAPY FOLLOWING HYALURONIC ACID GEL IMPLANTATION](#)

Program Directors

Bernard A. Cohen, MD

Professor of Pediatrics and Dermatology and Director of Pediatric Dermatology,
Johns Hopkins Children's Center
Baltimore, MD

Susan Matra Rabizadeh, MD, MBA

Department of Dermatology
Cedars-Sinai Medical Group
Beverly Hills, CA

Mark Lebwohl, MD

Professor and Chairman
Department of Dermatology
The Mount Sinai School of Medicine
New York, NY

Elizabeth Sloand, PhD, CRNP

Assistant Professor of Pediatric Nursing
The Johns Hopkins University
School of Nursing
Baltimore, MD

GUEST AUTHORS OF THE MONTH



Commentary & Reviews:

Jenny Kim, MD, PhD

Associate Professor of Clinical Medicine and Dermatology, David Geffen School of Medicine at UCLA
Chief of Dermatology, GLAHS VA
Los Angeles, California

Guest Faculty Disclosures

Jenny Kim, MD, PhD discloses that she has been a consultant for and received honoraria from Allergan, Inc. and Medicis within the last 12 months.

Jamie E. McInturff, MD discloses that she has no financial relationship with commercial supporters.



Commentary & Reviews:

Jamie E. McInturff, MD

Dermatology resident, Post-graduate year 4
UCLA/West Los Angeles VA Dermatology Residency Program
Los Angeles, California

Unlabeled/Unapproved Uses

The authors have indicated that there will be no reference to unlabeled or unapproved uses of drugs or products.

[Program Directors' Disclosures](#)

MARCH PODCAST



eMedicalDermatology Review is proud to continue our accredited **PODCASTS for 2010**.
[Listen here.](#)

The *eMedicalDermatology Review* podcast is a clinical discussion between our March authors, Jenny Kim, MD, Jamie McInturff, MD, and Robert Busker, *eMedicalDermatology Review's* Managing Editor. The topic is *Fillers*.

Participants can now receive 0.5 credits per podcast after completing an online [post-test](#). In addition to our monthly newsletters, there will be 4 podcasts for the year.

To learn more about podcasting and how to access this exciting new feature of *eMedicalDermatology*, please [visit this page](#).

Podcasts

Please remember that you don't need this



to listen to our podcasts. You can listen directly from your computer.

[back to top](#)

COMMENTARY

The variety of dermal fillers FDA approved for use in the United States has expanded greatly since the approval of bovine collagen in 1981. Bovine collagen, while useful in temporarily filling fine lines, is potentially allergenic, and requires skin testing prior to treatments. Also, its typical duration of action is only 3 months, and it may be inadequate for correcting areas of larger volume loss. Despite these short-comings, there was a lack of alternatives available until 2003.

Since 2003, the options for dermal fillers have expanded greatly. In addition to bovine collagen, FDA-approved products for soft-tissue augmentation in the United States now include bioengineered human collagen, porcine collagen, hyaluronic acid, polymethylmethacrylate with bovine collagen, poly-L-lactic acid, and calcium hydroxyapatite. In 2004, 221,000 patients had collagen injections; 40,000 had calcium hydroxyapatite injections; and 35,000 had poly-L-lactic acid injections.¹ In 2007, hyaluronic acid injections became the second most common non-surgical cosmetic procedure, with 1.4 million patients treated that year.²

 LISTEN TO OUR PODCAST

 RECOMMEND TO A COLLEAGUE

 NEWSLETTER ARCHIVE

With this wide variety of available fillers, in order to choose appropriate products to meet patient needs, practitioners need to become better-versed on the composition of these agents, indications for their use, techniques for injection, and reported adverse effects. This was once a difficult task given the limited number of comparative and long-term studies published. However, recent studies on hyaluronic acid such as the one by Dover et al discussed in this issue have demonstrated the safety and efficacy of this agent in large prospective randomized multicenter studies. Also, poly-L-lactic acid has emerged as the leading filler for HIV lipoatrophy. As this agent has been approved in Europe for 10 years and in the United States for 5 years, more long-term studies are appearing in the literature, such as the one by Levy et al, which provides 3 year follow-up data supporting the use of poly-L-lactic acid as a safe and effective treatment for HIV lipoatrophy.

