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RAPID COMMUNICATION

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Current otolaryngologic applications of the novel self-assembling RADA-16 peptide matrix

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1 | INTRODUCTION

While a plethora of products assist in hemostasis in otolaryngologic procedures, there are none specifically marketed to improve wound healing. A novel bioresorbable agent on the market is PuraGel® (3-D Matrix, Tokyo, Japan), a RADA-16 product that acts as a synthetic hemostatic and space-filling gel that promotes wound healing and prevents adhesion formation.[1–5] This synthetic 16-amino acid peptide spontaneously self-assembles into a mesh-like structure upon contact with physiologic fluids.[4] The nanofibrous hydrogel is placed as a thin film over a wound bed to fill tissue voids and eliminate dead space.[1,4,5] Procedural application was well studied in animal models.[4] It is used in general surgery to prevent intraabdominal adhesions and gastrointestinal and cardiovascular cases for hemostasis.[5–7] In 2019, RADA-16 received US FDA approval for nasal/sinus surgery.

There is limited literature discussing RADA-16 in otolaryngology. Given the reported benefits of accelerated wound healing and scar tissue prevention, there are multiple otolaryngologic applications where RADA-16 might improve outcomes.

2 | METHODS/RESULTS

This study was an investigator-initiated, retrospective survey review and did not require IRB approval. Our study utilized a survey to highlight current utilization and associated post-operative complications with this product. The 3-D Matrix company provided a complete list of the 13 academic centers using the RADA-16 product at the time. At the time of the distribution of this survey, the product was only used by a limited number of practitioners with the vast majority being at academic centers. A survey was distributed via email to query the anecdotal experiences, number and type of cases RADA-16 was utilized in, and any post-operative complications and observations. Responses were received from 10 academic otolaryngologic

TABLE 1 Summary of otolaryngologic procedures utilizing RADA-16 ($n = 239$; overall complication rate 6.28%). Majority of use were in FESS, septoplasty/turbinate reductions, and tonsillectomies (49.79%, 23.43%, and 7.53%, respectively). When separated by site, the rate of complications in the nasal/sinus surgery and other groups were 5.50% (12) and 16.67% (3), respectively. Of note, the 16.67% was comprised only of post-tonsillectomy cases. Locations of sinonasal scarring/stenosis were ethmoid, frontal, and maxillary sinuses, and nasal cavity—three of these cases required reoperation.

Site and procedure type	Number (*n*)	Percentage (%)	Complication number and percentage%
Nasal/sinus surgery	218	91.21%	12, 5.50%
FESS	119	49.79%	
Septoplasty/Turbinate reduction	56	23.43%	
Medial maxillectomy	14	5.86%	
Nasoseptal flap	11	4.60%	
Sinonasal tumor resection	6	2.51%	
Nasal stenosis repair	5	2.09%	
Draf III frontal sinusotomy	4	1.67%	
Nasopharyngeal stenosis	1	0.42%	
Dacryocytorhinostomy	1	0.42%	
Choanal atresia repair	1	0.42%	
Other	21	8.79%	3, 16.67%
Tonsillectomy	18	7.53%	
Expansion palatoplasty	2	0.84%	
Subglottic stenosis dilation	1	0.42%	
Total	239		15, 6.28%

institutions for a total of 239 cases. This paper's data analysis involved simple, descriptive statistics.

3 | DISCUSSION

The purpose of this study was to determine the current practice patterns for RADA-16 in otolaryngology. There were 239 cases total and complications were reported in 6.28% (15) of cases (Table 1). The top reported uses were FESS, septoplasty/turbinate reduction, and tonsillectomy. When separated by site, the rate of complications in nasal/sinus surgery and tonsillectomy were 5.50% (12) and 16.67% (3), respectively.

Previous studies highlighted the hemostatic applications of RADA-16, notably in gastrointestinal and cardiac procedures.[6–9] RADA-16 is transparent on application, allowing visualization of incisional sites after placement. Subramaniam et al quantified RADA-16's average time to hemostasis being 69.5 s.[8] Friedland et al reviewed RADA-16 in 28 complete FESS and 66 limited FESS in the absence of other nasal packing; yielding a post-operative bleed rate of 4.25%.[5] All three primary bleeds were treated with cautery and absorbable gel foam. Of the delayed bleeds, one required reintervention with nonabsorbable packing and this case involved dual antiplatelet therapy. Lee et al had zero post-operative bleeds or adhesions after RADA-16 in 60 patients who underwent turbinate reductions.[3] Our study's post-operative bleed rate was 1.38% after nasal/sinus surgery and 16.67% after tonsillectomy. Intraoperative hemostasis measures were not recorded by the authors. However, subjectively, authors felt minor bleeding was controlled by the product, while more significant bleeding from either named vessels or from severely vascular/inflamed areas such as polyps was better controlled with space-filling products. The post-tonsillectomy bleeding rate is somewhat conspicuous, but this may be a product of selection bias as the sample size was quite small and only represented two surgeons. A larger comparative study evaluating RADA-16 in a larger cohort of tonsillectomy patients may yield helpful results.

