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VIEWPOINT

Indications for absorbable steroid-eluting sinus implants: Viewpoint via the Delphi method

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Abstract

Absorbable steroid-eluting sinus implants provide targeted corticosteroid release over a sustained period and are designed to prevent both undesirable adhesion formation and sinus ostia restenosis. Here, we highlight the key evidence of these implants to date and query a group of experts via a Delphi process on the indications and optimal timing for intraoperative or in-office placement of these implants. Six of a total of 12 statements reached consensus and were accepted. Overall, experts largely agree that intraoperative or in-office use of steroid-eluting stents could be considered for patients: (1) who are diabetic or intolerant of oral steroids, (2) undergoing extended frontal sinus surgery, and (3) with recurrent stenosis. Given the lack of expert consensus on other key statements, clinicians should carefully consider these treatment options on a case-by-case basis after shared decision-making.

KEYWORDS
endoscopic sinus surgery, PROPEL, SINUVA, steroid-eluting implants

1 | INTRAOPERATIVE ETHMOID SINUS USE

The first implant to reach the market was the PROPEL implant (Intersect ENT, now acquired by Medtronic, Ireland), which was approved by the US Food and Drug Administration (FDA) in 2011 for patients aged ≥18 years with chronic rhinosinusitis with nasal polyps (CRSwNPs) and chronic rhinosinusitis without nasal polyps (CRSsNPs) following endoscopic sinus surgery (ESS).[1] The implant continuously releases a total of 370 μg of mometasone furoate over 30 days with the goals of maintaining the patency of the ethmoid cavity and reducing the need for postoperative interventions.[2] Approval of this device was based on two prospective double-blind placebo-controlled, randomized trials using an intrapatient control design. The randomized controlled trials found a significant decrease in polyp recurrence and decreased rate of adhesions on the implant side for up to 90 days postoperatively.[3,4]

2 | INTRAOPERATIVE FRONTAL SINUS USE

Other steroid-eluting stents include the PROPEL Mini, intended for use in the ethmoid and frontal sinuses, and the PROPEL Contour (both Intersect ENT, now acquired by Medtronic, Ireland), intended for use in the maxillary and frontal sinuses. Similar to the original implant, both the Mini and Contour stents contain 370 μg of mometasone released over 30 days and are designed for insertion in the frontal sinus opening.

The efficacy of the Mini implant placement and the PROPEL Contour in the frontal sinus opening have been assessed in a prospective double-blind placebo-controlled randomized trial also using an intrapatient control design.[5,6] A meta-analysis of these two studies showed decreased restenosis or occlusion rates for the implant side up to 90 days postoperatively, irrespective of asthma status, previous endoscopic sinus surgery, extent of surgery, or extent of polyps.[7]

3 | POSTOPERATIVE USE

SINUVA (Intersect ENT, now acquired by Medtronic, Ireland) is the most recently approved steroid-eluting sinus implant, obtaining initial approval in late 2017.[8] SINUVA, unlike the other stents, is approved in the United States as a drug rather than a device and is intended for patients with recurrent CRSwNP after prior ethmoid sinus surgery. The SINUVA implant contains 1350 μg of mometasone furoate released over 90 days and can be placed in the outpatient setting.[2,9] Two studies examined candidates for revision ESS who were randomized to bilateral implant placement or a sham procedure (the device was inserted without deployment).[10,11] Both found significant decreases in both nasal obstruction/congestion score and bilateral polyp grade and decreased indication for revision ESS in the treatment compared with the sham group.

4 | COMPLICATIONS

In the abovementioned clinical trials, there were no serious, life-threatening adverse events that were reported. Common adverse events reported in these studies included nasal discomfort, sinusitis, adhesions, epistaxis, and nasopharyngitis, all of which resolved without any sequelae. The US FDA's Manufacturer and User Facility Device Experience (MAUDE) database was recently queried for any reported adverse events related to the current commercially available implants and a total of 28 adverse events were reported. Of all adverse events, 39% were attributable to postoperative infections, while migration of the stent was the second most common complication. Eight patients in the cohort required reintervention to remove the implant.[12]

5 | ALTERNATIVES TO STEROID-ELUTING STENTS

The commercially available steroid-eluting stents are not available in all countries. Alternatives include synthetic, bioresorbable products, which can be manually steroid-impregnated before placement into the middle meatus or ethmoid bed; however, adding steroids to a bioabsorbable implant is not FDA-approved.[13–17] Most implant products currently on the market require prior surgical dissection of the ethmoid area although stents that do not require prior dissection are currently undergoing clinical trials. Further clinical trials are warranted to evaluate both the efficacy and cost-effectiveness of steroid-impregnated alternatives to the current stents.