Dermal fillers are powerful tools which allow the clinician to not only fill wrinkles but also restore volume to the aging face, resulting in a more natural youthful appearance. Although the non-collagen fillers last several months, they are not permanent, so the clinician must adapt future treatments to a particular patient's aging process. These agents also provide the cosmetic patient with little downtime and less risk of serious side-effects compared to that of conventional cosmetic surgery. In addition, they offer patients with HIV-lipoatrophy a treatment which may make their disease less visible to others.

In the future, the field of dermatology would benefit from research studies addressing the safety and efficacy of filler use in conjunction with other procedures such as laser and botulinum toxin injections. The study by Goldman et al, discussed herein, addresses the use of laser immediately following hyaluronic acid filler injection—however, this was a small study, and further data to support its findings are largely lacking. Also, there are few studies addressing the use of fillers in patients with darker skin types and the potential side-effects of hyperpigmentation and keloid formation. The latter is a significant oversight, as in 2007 racial and ethnic minorities accounted for 22% of cosmetic procedures in the United States.²

Finally, given the relative ease of use of these fillers, there is legitimate concern regarding the rise of non-physician injectors of these substances. Also of great concern are the reports of unethical practitioners injecting impure and non-FDA approved products, sometimes with serious consequences of infection and disfigurement. Therefore, it is important to educate our patients that the injection of dermal fillers is a medical procedure that requires the use of pure, high quality products, as well as the hands of an experienced clinician.

Commentary References

1. 2004 Cosmetic Surgery National Data Bank Statistics. [The American Society of Aesthetic Plastic Surgery website.](#)
2. 2004 Cosmetic Surgery National Data Bank Statistics. [The American Society of Aesthetic Plastic Surgery website.](#) 11.7 *Cosmetic Procedures in 2007 page.*

[back to top](#)

THE EFFICACY, DURABILITY, AND SAFETY OF HYALURONIC ACID FILLERS

Dover JS, Rubin MG, Bhatia AC. **Review of the efficacy, durability, and safety data of two nonanimal stabilized hyaluronic acid fillers from a prospective, randomized, comparative, multicenter study.** *Dermatol Surg.* 2009 Feb;35 Suppl 1:322-330; discussion 330-331.

(For non-subscribers to this journal, an additional fee may apply to obtain full-text articles.)



[View journal abstract](#)

In December of 2003, the non-animal stabilized hyaluronic acid (NASHA) small gel known as Restylane® became approved by the Food and Drug Administration for soft tissue augmentation of the nasolabial folds. This was followed by the later development of large-particle hyaluronic acid gels such as Perlane®. These products are both bioengineered from bacteria and are formulated to have the same concentration of hyaluronic acid (20mg/cc). They differ only in particle size, in that the large-particle gel contains about 10,000 particles per cc versus the small-particle gel which contains 100,000 particles per cc.



To assess the efficacy, durability, and safety of both small and large particle NASHA gels, the authors conducted a blinded, prospective, randomized study at 17 sites with a total of 248 subjects enrolled. These subjects were randomized to receive either the large-particle NASHA gel through a 27 gauge needle or the small-particle NASHA gel through a 30 gauge needle into both nasolabial folds. The investigators were instructed to fully correct the nasolabial folds, but the method, depth, and volume per injection were at the discretion of the investigator.

All of the adverse experiences were largely equal between the large and small-particle groups. The most common adverse event was bruising (26% of large-gel group and 29% of small-gel group), followed by edema (6% of large-gel group and 4% of small-gel group), and then tenderness (4% of large-gel group and 5% of small-gel group).

Three subjects in each treatment group developed inflammatory nodules in the nasolabial folds. Most subjects had spontaneous resolution of the nodules within 2 weeks; however, in the large-gel group, one subject required 3 courses of clarithromycin, 3 injections with intralesional steroids, and needle evacuation for resolution. Also, one subject of the small-gel group was treated with amoxicillin clavulanate for 9 days before resolution.

This randomized study is notable in that it allowed for direct comparison of the efficacy and adverse events between a large and a small particle hyaluronic acid dermal filler. Importantly, no significant difference was seen between the 2 products in terms of adverse experiences, efficacy, or longevity.

One limitation to this study is that the volumes injected may not accurately reflect the volumes used in most practices. In the study, there was a significant range in the total volume injected per subject, with subjects receiving 0.8 to 9cc of the large gel and 1.0 to 8.8cc of the small gel. However, the inclusion of patients receiving greater volumes of product than that recommended by the package inserts (6cc for the large gel and 1.5cc per nasolabial fold for the small gel) demonstrates that the use of these larger volumes may also be safe and effective.

