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ORIGINAL RESEARCH

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Porcine small intestine graft for reconstruction of oral defects

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Abstract

Objective: To evaluate the feasibility and outcomes of porcine submucosal allograft (Biodesign Sinonasal Repair Graft [Cook Medical, Bloomington, IN]) in oral cavity and oropharynx reconstruction after ablative surgery.

Methods: We conducted a prospective and retrospective review of patients who underwent Biodesign Sinonasal Repair Graft reconstruction for oral and oropharyngeal surgical defects at a single institution between 2018 and 2020. A total of 11 patients were included in the study. Data points included their perioperative medical and demographic data, immediate postoperative course, and follow-up visits at 10 days and at 2 months. The clinicopathologic characteristics of their disease, postoperative esthetic, and functional outcomes were recorded and analyzed.

Results: Eleven procedures have been performed, and all patients received Biodesign reconstruction either immediately after ablation or after they failed a previous reconstruction. None of the patients had bone exposure. The subsites included oral tongue ($n = 6$), floor of the mouth ($n = 3$), buccal mucosa ($n = 1$), and soft palate ($n = 1$). In all cases, the operations and the postoperative course were uneventful. The mean defect size was 22 cm^2. The median start of oral intake was at 2 days postoperatively. The Biodesign graft healed well in all patients with no total graft loss. There was one complication that required revision surgery due to obstruction of Wharton's duct by the Biodesign material.

Conclusions: Biodesign can be a viable option for small and medium-sized oral and oropharyngeal defects in patients who are medically unfit or do not want to undergo a free flap surgery.

Level of Evidence: 4.

KEYWORDS

Biodesign, oral cavity reconstruction, porcine small intestine submucosa, tongue reconstruction, xenograft

Approval body: UTHSC IRB (University of Tennessee Health and Science Center Institutional Review Board)

1 | INTRODUCTION

Oral cancer and benign oral lesions are typically managed with surgery. Despite largely favorable results with local control, surgical excision may negatively impact functional outcomes and quality of life. Altered anatomy of the site may affect speech, swallowing, or tongue mobility. Reconstructive surgery aims to optimize these outcomes, whether through primary wound closure, secondary intention, skin grafting, local flap, or vascularized free tissue transfer.[1]

Over the past two decades, microvascular free flap reconstruction has become increasingly common in reconstructing complex oral cavity defects. Initially, the radial forearm flap was the standard choice as it provides thin pliable skin that can be folded to fit the defect and has a long vascular pedicle.[2] In more recent years, the anterolateral thigh flap has become more popular among surgeons for non-obese patients due to its minimal donor site morbidity and ability to be harvested simultaneously in a two-team approach.[2-5] Microvascular free flap reconstruction comes with challenges, such as the need for longer operative time, increased overall costs, prolonged hospital stays, and the potential for donor site morbidity. Presence of non-mucosal tissue in the oral cavity can worsen xerostomia, particularly if combined with radiation. In effort to minimize this, jejunal patches and colon autologous flap patches have been used for floor-of-mouth reconstruction.[6-8] These flaps combine thinness and pliability with the capacity to produce mucus. Although authors have reported success with this approach, abdominal surgery is a necessary part of the procedure, and the ability of these flaps to withstand radiation has been brought into question.[9] For these reasons, they are not commonly used.

Extensive research has been done in the field of non-autologous grafts—xenografts and allografts. These products do not require harvesting autologous tissue and have characteristics that promote wound healing. The porcine small intestine submucosa xenograft (Biodesign; COOK Medical, Bloomington, Indiana) is an acellular biomaterial sheet derived from the extracellular matrix of porcine small intestinal submucosa (SIS).[10] Located between the mucosal and muscular layers of the porcine small intestine, the SIS is harvested and treated to remove cellular elements leaving the extracellular matrix intact.[11] The resulting biomaterial is a matrix composed of collagen, glycosaminoglycans, proteoglycans, and bioactive substances.[12,13] The matrix provides a framework for cellular integration of the host tissue while remaining relatively inert to immunogenic response.[14] It has been shown to maintain its strength with repeated physiologic load bearing,[15] and published reports support its safe and effective use in the repair of congenital diaphragmatic hernia,[16] vaginal prolapse,[17] urologic procedures, and in skull base and orbital reconstructions.[11,18,19] Two Biodesign SIS products are specifically intended for the use in otolaryngology: the Biodesign Sinonasal Repair Graft (SRG) and the Biodesign Otologic Repair Graft. The Biodesign Sinonasal Repair Graft was approved by the U.S. Food and Drug Administration in 2013. Although publications exist on the clinical application of the Biodesign SRG in nasal cavity defects,[20,21] this is the first reported application of its use in the oral cavity and oropharynx. This case series aims to describe our institution's experience with Biodesign Sinonasal Repair Graft in the reconstruction of oral and oropharyngeal defects.