6 | DELPHI PROCESS

To collect the individual opinions of rhinology experts on the intraoperative and in-office use of absorbable steroid-eluting stents, a Delphi process was performed. Institutional review board exemption was obtained from the University of Southern California Keck School of Medicine. All experts had prior experience with intraoperative stent placement; however, not all experts had placed stents specifically designed for office use. A group of five authors (V.S.L., P.P., D.O., G.A.S., and E.F.), who were members of the American Academy of Otolaryngology Outcomes and Evidence Based Medicine Committee and who had published an *ENT Bulletin* article on the evidence regarding steroid-eluting sinus stents, determined the wording of the original questions through a series of discussions.[18] Experts were then asked to anonymously answer 12 questions (Q1–Q12) by responding whether they strongly agree/agree/neutral/disagree/strongly disagree. A cutoff of 80% was used for consensus, with pooling of the categories agree and strongly agree and the categories disagree and strongly disagree. Two iterations of the Delphi survey were performed. The initial group of authors extensively discussed the results of each item after the first Delphi survey. Items that reached consensus were accepted. Items that did not meet consensus after the first survey were discussed to determine whether: (1) the wording or specific language was pivotal in the item not reaching consensus, or (2) not meeting consensus was instead caused by a true lack of consensus. The second survey was used to reassess items for which there was near consensus or for items in which there was suggestion of significant alterations in wording that could have affected survey results. All items reaching consensus after the second round were accepted.

7 | DELPHI RESULTS

The survey results are displayed in Tables 1 and 2 with statements ultimately reaching consensus highlighted. Fourteen experts answered the first survey and 12 experts answered the second; survey results were anonymous. Of the 12 experts, seven reported having used SINUVA in the past, with five of them continuing its use at the time of the survey. Similarly, all 12 experts reported having used PROPEL in the past, with 10 of them continuing its use at the time of the survey.

An overwhelming majority of experts find a potential, beneficial role for implants after ESS for CRSsNPs (Q2). Conversely, experts did not reach consensus on whether implants should be primarily used for patients with CRSwNPs (Q1). The majority of experts agreed that implants can be used in patients who are diabetic (Q3) or have intolerance to oral steroids (Q4). All of the experts agreed that implants could be considered for extended frontal sinus surgeries (Q5). No consensus was reached by the experts on the optimal number of steroid-eluting stents to be placed in each sinonasal cavity (Q6) or whether steroid-eluting implants should be considered in patients who are poorly compliant with postoperative rinses after ESS (Q7).

When questioned about the in-office use of steroid-eluting implants, the majority of the experts agreed that implants could be used for patients who have recurrent stenosis (Q10) and that SINUVA is most optimally positioned only if a total ethmoidectomy has been performed (Q11). No consensus was reached when asked whether SINUVA could be an alternative to biologics for recurrent

