SMGroup

SM Dermatology Journal

Research Article

# Polymethyl Methacrylate Microspheres in the Treatment of Facial Rejuvenation: A Large Retrospective Series

**Nasrin Mani[1]*, Majid Mani[2], Daniel N Sauder[2] and Marcella R Bothwell[3]**

[1]*La Jolla Cosmetic Laser Clinic and California Retina Associates, San Diego, CA, USA*
[2]*Division of Dermatology, University Hospital at Princeton, Princeton, NJ, USA*
[3]*Department of Surgery and Division of Otolaryngology, University of California San Diego, San Diego, CA, USA*

**Article Information**

Received date: Oct 18, 2016
Accepted date: Dec 15, 2016
Published date: Dec 22, 2016

***Corresponding author**

Nasrin Mani, La Jolla Cosmetic Laser Clinic, 7720 Fay Avenue, La Jolla CA 92037, USA, Tel: 858-454-2700; Fax: 858-454-2782; Email: drmani@lajollalaser.com



**Keywords** Filler; Rejuvenation; Polymethyl methacrylate (PMMA) microspheres

## Abstract

**Study Background:** Soft tissue temporary and semi-permanent fillers continue to increase in popularity worldwide for facial rejuvenation. The study aims to review the cosmetic use and complication rate in large retrospective case series of Polymethyl Methacrylate (PMMA) microspheres in facial rejuvenation.

**Methods:** The study is a retrospective case series of 779 patients that underwent PMMA filler by one senior provider (NM) for facial rejuvenation to 7 consistent and reproducible areas of the face determined from chart review in order of preference: Peri-oral (589), Infra-orbital (395), Nasolabial folds (379), Temporal (212), Cheek (161), Glabella (99), and Scar area (8) from February 2009 to September 2015 and the chart review was completed in May 2016.

**Results:** The average age at first injection was 51.4 years old with standard deviation of 12.2 years. Seven-hundred and six patients were female and 73 were male. Forty-three (5.4%) patients injected with PMMA had nodular complications. The average time to first sign of complication was 1.2 years with a range of .02 to 4.61 years. Prior blepharoplasty, rhytidectomy, rhinoplasty, Fitzpatrick skin classification, or history of autoimmunity was not significant to nodular complication. Thirty-four patients resolved with multiple steroid injections averaging 3.7 injections to resolution. Five were lost to follow up. Four have had ongoing injections with one undergoing surgical resection for multiple infra-orbital and peri-oral nodules.

**Conclusions:** Injection of permanent PMMA filler using a subdermal technique in the context of facial rejuvenation is possible with clinically significant cosmetic benefit. Since this is an off-label use of PMMA filler, caution must be taken with full disclosure to the patient leading to informed consent.

## Introduction

Soft tissue fillers are continuing to increase in popularity throughout North America and worldwide as a means of wrinkle and fold reduction, facial volume restoration, and contour enhancement [1]. A 3% increase in soft tissue fillers was noted in one year from 2013 to 2014 in the American Society of Plastic Surgery report 2014 [2]. Yet fillers are implants and essentially foreign bodies that can potentially trigger an inflammatory response in some individuals [3].

Most fillers are only FDA approved for limited areas however it is common practice to expand their use in other areas of the face in the context of the non-surgical facelift (rhytidoplasty) or non-surgical rhinoplasty. The authors have previously reported on the safety and effectiveness of the infraorbital area [4]. In the context of the non-surgical movement in aesthetics, the authors wish to report the safety of PMMA in all patients treated in a single clinic who received PMMA filler in the context of facial rejuvenation.