Another limitation of this study was that the injection technique was not standardized, and the overall incidence of bruising in this study was very high compared to other studies. However, this lack of standardization provided some additional information regarding optimal injection techniques: the investigators found that the fanning injection technique was associated with a higher incidence of adverse events than the linear threading or serial puncture techniques. Also, those reporting longer than average injection times had less adverse experiences reported.

[back to top](#)

THE DURABILITY OF CROSS-LINKED HYALURONIC ACID GEL IN THE TREATMENT OF SEVERE NASOLABIAL FOLDS

Lupo MP, Smith SR, Thomas JA, Murphy DK, Beddingfield FC 3rd. **Effectiveness of Juvederm® Ultra Plus dermal filler in the treatment of severe nasolabial folds.** *Plast Reconstr Surg.* 2008 Jan;121(1):289-297.

(For non-subscribers to this journal, an additional fee may apply to obtain full-text articles.)



[View journal abstract](#)



[View full article](#)

One limitation of dermal filler studies is their generally limited length of follow-up to objectively assess durability of product. This study—a multicenter, double-blind, randomized, and controlled within-subject design comparing Juvederm® Ultra Plus (a 24 mg/cc and cross-linked form of hyaluronic acid) to Zyplast® (a bovine collagen)—had an extended follow-up period of one year for a subset of patients.

Out of the total 439 subjects enrolled, 87 were deemed to have “severe” nasolabial folds per the 5 point Wrinkle Assessment Scale. These 87 subjects were randomized to receive treatment with Juvederm Ultra Plus into one nasolabial fold and Zyplast into the contralateral fold. There were no significant differences in side-effects between the 2 products in this study. All adverse reactions were minor (erythema, bruising, or induration), and all resolved within one week without intervention. Also, both products were able to achieve the same level of correction at 2 weeks after treatment.

 RECOMMEND TO A COLLEAGUE

 NEWSLETTER ARCHIVE

However, at the end of the initial 24 week follow-up period, the nasolabial folds treated with Zyplast had wrinkle severity scores near their baseline, while two-thirds of the Juvederm Ultra Plus sites had at least a 2 point improvement in wrinkle severity score. At the one year follow-up, 81% still had at least a 1 point improvement from their baseline wrinkle severity score, and 38% still had at least a 2 point improvement. Notably, those undergoing retreatment at 1 year required much less volume to achieve complete correction; the median volume for full correction at the initial treatment visit was 1.6cc, while treatment after the one year period required only a median of 0.7cc for full correction.

This study is significant in that it indicates the cross-linked form of hyaluronic acid may last longer than expected based on the durability data from other studies of non-cross-linked hyaluronic acids. However, this claim should not be overstated, as cross-linked and non-cross-linked hyaluronic acid fillers were not directly compared in this study. Additional long term studies with a greater number of subjects comparing the durability of cross-linked and non-cross-linked hyaluronic acids are needed to more clearly delineate the duration of action of this product.

[back to top](#)

THE SAFETY AND EFFICACY OF CALCIUM HYDROXYLAPATITE

Sadick NS, Katz BE, Roy D. **A multicenter, 47-month study of safety and efficacy of calcium hydroxylapatite for soft tissue augmentation of nasolabial folds and other areas of the face.** *Dermatol Surg.* 2007 Dec;33 Suppl 2:S122-6; discussion S126-S127.

(For non-subscribers to this journal, an additional fee may apply to obtain full-text articles.)



[View journal abstract](#)

Calcium hydroxylapatite (CaHA) was first approved in the United States for augmentation of the vocal folds, radiographic tissue marking, and for use in craniofacial implants. Then, in 2006, Radiesse® (composed of CaHA microspheres in an aqueous polysaccharide gel), was FDA approved both for use in correction of facial lipoatrophy associated with antiretroviral treatment in HIV and as a dermal filler to correct facial lines and wrinkles. The CaHA particles are believed to serve as a matrix for fibroblast growth, with the particles slowly metabolizing into calcium and phosphate ions over time.

This study aimed to assess the safety and efficacy of CaHA as a soft-tissue filler in the face. It was performed at 2 treatment centers with a total of 113 subjects over a 47 month period. While 86 of the patients had treatment of the nasolabial folds, a variety of other sites were injected. The nasolabial folds were injected with a linear threading technique; however the method of injection varied for other treatment sites. In this study, all patients with a known history of oral HSV were given acyclovir prophylaxis.