TABLE 1 Delphi process results for the original survey*

Question	Intraoperative/ In-office use	Question/statement	Resurveyed (yes/no)	Consensus (all others voted neutral)		Accepted (yes/no)
				Agree	Disagree	
1	Intraoperative	Steroid-eluting stent placement should only be considered in sinus surgery for chronic rhinosinusitis with nasal polyps	Yes	8%	67%	No
2	Intraoperative	Steroid-eluting stent placement could be considered in sinus surgery for chronic rhinosinusitis without nasal polyps	Yes	92%	8%	Yes
3	Intraoperative	Steroid-eluting stent placement should be considered in sinus surgery for patients intolerant of oral steroids	No	92%	8%	Yes
4	Intraoperative	If a patient has diabetes, then steroid-eluting stents could be considered instead of oral steroids after endoscopic sinus surgery	No	92%	0%	Yes
5	Intraoperative	For extended frontal sinus approaches/surgeries, steroid-eluting stents could be considered	No	100%	0%	Yes
6	Intraoperative	No more than 2 steroid-eluting stents should be placed in each sinonasal cavity	Yes	50%	0%	No
7	Intraoperative	For patients with poor compliance with postoperative rinses, steroid-eluting stent placement could be considered in primary sinus surgery	No	58%	17%	No
8	Intraoperative	Propel should never be placed in an acutely infected field	Yes	42%	17%	No
9	In-office	SINUVA placement could be considered for ethmoid or frontal recess recurrent polyps after surgery as an alternative to biologic therapy	No	75%	0%	No
10	In-office	If a patient has recurrent stenosis, then a steroid-eluting stent could be used in the office	No	92%	0%	Yes
11	In-office	SINUVA is most optimally positioned only if total ethmoidectomy has been performed	Yes	83 %	17%	Yes
12	In-office	PROPEL should be removed within 21 days of surgery	No	50%	17%	No

*Shaded statements reached consensus and were accepted (n = 14). Note: Question 2 was resurveyed despite reaching agreement as it was directly correlated with question 1.

CRSwNP (Q9) or regarding whether PROPEL should be removed within 21 days of surgery (Q12).

8 | DISCUSSION

Currently available evidence, although largely funded by industry, has consistently demonstrated a high level of evidence that absorbable steroid-eluting implants can be beneficial, particularly in the frontal sinus. Accordingly, experts agree that steroid-eluting stents can be considered intraoperatively for patients with CRSwNPs or CRSsNPs and if the patient is intolerant of oral steroids. In the office, experts agree that stents can be considered for patients with stenosis and they recommend that SINUVA is optimally placed if a total ethmoidectomy has previously been performed.

No consensus was reached by the experts when asked whether steroid-eluting implants should be considered in patients who are poorly compliant with postoperative

TABLE 2 Delphi process results for statements rewritten and resurveyed (n = 12)

Question	Round	Question/statement	Consensus (% agree, disagree [all others neutral])	Accepted (yes/no)
1	1	Steroid-eluting stent placement should only be considered in sinus surgery for chronic rhinosinusitis with nasal polyps	14%, 57%	
	2	Steroid-eluting stent placement should primarily be considered in sinus surgery for chronic rhinosinusitis with nasal polyps	67%, 16%	No
2	1	Steroid-eluting stent placement could be considered in sinus surgery for chronic rhinosinusitis without nasal polyps	92%, 8%	
	2	Steroid-eluting stent placement could be considered in sinus surgery for chronic rhinosinusitis without nasal polyps	92%, 0%	Yes
6	1	No more than 2 steroid-eluting stents should be placed in each sinonasal cavity	50%, 0%	
	2	Only one steroid-eluting stent should generally be used in each sinonasal cavity	58%, 25%	No
8	1	Propel should never be placed in an acutely infected field	25%, 21%	
	2	PROPEL can be considered for placement in an acutely infected field if the surgeon believes it is in the best interest of the patient	58%, 25%	No
11	1	SINUVA should only be placed if a total ethmoidectomy has been performed	71%, 14%	
	2	SINUVA is most optimally positioned only if total ethmoidectomy has been performed	83%, 17%	Yes

Note: Question 2 was resurveyed despite reaching agreement as it was directly correlated with question 1.

rinses after ESS (Q7). This may be caused by the perceived tendency of steroid-eluting implants to crust and the clinical benefit of daily postoperative rinses over these implants in managing crusts and surgical debris to promote healing and prevent infection during the postoperative period. Additionally, when asked about the optimal number of steroid-eluting stents to be placed in each sinonasal cavity (Q6), no consensus was reached. This may reflect a more patient-tailored approach in which the optimal number of steroid-eluting implants to be placed is determined by anatomy, severity of the patient's sinonasal disease, and the experience of the surgeon. It could also represent different opinions by various experts on the cost versus benefit of additional stent placement in the operated cavity.