## Materials and Methods

A retrospective case series of 779 patients desiring facial rejuvenation was reviewed for long-term complications of PMMA in an outpatient cosmetic dermatology clinic by one senior provider (NM). Microsoft Excel® (Redmond, Washington, USA was reviewed from prior data and updated to 2016 with numeric identifiers replacing patients identifying features to preserve anonymity. Data were then transferred into SPSS database version 23 (IBM Corporation, Armonk, NY, USA) for statistical analysis. Basic demographic data were analyzed with calculation of the frequency, mean, minimum, and maximum of variables. Due to the nonparametric type of data, chi-square analysis was performed to analyze independent variables and their influence on statistical outcomes.

## Results

The study is a retrospective case series of 779 patients that underwent PMMA filler to 7 consistent and reproducible areas of the face determined from chart review in order of preference: Peri-oral (589), Infra-orbital (395), Nasolabial folds (379), Temporal (212), Cheek (161), Glabella (99), and

Scar area (8) from February 2009 to September 2015 and the chart review was completed in May 2016.

The average age at first injection was 51.4 years old with standard deviation of 12.2 years. Seven-hundred and six patients were female and 73 were male. Patients' race and skin type were diverse: Caucasian (557), Hispanic or South/Central American (82), and Middle Eastern (59), Asian (36), African American (5), Other (20). Fitzpatrick skin type of patients varied from type 2(9) type 3 (447), type 4 (317), type 5 (4) and type 6 (1).

Other facial cosmetic surgical procedures reported in the affirmative on chart review were: rhytidoplasty (123), blepharoplasty (77), and rhinoplasty (40). Other cosmetic procedures reported in the affirmative by chart review were: Neuromodulator (Botox, Allergan and Dysport, Galderma Laboratories) (634), Laser, NOS (197), Photo-rejuvenation or IPL (114), Thermage®, Valeant Pharmaceutical North America, LLC (196), and Ultherapy®, Merz Pharma (205). Other HA (hyaluronic acid type fillers reported in the affirmative by these patients included: Restylane®, Galderma Laboratories (222) and Juvederm®, Allergan (278). Other fillers reported: Radiesse® (Calcium hydroxylapatatite), Merz Pharma and Sculptra® (Poly-L-Lactic acid), Galderma Laboratories (355).

As of May, 2016, 43 patients with nodular complications were reported in clinic notes of the 779 patients. However, 10 patients had complications in multiple facial areas (Table 1).

The average time to first sign of complication for all complications was 1.2 years. Data was grouped based on infra-orbital and "other areas of face" based on prior data collection. The other "areas of face regions" time to complication was 1.45 years with a range of 0.02 to 4.61 years. The average time to first sign of complication in the infra-orbital region was slightly less at 1.1 year with a range of 0.03 to 3.8 years.

Prior facelift, blepharoplasty, Fitzpatrick skin classification was not associated with increased risk of nodular complication of the infra-orbit area or other areas of the face. Autoimmunity was approaching significance in the complication of the other areas of the face at $p = 0.07$ but not with the infra-orbital group.

Of the forty-three patients, 34 resolved with multiple steroid injections averaging 3.7 injections to resolution. Five were lost to follow up. Four have had ongoing injections with one of these patients undergoing surgical resection of multiple eye and peri-oral biopsy confirmed granulomas.

General treatment consisted of intra-lesional Triamcinolone 40mg/ml of the nodule at injection site. If no improvement was noted at 6 weeks, a 50:50 mixture of Triamcinolone and Fluorouracil (5-FU) was utilized as per Vent and Lemperle in 2014 [5]. Fluorouracil in combination with intra-lesional triamcinolone was also utilized as per Lemperle et al in 2006 [6].

## Discussion

Bellafill (Suneva Medical, San Diego, CA) is the only FDA-approved PMMA injectable filler available in the United States. First approved as Artefill in 2007 as dermal filler for NL folds, it recently became approved for acne scarring in 2014 for the treatment of moderate to severe, facial acne scars. PMMA is recommended to be injected either subdermal or epi-periosteum only. In this large retrospective study, the complication rate for NL fold injection is 1.6 % which is slightly lower than Cohen et al who reported in 2015 a rate of 1.7% [7]. Both of which are higher than the previously reported 0.1% [8]. Karnik et al showed substantial effectiveness in the treatment of atrophic acne scars in the face with only mild, reversible adverse events [9]. Lee and Lorenc report, patients best treated by PMMA are those with atrophic distensible acne scarring and injecting into the deep dermis [10]. In this study, complication of injection of PMMA into scar was 0% but with a limited sample size of 8 patients.