The most common side effects reported included mild erythema and edema lasting up to a few days post-injection. There were also reports of transient firmness which resolved within 2 weeks for all affected subjects. Importantly, 2 out of 14 patients receiving CaHA for lip augmentation in this study experienced submucosal nodule formation. While these nodules in the study patients responded to intralesional steroid injections, the incidence of 15% of patients developing this complication is high. This finding supports the statements by other authors that caution against the use of CaHA in the lips.^{1,2,3}

A major short-coming of this study is that only 41 of these patients underwent 3-month and 6-month follow-up evaluations to assess efficacy. At these visits, both the patients and physicians were asked to rate their satisfaction with the look and feel of the implant on a scale of 1 through 5 (1=unsatisfactory, 2=poor, 3=satisfactory, 4=very good, 5=excellent). At 3 months, the mean patient score of the implant was 4.6 for both look and feel while the physician score was 4.5 for look and 4.6 for feel. At 6 months, these ratings were slightly higher by both patient and physician assessment. However, as the methods of the paper did not clarify if there was a selection process to determine which patients were chosen for follow-up, it is unclear if these results can be generalized to the entire study group.

With regards to the durability of the product, the authors state that the product was durable for approximately 8 months. However, it is unclear per their methods how this was determined. Given that some forms of hyaluronic acid have been shown to last this long as well, the durability of this product may not be a unique feature.

 RECOMMEND TO A COLLEAGUE

 NEWSLETTER ARCHIVE

References

1. Tzikas TL. [Evaluation of the Radiance FN soft tissue filler for facial soft tissue augmentation.](#) *Arch Facial Plast Surg* 2004. 2004, 6:234–239.
2. Sklar JA and White SM. [Radiance FN: a new soft tissue filler.](#) *Dermatologic Surgery*. 2004, 30:764-768.
3. Berlin A, Cohen JL, Goldberg DJ. [Calcium hydroxylapatite for facial rejuvenation.](#) *Seminars Cutaneous Medicine and Surgery*. 2006; 25:132-137.

[back to top](#)

CORRECTION OF HIV AND NON-HIV LIPOATROPHY WITH POLY-L-LACTIC ACID

Levy RM, Redbord KP, Hanke CW. **Treatment of HIV lipoatrophy and lipoatrophy of aging with poly-L-lactic acid: a prospective 3-year follow-up study.** *J Am Acad Dermatol*. 2008 Dec;59(6):923-933.

(For non-subscribers to this journal, an additional fee may apply to obtain full-text articles.)



[View journal abstract](#)



[View full article](#)

Poly-L-lactic acid is a non-animal derived product that is believed to induce neocollagenesis and has been largely marketed for volume restoration. Poly-L-lactic acid is believed to slowly break down into lactic acid over a period of years. The initial FDA approval was solely for treatment of HIV-associated facial lipoatrophy, but in July of 2009, the FDA expanded the approval to include the correction of nasolabial folds and other facial wrinkles in immune-competent individuals.

This prospective cohort study is notable in that it provides long-term safety and efficacy data for this product in both HIV-positive and –negative individuals. A total of 65 patients with facial lipoatrophy were enrolled in this study (27 HIV positive and 38 HIV negative), and treated at 4 to 6 week intervals until the desired effect was achieved. Each vial of product was diluted with 3cc of sterile water the night before injection, with the addition of 2cc of 1% lidocaine on the day of the procedure. These vials were thoroughly vortexed, and they were re-vortexed during the procedure to adequately resuspend any precipitated product.

Based on the degree of lipoatrophy, either one half or whole vial was injected into the subcutaneous tissue of each cheek through a 25 gauge 1 inch needle with a fanning retrograde injection technique. Aftercare involved massage of the area for 5-10 minutes by a medical assistant and icing of the areas 15 minutes per hour for the following 12-24 hours while awake.

Efficacy was determined by both blinded evaluation of patient photographs (which were scored using the Facial Lipoatrophy Grading Scale) as well as patient satisfaction scores. For HIV-positive patients there was an average of 2.5 points of improvement on the Facial Lipoatrophy Grading Scale at 3 years; in contrast, for HIV-negative patients the net improvement at 3 years was 1.11 points on this scale. The patient satisfaction scores at 3 years likewise revealed that 100% of HIV-positive patients were “very satisfied” or “somewhat satisfied” with the results, in contrast to 86% of the HIV-negative patients. This study also shows that correction may persist for at least a year from the last injection, as many patients did not receive additional treatments in the third year of the study but maintained the same level of correction as during year 2.