To obtain a broad survey of rhinology experts, we included surgeons who practice outside of the United States who might not have routine access to these implants in their health systems. We expected that access to implants in practice and varying personal experience would affect responses to the statements but we wanted to include a range of opinions. All experts had used the products. We did not specifically query why experts who had used the products previously no longer used them at the time of the survey. We also did not query why experts who had access to office-based stents had not used them. Further studies are necessary to determine decision-making patterns regarding availability and utilization. Our experts are primarily affiliated with academic medical centers, although two were community-based and therefore may utilize steroid-eluting stents differently than general otolaryngologists or surgeons who practice in different types of health systems. Two experts did not respond to the second survey round and therefore specific practice patterns may be differently represented in the five follow-up questions, which failed to reach initial agreement.

No consensus was reached when asked whether SINUVA could be an alternative to biologics for recurrent CRSwNP (Q9). While biologics have provided clinicians with a promising new option in the treatment of CRSwNP, several cost-utility analyses have demonstrated unfavorable cost-effectiveness compared with surgery.[19] Similarly, newer treatment options such as SINUVA should be compared with other postsurgical treatment options such as biologics to determine appropriate patient selection in the treatment of recurrent CRSwNP. The reported change in nasal polyp score for SINUVA is smaller than the reported change in nasal polyp score for dupilumab at comparable time points, and a direct comparison study would be illuminating.[10,11,20] As for the duration that these implants should remain in the sinonasal cavities, no consensus was reached by the experts when asked whether PROPEL should be removed within 21 days of surgery (Q12). The PROPEL stents are designed to dissolve between 30 and

45 days. Some panelists report removing the stents early to prevent postoperative crusting as the stents break apart.

9 | CONCLUSION

A panel of experts agreed that steroid-eluting stents can be considered intraoperatively for patients with CRSwNPs or CRSsNPs, especially in cases when patients are intolerant of oral steroids or when an extended frontal dissection has been performed. Steroid-eluting stents can be considered in the office for stenosis. However, newer more rigid office stents are best placed when a total ethmoidectomy has been performed. The impact on patient-reported outcomes in these contexts and the role of these implants in the wake of newer therapies, such as biologics, need to be investigated to better determine the role of steroid-eluting stents.

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CONFLICTS OF INTEREST

Greg Davis: Intersect ENT (consultant). Amber U. Luong: Aerin Medical (Austin, TX, USA), Glaxo-SmithKline (Brentford, UK), Lyra Therapeutics (Watertown, MA, USA), Sanofi (Paris, France), Stryker (Kalamazoo, MI, USA), ENTvantage Dx (Austin, TX, USA), Third Wave Therapeutics (San Francisco, CA, USA), and AstraZeneca (Cambridge, UK). Prior agreement with IntersectENT and Acclarent. Robert Kern: Lyra Therapeutics (Chief Medical Officer). Raewyn G. Campbell: Acclarent, prior agreement; Medtronic (Jacksonville FL, USA), Seqirus (Maidenhead, UK). Rakesh Chandra: Acclarent, prior agreement; Joseph Han: Acclarent, prior agreement; Jivianne Lee: Acclarent, prior agreement; David Poetker: Acclarent, prior agreement. Sarah Wise: consultant NeuroENT, Chitogel; Advisory board Optinose, Genentech. None of these companies were involved in the research in the present study.