PMMA has been reported as a semi-permanent filler used in other areas of the face by respected practitioners. Thomas in 2016 discussed that there are multiple other injectable fillers that can be used in nasal reconstruction. Examples include silicone, both liquid and solid/sheet form; Artecoll, which is bovine collagen; and PMMA [11]. Mills reported successful use in malar atrophy with an 87.5% success rate and no adverse reactions in 24 patients [12].

PMMA's use has been expanded in cosmetic facial rejuvenation to other areas of the face or hands. In the Author's clinic, patients seeking a more long-lasting response to filler injection were informed of the "off-label" use of the semi-permanent PMMA filler. Patients who wished to proceed received 1- 7 injections of PMMA to regions of the face including: Peri-oral (589), Infra-orbital (395), Nasolabial folds (379), Temporal (212), Cheek (161), Glabella (99), and Scar area (8). Given the potential for nodular and granuloma complications, these patient's charts were reviewed for these complications. In this retrospective study, we present the largest patient review of PMMA filler used for multiple facial rejuvenation sites to date.

The infra-orbital area was the most common place to have the nodular complication reported. It is possible that the rate of nodular

**Table 1:** Demonstration sites of PMMA injected, number of injections, number of nodular complications per site and percent rate of complications.

| Site of Injection | Patients injected per Site | Patients with Complications | Percent Complication |
|---|---|---|---|
| PERI-ORAL | 589 | 18 | 3.06% |
| INFRA-ORBITAL | 395 | 24 | 6.08% |
| NASOLABIAL | 379 | 6 | 1.58% |
| TEMPORAL | 212 | 1 | 0.47% |
| CHEEK | 161 | 3 | 1.86% |
| GLABELLA | 99 | 1 | 1.01% |
| SCAR | 8 | 0 | 0.00% |
| TOTAL NUMBER OF PATIENTS | 779* | 43 | 5.52% |

*Note: Patients may have had more than one site of injection.

reactions might be the same as for other areas but the detection of the nodules may be more obvious. The infra-orbital thin skin being less forgiving to practitioner and patient than the thicker skin in other areas of the face. For example, in the peri-oral area, nodular complications were less obvious and mostly palpable. Lemperle et al recommended a strictly epi-periosteal injection beneath the orbicularis oculi muscle and just superficial to the insertion of the orbital septum [5,13].

While the overall nodularity complication rate was 5.4%, the infra-orbital (6.1%) and peri-oral (3.1%) areas which had higher complications may have some common issues as well. The infra-orbital and peri-oral sphincters have similarities regarding the circumferential muscular motion. Jordan and Stoica reported 3 patients with filler migration and made an excellent review on possible mechanisms for this migration. Motion of the orbicularis muscle or muscles of facial expression could promote dislocated granulomas from filler [1].

Ten patients had nodularity in multiple facial areas injected with PMMA. Looking specifically at these patients, we could find no statistical test to infer causation or correlation including number of injections which varied widely. One of these patients, after resolution of small granuloma wished to proceed again with PMMA filler later which was discouraged.

Limitations to the study include lack of excisional or incisional biopsy in most patients. Nodular complication was defined as any lumpiness that required treatment with injection regardless of before or after 90 days. While Cohen separated "early" (<90 days) associated with implant procedure and "late" potentially a granulomatous process, we elected to treat any unwanted nodule needing steroid treatment as a complication [7].