The most common complication was subcutaneous papule formation, which occurred in 11% of patients. More HIV-positive than -negative patients developed these papules, a finding attributed to the larger amount of product used in the HIV-positive patients in this study. For the 4 patients who developed papules during the first 2 years of the study, all had spontaneous improvement. For one patient, further improvement was achieved after subcision of her nodules with a 19 gauge needle. Notably, this study revealed that some papule formation may be late-onset, as 2 patients reported papules in the third year of the study despite having not received further injections of product after the second year.

The authors state there is a higher risk of papule formation with higher cumulative volumes of product use in an individual, less dilution of the product, injection into the dermis instead of the subcutaneous tissue, injection of precipitated product that has not been re-vortexed, failure to massage after injection, or treatment of areas more prone to

 RECOMMEND TO
A COLLEAGUE

 NEWSLETTER
ARCHIVE

form subcutaneous papules (temple, above the orbital rim, or below the mandible). Per the authors' experience, these papules are best treated with observation and reassurance.

Another investigator reported that recurrent inflammatory nodules can develop with this product several months to years after injection, which were treated with intralesional steroids.¹ This complication was not observed in this study.

References

1. Hamilton DG, Gauthier N, Robertson BF. [Late-onset, recurrent facial nodules associated with injection of poly-L-lactic acid](#). *Dermatol Surg*. 2008; 34:123-126.

[back to top](#)

COMPLICATIONS OF DERMAL FILLERS

Cohen JL. **Understanding, avoiding, and managing dermal filler complications.** *Dermatol Surg*. 2008 Jun;34 Suppl 1:S92-S99.

(For non-subscribers to this journal, an additional fee may apply to obtain full-text articles.)



[View journal abstract](#)

This paper presents a summary of the complications associated with dermal filler use and the management of these complications, as reported in peer-reviewed publications, manufacturer prescribing information, and presentations from professional meetings. The author discusses both common and rare side-effects of dermal filler use, including injection site reactions, inappropriate placement of product, product sensitivity, infection, and skin necrosis.

This author reports that the most common adverse effects of dermal filler use are injection site reactions, including swelling, redness, tenderness, pain, bruising, and itching. These reactions typically last for less than 7 days. Bruising may be minimized by avoiding unnecessary medications or supplements that promote bleeding for the week prior to the procedure (aspirin, NSAIDs, vitamin E, ginger, ginseng, ginkgo biloba, garlic, kava kava, celery root, and fish oils).

Inappropriate placement of product can also produce undesirable effects. With hyaluronic acid fillers, injection too superficially may lead to the appearance of bluish bumps under the skin. These can usually be treated with massage, aspiration, incision and drainage, or hyaluronidase injection. Importantly, since hyaluronidase is animal-derived, skin testing is recommended prior to use. In contrast, the superficial placement of calcium hydroxylapatite can lead to visible white nodules. Likewise, injection of this filler into areas of very thin skin such as the tear trough may also produce visible white nodules of product. Also, in the lips, calcium hydroxylapatite has been reported to migrate superficially, creating nodules which may be corrected through incision and drainage.

With regards to product sensitivity, as all non-autologous fat fillers are foreign material to the host, all dermal fillers have the potential to generate an immune response. For bovine collagen, 2 skin tests are recommended prior to product use to evaluate for sensitivity reactions. In patients with 2 negative bovine collagen skin tests, risk for a granulomatous reaction with use of the product may be as low as 0.5%. Of note, reactions to human collagen appear to be much lower, and skin testing is not required prior to its use.

For poly-L-lactic acid, subcutaneous papule formation is more common, but with improved protocols for injection, the incidence is not as high as reported in the early studies from Europe. Reconstitution of the product with at least 5cc of sterile water for at least 8 hours prior to injection and placement of the product into the high fat instead of the dermis is believed to decrease the risk of papule formation. While most of these nodules have been reported to be palpable and not visible, observation is recommended as spontaneous resolution has been reported to occur. In addition, excision and subcision of these nodules has been reported to be effective. In contrast, hypersensitivity reactions and persistent nodules have been only very rarely reported with hyaluronic acid fillers, and have been reported to disappear rapidly with hyaluronidase injection.

To minimize the risk of infection, antiviral prophylaxis is recommended for patients with a history of oral herpes prior to injection into the lips. It is also recommended that the injections not be performed if a patient has evidence of an active herpes infection. In addition, non-FDA approved products should be avoided, as there have been reports of

 RECOMMEND TO
A COLLEAGUE

 NEWSLETTER
ARCHIVE

mycobacterial infections with these agents. To avoid infections from injection of any product, removal of all make-up in the area and preparation of the skin with isopropyl alcohol or chlorhexidine is recommended. If infection is suspected, empiric treatment with clarithromycin is prudent while awaiting culture results.