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REFERENCES

1. United States Food and Drug Administration. US FDA Premarket Approval Medical Devices Database. Available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm. Accessed March 1, 2021.
2. Intersect ENT. Available at https://www.intersectent.com. Accessed March 1, 2021
3. Murr AH, Smith TL, Hwang PH, et al. Safety and efficacy of a novel bioabsorbable, steroid-eluting sinus stent. *Int Forum Allergy Rhinol*. 2011;1(1):23–32.
4. Marple BF, Smith TL, Han JK, et al. Advance II: a prospective, randomized study assessing safety and efficacy of bioabsorbable steroid-releasing sinus implants. *Otolaryngol Head Neck Surg*. 2012;146(6):1004–1011.
5. Smith TL, Singh A, Luong A, et al. Randomized controlled trial of a bioabsorbable steroid-releasing implant in the frontal sinus opening. *Laryngoscope*. 2016;126(12):2659–2664.
6. Luong A, Ow RA, Singh A, et al. Safety and effectiveness of a bioabsorbable steroid-releasing implant for the paranasal sinus ostia: a randomized clinical trial. *JAMA Otolaryngol Head Neck Surg*. 2018;144(1):28–35.
7. Singh A, Luong AU, Fong KJ, et al. Bioabsorbable steroid-releasing implants in the frontal sinus ostia: a pooled analysis. *Int Forum Allergy Rhinol*. 2019;9(2):131–139.
8. United States Food and Drug Administration. US FDA Drug Approvals and Databases. Available at https://www.accessdata.fda.gov/drugsatfda_docs/nda/2017/209310Orig1s000SumR.pdf. Accessed on March 1, 2021
9. Han JK, Forwith KD, Smith TL, et al. RESOLVE: a randomized, controlled, blinded study of bioabsorbable steroid-eluting sinus implants for in-office treatment of recurrent sinonasal polyposis. *Int Forum Allergy Rhinol*. 2014;4(11):861–870.
10. Forwith KD, Han JK, Stolovitzky JP, et al. RESOLVE: bioabsorbable steroid-eluting sinus implants for in-office treatment of recurrent sinonasal polyposis after sinus surgery: 6-month outcomes from a randomized, controlled, blinded study. *Int Forum Allergy Rhinol*. 2016;6(6):573–581.
11. Kern RC, Stolovitzky JP, Silvers SL, et al. A phase 3 trial of mometasone furoate sinus implants for chronic sinusitis with recurrent nasal polyps. *Int Forum Allergy Rhinol*. 2018;8(4):471–481.
12. Narwani V, Torabi SJ, DA Kasle, et al. Adverse events associated with corticosteroid-eluting sinus stents: a MAUDE database analysis. *Otolaryngol Head Neck Surg*. 2021;166(1):179–182.
13. Adriaensen GFJPM, Lim KH, Fokkens WJ. Safety and efficacy of a bioabsorbable fluticasone propionate-eluting sinus dressing in postoperative management of endoscopic inus surgery: a randomized clinical trial. *Int Forum Allergy Rhinol*. 2017;7(8):813–820.
14. Xu J, Park SJ, Park HS, et al. Effects of triamcinolone-impregnated nasal dressing on subjective and objective outcomes following endoscopic sinus surgery. *Eur Arch Otorhinolaryngol*. 2016;273(12):4351–4357.
15. Zhao KQ, Yu YQ, Yu HM. Effects of mometasone furoate-impregnated biodegradable nasal dressing on endoscopic appearance in healing process following endoscopic sinus surgery: a randomized, double-blind, placebo-controlled study. *Int Forum Allergy Rhinol*. 2018;8(11):1233–1241.

16. Côté DW, Wright ED. Triamcinolone-impregnated nasal dressing following endoscopic sinus surgery: a randomized, double-blind, placebo-controlled study. *Laryngoscope*. 2010;120(6):1269–1273.
17. Li W, Lu H, Wang H, et al. Efficacy and safety of steroid-impregnated implants following sinus surgery: a meta-analysis. *Laryngoscope*. 2020;130(12):2754–2759.
18. Out of Committee: Outcomes Research and Evidence-Based Medicine | Absorbable Steroid-Eluting Sinus Implants: What We Do and Don't Know | AAO-HNSF Bulletin. https://bulletin.entnet.org/aao-hnsf-2021/article/21295901/out-of-committee-outcomes-research-and-evidencebased-medicine-absorbable-steroideluting-sinus-implants-what-we-do-and-dont-know. Accessed March 19, 2022.
19. Scangas GA, Wu AW, Ting JY, et al. Cost utility analysis of dupilumab versus endoscopic sinus surgery for chronic rhinosinusitis with nasal polyps. *Laryngoscope*. 2021;131(1):E26–E33.
20. Bachert C, Han J, Desrosiers M, et al. Efficacy and safety of dupilumab in patients with severe chronic rhinosinusitis with nasal polyps (LIBERTY NP SINUS-24 and LIBERTY NP SINUS-52): results from two multicenter, randomized, double-blind, placebo-controlled, parallel-group phase 3 trials. *The Lancet*. 2019;394(10209):1638–1650.

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