Other limitations include the retrospective chart review and patients lost to follow up. Significant complications, however, are unlikely to be missed or lost to follow up in the population of cosmetic patients. Concerning medical issues while noted on intake exam, autoimmunity takes many years to diagnose and is sometimes not considered relevant in the patient's mind when entering a cosmetic facility. The authors noted it was approaching statistical significance at p= 0.07 in the complication "other areas of face" stratified group. It may be wise to specifically question patients about this history.

In conclusion, this study has shown that injection of a permanent PMMA filler in the context of facial rejuvenation while possible to create clinically relevant results, may produce the possibility of nodular complication in a significant number of patients. The incidence of granuloma complication is reported in the nasolabial fold is 1.7% [7]. While not biopsy confirmed, comparable rates of nodularity were noted in the nasolabial fold area but were much higher in the infra-orbital and peri-oral areas. Also, adverse reactions may occur as late as 4.6 years. The 'Holy Grail' of cosmetic filler for patients is to not have to re-inject the fillers at intervals. At present, the tenacity of the PMMA filler with incomplete dissolution may be ill suited to some patients and some regions of the face. Even where PMMA filler is FDA approved in the face, significant caution must be taken with full disclosure to the patient leading to informed consent. Longer term follow-up seems to be necessary and beneficial to a cosmetic practice.

## References

1. Jordan DR, Stoica B. Filler Migration: A Number of Mechanisms to Consider. Ophthal Plast Reconstr Surg. 2015; 31: 257-262.
2. American Society of Plastic Surgeons. Http://www.plasticsurgery.org. 2014.
3. Eun YS, Cho SH, Lee JD, Kim HS. Periorbital lipogranuloma related to filler migration: a rare compication of facial fillers. J Cosmet Laser Ther. 2014; 16: 149-150.
4. Mani N, McLeod J, Sauder M, Sauder DN, Bothwell MR. Novel use of polymethyl methacrylate (PMMA) microspheres in the treatment of infraorbital rhytids. J Cosmet Dermatol. 2013; 12: 275-280.
5. Vent J, Lemperle G. Prevention and treatment of complications after polymethylmethacrylate-microspheres injections. Facial Plast Surg. 2014; 30: 628-634.
6. Lemperle G, Rullan PP, Gauthier-Hazan N. Avoiding and treating dermal filler complications. Plast Reconstr Surg. 2006; 118: 92S-107S.
7. Cohen S, Dover J, Monheit G, Narins R, Sadick N, Werschler WP, et al. Five-Year Safety and Satisfaction Study of PMMA-Collagen in the Correction of Nasolabial Folds. Dermatol Surg. 2015; 41: S302-313.
8. Gladstone HB, Cohen JL. Adverse effects when injecting facial fillers. Semin Cutan Med Surg. 2007; 26: 34-39.
9. Karnik J, Baumann L, Bruce S, Callender V, Cohen S, Grimes P, et al. A double-blind, randomized, multicenter, controlled trial of suspended polymethylmethacrylate microspheres for the correction of atrophic facial acne scars. J Am Acad Dermatol. 2014; 71: 77-83.
10. Lee JC, Lorenc ZP. Synthetic Fillers for Facial Rejuvenation. Clin Plastic Surg. 2016; 43: 497-503.
11. Thomas WW, Bucky L, Friedman O. Injectables in the Nose Facts and Controversies. Facial Plast Surg Clin North Am. 2016; 24: 379-389.
12. Mills DC, Camp S, Mosser S, Sayeg A, Hurwitz D, Ronel D. Malar augmentation with a polymethylmethacrylate-enhanced filler: assessment of a 12-month open-label pilot study. Aesthet Surg J. 2013; 33: 421-430.
13. Lemperle G, Knapp TR, Sadick NS, Lemperle SM. ArteFill permanent injectable for soft tissue augmentation: I. Mechanism of action and injection techniques. Aesthetic Plast Surg. 2010; 34: 264-272.