RADA-16's wound healing properties has been discussed in small series of nasopharyngeal stenosis, turbinate reduction, FESS, and facelifts.[1–5,8,10] Wong et al reported RADA-16 in a post-radiated bed with successful treatment of nasopharyngeal stenosis and prevention of adhesions when used in adjunct with Dexamethasone injections.[2] RADA-16 proved useful in eliminating dead space and expediting healing in facelifts.[1,10] Our authors' early adoption of this new technology was based on potential improvement of wound healing. In sinus surgery, optimizing mucosal wound healing can lead to improved patient outcomes with less obstructive adhesions and reoperation rates. This is especially important along areas of denuded bone/cartilage as in Draf IIIs or sinonasal tumor excisions.

Our study was a survey-based study sent to academic otolaryngologists utilizing the product across the country; therefore, limitations include the relatively small sample size and selection bias. While this product may be currently utilized more broadly, at the time of the survey distribution, it was available mainly to a smaller number of academic centers leading to potential selection bias. Additionally given that it is a novel product, the surgeon may have consciously or unconsciously chosen to use it in only select cases. Other impactful information including

patient demographics, comorbidities, intraoperative data including extent of disease, post-operative medical compliance, and Lund-Kennedy endoscopy scores were not recorded. Further prospective studies comparing RADA-16 versus a control group are critical.

To our knowledge, this is one of the first studies surveying RADA-16 in common otolaryngologic surgeries across academic rhinologists in the United States. and overall utilization of RADA-16 in otolaryngology. This product is currently not yet widely utilized; therefore, there is a better probability that this study may report an accurate description of the utilization of this product.

4 | CONCLUSION

RADA-16 hydrogels have innovative uses to promote mucosal healing by providing a matrix for migrating cells to repopulate and heal denuded tissue. Further studies will be helpful to determine appropriate use and applications of this novel product.

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CONFLICT OF INTEREST STATEMENT

We have no conflicts of interest to disclose.

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REFERENCES

1. Baker DC. Lateral SMASectomy, plication and short scar facelifts: indications and techniques. *Clin Plast Surg*. 2008;35(4):533-550. doi:10.1016/J.CPS.2008.06.003
2. Wong E, Ho J, Smith M, Sritharan N, Riffat F, Smith MC. Use of Purastat, a novel haemostatic matrix based on self-assembling peptides in the prevention of nasopharyngeal adhesion formation. *Int J Surg Case Rep*. 2020;70:227-229. doi:10.1016/j.ijscr.2020.04.027
3. Lee MF, Ma Z, Ananda A. A novel haemostatic agent based on self-assembling peptides in the setting of nasal endoscopic surgery, a case series. *Int J Surg Case Rep*. 2017;41:461-464. doi:10.1016/J.IJSCR.2017.11.024
4. Sankar S, O'Neill K, Bagot D'Arc M, et al. Clinical use of the self-assembling peptide RADA16: a review of current and future trends in biomedicine. *Front Bioeng Biotechnol*. 2021;9:9. doi:10.3389/FBIOE.2021.679525
5. Friedland Y, Bagot D'Arc M, Ha J, Delin C. The use of self-assembling peptides (PuraStat™) in functional endoscopic sinus surgery for Haemostasis and reducing adhesion formation. A case series of 94 patients. *Surg Technol Int*. 2022;41:1594. doi:10.52198/22.STI.41.GS1694
6. Stenson KM, Loftus IM, Chetter I, et al. A multi-Centre, single-arm clinical study to confirm safety and performance of PuraStat®, for the Management of Bleeding in elective carotid artery surgery. *Clin Appl Thromb Hemost*. 2022;28:28. doi:10.1177/10760296221144307
7. Branchi F, Klingenberg-Noftz R, Friedrich K, et al. PuraStat in gastrointestinal bleeding: results of a prospective multicentre observational pilot study. *Surg Endosc*. 2022;36(5):2954-2961. doi:10.1007/s00464-021-08589-6
8. Subramaniam S, Kandiah K, Thayalasekaran S, Longcroft-Wheaton G, Bhandari P. Haemostasis and prevention of bleeding related to ER: the role of a novel self-assembling peptide. *United European Gastroenterol J*. 2019;7(1):155-162. doi:10.1177/2050640618811504
9. Giritharan S, Salhiyyah K, Tsang GM, Ohri SK. Feasibility of a novel, synthetic, self-assembling peptide for suture-line haemostasis in cardiac surgery. *J Cardiothorac Surg*. 2018;13(1):68-75. doi:10.1186/S13019-018-0745-2
10. Few J. Facelift patients receiving intraoperative Administration of a Self-assembling Hemostat Agent Experienced Minimal Bruising and No Acute Hematomas: a pilot study. *Aesthet Surg J Open Forum*. 2022;4:4. doi:10.1093/ASJOF/OJAC037

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