Letter

Retrospective analysis of filler complications reported in the manufacturer and user facility device experience database from 2015 to 2025

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To the Editor

Dermal fillers, including biostimulatory and hyaluronic acid (HA) fillers, are commonly used for facial rejuvenation. Biostimulatory fillers, including calcium hydroxylapatite (CaHA), poly-L-lactic acid (PLLA), and polymethylmethacrylate (PMMA), stimulate collagen production but are associated with late inflammatory reactions (LIRs). Although vascular occlusion is a known risk across all filler types, LIRs with biostimulatory fillers warrant closer scrutiny. We evaluated complication patterns using a national database to determine whether current injection protocols should be reassessed.

On February 20, 2025, the FDA Manufacturer and User Facility Device Experience (MAUDE) database was queried for medical device reports from 2015 to 2025 describing adverse events (AEs) reported with biostimulatory fillers. After excluding duplicates and secondary treatments, 874 unique AE reports were analyzed.

PLLA (n = 245) was primarily associated with subcutaneous nodules (n = 41), swelling/edema (n = 34), and inflammation (n = 25), with severe cases including abscesses (n = 8), vision loss (n = 6), anaphylactic shock (n = 5), and necrosis (n = 5). For CaHA (n = 482), vascular occlusion (n = 118) was most common, followed by swelling/edema (n = 39) and necrosis (n = 37). PMMA (n = 147) was linked to granulomas (n = 30), swelling/edema (n = 23), and foreign body reactions (n = 22), with severe outcomes including disfigurement (n = 18), necrosis (n = 15), and infection (n = 6) (**Table 1**).

We found that biostimulatory fillers were associated with subcutaneous nodules, granulomas, and vascular occlusion. Our dataset showed that occlusion represented a high proportion of CaHA complications. Similarly, a cross-sectional review of 2813 AEs across HA and biostimulatory fillers (CaHA = 288) found that 0.0008% of CaHA injections resulted in necrosis, visual symptoms, or occlusion.[1] Compared to other fillers, visual symptoms and intra-arterial injections were most common with CaHA ($P < .01$), and necrosis was most common with CaHA and PMMA ($P < .01$).[1] We also found that biostimulatory fillers, particularly PLLA and PMMA, were associated with late-onset granulomas and nodules. Similarly, a cross-sectional review of 1748 AEs across filler types (PLLA = 47) identified subcutaneous nodules as the most frequent complication for PLLA (36.1%, 17/47).[2] An observational study identified 55 patients with biostimulatory filler complications, of which 69.1% were associated with PLLA and 23.6% with CaHA; 89.1% developed subcutaneous nodules and 60% appeared more than 1 month following treatment.[3]

Our findings raise the question of what proportion of these complications result from LIRs. We hypothesize subclinical bacterial colonization or biofilm formation as potential drivers. A systematic review of 197 articles on LIRs found a local presence of histiocytes and giant cells in 295 patients across 14 studies using histochemical techniques, and *Staphylococcus epidermidis* in 98% of positive cultures from the lips, cheek, or mandibular border over 10 studies, suggesting roles for both immune response and bacterial involvement.[4]

This study is subject to reporting biases inherent to the MAUDE database, such that severe complications are more likely to be documented than transient or minor AEs. Additionally, the denominator of total filler procedures performed is unknown, limiting calculation of true incidence rates. Our findings underscore the need for post-procedural monitoring and real-time imaging technologies to detect and manage delayed inflammatory complications before they become persistent. Given the higher-than-expected rates of inflammatory complications, prospective, long-term studies are needed to track delayed outcomes.

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Potential conflicts of interest

The authors declare no conflicts of interest.

Table 1. *Top 10 Most Frequent AEs for Each Biostimulatory Filler.*

Filler Type	AE	Frequency
PLLA	Subcutaneous nodule	41
	Swelling/edema	34
	Inflammation	25
	Pain	18
	Granuloma	18
	Allergic/hypersensitivity reaction	18
	Abscess	8
	Visual impairment	6
	Anaphylactic shock	5
	Necrosis	5
CaHa	Obstruction/occlusion	118
	Swelling/edema	39
	Necrosis	37
	Subcutaneous nodule	35
	Allergic/hypersensitivity reaction	20
	Cellulitis	19
	Pain	18
	Deposits	16
	Inflammation	15
	Erythema	13
PMMA	Granuloma	30
	Swelling/edema	23
	Foreign body reaction	22
	Pain	21
	Deformity/disfigurement	18
	Swelling	17
	Necrosis	15
	Subcutaneous nodule	7
	Abscess	6
	Infection	6

Abbreviations: AE, adverse event; CaHa, calcium hydroxylapatite; PLLA, poly-L-lactic acid; PMMA, polymethylmethacrylate.

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