Finally, necrosis of the skin has been reported to occur. It is believed that necrosis happens when vessels are externally compressed by product or when product is directly injected into a vessel. The glabellar region is believed to be at greatest risk for necrosis from filler injection. If fillers are used in this area, to minimize the risk of necrosis, it is recommended that only collagen products which are injected more superficially be used. Also, product should be placed more medially at low volumes, and aspiration before injection should be practiced in this area. If there are clinical signs of potential necrosis of the skin, the author of this review recommends applying warm gauze or nitroglycerin paste to the area to stimulate blood flow. He also cites a case where hyaluronidase was used successfully to reverse possible compression of a vessel with hyaluronic acid.

[back to top](#)

THE INFLUENCE OF LASER, RADIOFREQUENCY, AND INTENSE PULSED LIGHT THERAPY FOLLOWING HYALURONIC ACID GEL IMPLANTATION

Goldman MP, Alster TS, Weiss R. **A randomized trial to determine the influence of laser therapy, monopolar radiofrequency treatment, and intense pulsed light therapy administered immediately after hyaluronic acid gel implantation.** *Dermatol Surg.* 2007 May;33(5):535-542.

(For non-subscribers to this journal, an additional fee may apply to obtain full-text articles.)



[View journal abstract](#)



[View full article](#)

In facial rejuvenation, it has become common practice to use more than one modality to achieve the desired effect. However, there is a theoretical concern about performing treatment with a laser, light, or radiofrequency device immediately after implantation of a dermal filler, given the fear that the heat generated by the device could distort or degrade the filler.

The authors designed this randomized, evaluator-blind, split-face study to address this concern. They enrolled 36 patients who underwent treatment with hyaluronic acid gel into the bilateral nasolabial folds and posterior auricular regions. This was immediately followed by treatment with either the Nd:YAG laser, diode laser, monopolar radiofrequency device, or intense pulse light therapy to the nasolabial fold and posterior auricular region of only one side of the face. The patients were then reassessed at days 14, 28, and 56 after their treatment. At days 0, 14, and 28, all of the patients underwent skin biopsies from the bilateral posterior auricular regions.

Importantly, there was no statistically significant difference in wrinkle severity scores between the areas treated with hyaluronic acid alone and those with hyaluronic acid immediately followed by treatment with each of the four devices tested at all follow-up visits. Therefore, this study did not demonstrate any clinically apparent effect of laser, light, or radiofrequency treatment on the implant.

Unfortunately, the biopsies obtained were inadequate to demonstrate if there was a histological effect from the laser, light, or radiofrequency treatment. Only 8.6% of the biopsies had detectable filler, likely because the biopsies were too superficial. However, there have been animal studies published that demonstrated clearly with pathology that non-ablative lasers and light as well as superficial ablative lasers had no effect on both small and large-particle hyaluronic acid gels.¹ This was in contrast to the deep ablative laser treatments for which there was sign of laser-filler interaction on histopathology.¹ In addition, one study on the use of radiofrequency devices immediately after the implantation of hyaluronic acid gel into the forearms of human subjects showed no difference on histopathology or clinical evaluation.²

References

1. Farkas JP, Richardson JA, Brown S, Hoopman JE, Kenkel JM. [Effects of common laser treatments on hyaluronic acid fillers in a porcine model.](#) *Aesthet Surg J.* 2008 Sep-Oct;28(5):503-511.

RECOMMEND TO
A COLLEAGUE

NEWSLETTER
ARCHIVE

COMPLETE THE POST-TEST

Step 1.
Click on the appropriate link below. This will take you to the post-test.

Step 2.
If you have participated in a Johns Hopkins online course, login. Otherwise, please register.

Step 3.
Complete the post-test and course evaluation.

Step 4.
Print out your certificate.

PHYSICIAN
POST-TEST

NURSE
POST-TEST

2. Alam M, Levy R, Pajvani U, et al. [Safety of radiofrequency treatment over human skin previously injected with medium-term injectable soft-tissue augmentation materials: a controlled pilot trial.](#) *Lasers Surg Med.* 2006 Mar;38(3):205-210.

[back to top](#)

© 2010 JHUSOM, IJHN and *eMedicalDermatology Review*

Presented by JHUSOM in collaboration with [DKBmed](#).