2 | METHODS

This retrospective and prospective project was approved by Institutional Review Board at University of Tennessee Health and Science Center as an observational study. From December 2018 through July 2020, 11 patients were identified and consented for collection of their medical information and photographs. Six patients were men and 5 were women, with a median age at the time of surgery 62 years (range 37 to 86 years). All patients underwent a reconstructive procedure at Methodist University Hospital in Memphis, Tennessee with the use of Biodesign Sinonasal Repair Graft. Only the subjects with more than 3 months of follow-up were included in the study.

2.1 | Data collection

Patient demographics, along with preoperative, perioperative, and postoperative data were collected from our electronic medical records. Course of healing, presence of tongue tethering, dysarthria or dysphagia were collected and obtained from electronical medical records and from direct discussion with the surgeons after the clinic visits.

2.2 | Surgical approach

The procedures were performed under general anesthesia in the supine position. The lesions were excised and in oncologic cases the margins were cleared with frozen section analysis. Neck dissection was performed in indicated cases. In all cases, there was no bone exposure. Following the ablative portion of the surgery, a Biodesign SRG was brought into the field (7 $\times$ 4 cm, 0.2 mm of thickness) and cut to the appropriate size and shape fitted to the recipient defect. The xenograft was then placed in the wound and secured with vicryl tacking sutures, then sewn circumferentially with 4-0 chromic suture. Several piecrust incisions were made in the graft to prevent fluid collection and help with adherence to the tissue. In certain cases, to keep the graft firmly in position for healing, it was felt that a temporary bolster would be appropriate. A bolster was made using Xeroform wrapped around cotton gauze and secured with Nylon sutures on top of the graft. In several cases, a nasogastric Dobhoff feeding tube was placed for postoperative nutrition support.

2.3 | Postoperative care

Depending on the extent of surgery and medical comorbidities, some patients were discharged on the day of surgery and others stayed in

TABLE 1 Patient characteristics

Patient #	Age (years)	Indication for reconstructive surgery	Reason for use of Biodesign	Staging	Duration of surgery (min)	Defect size (cm^2)	Graft size (cm^2)	Hospitalization (days)	Feeding tube (days)	Complications related to Biodesign graft
1	75	Oral tongue SCC	Patient refused free flap surgery	pT2N2b	209	4.5 × 3.5	4.5 × 3.5	2	2	No
2	60	Oral tongue SCC after free flap failure	Patient refused revision free flap surgery	pT3N3b	192	4 × 8	4 × 7	8	6	No
3	86	Oral tongue SCC	Free flap deemed too morbid, patient preferred quick procedure	pT2N0	150	4 × 7	4 × 7	2	2	Tongue tethering (mild)
4	48	Tongue scar with tethering after previous SCC resection with skin graft	Patient preferred simplest approach	—	105	4 × 7	4 × 7	2	2	Dysarthria (mild)
5	66	Buccal mucosa SCC	Patient preferred simplest approach	pT1N0	133	4 × 7	4 × 7	0	0	No
6	61	Floor of mouth SCC	Primary closure would lead to ankyloglossia	pT1N0	97	3 × 6	4 × 7	2	2	Obstructive sialadenitis
7	61	Lichen planus of oral tongue and floor of mouth	Primary closure would lead to ankyloglossia	pT0N0	113	4 × 6	4 × 7	1	0	No
8	37	Soft palate pleomorphic adenoma	Primary closure not possible, graft was preferable to secondary intention	—	75	2 × 5	2 × 5	1	0	No
9	74	Oral tongue SCC	Primary closure would lead to ankyloglossia	pT1N0	66	3 × 2.5	3 × 3	0	0	No
10	48	Revision excision of oral SCC	Primary closure would lead to ankyloglossia	pT1N0	182	4 × 6	4 × 7	0	0	Self-limited tongue tethering, later resolved
11	66	Ventral tongue SCC	Primary closure would lead to ankyloglossia	pT2N0	312	3 × 5	3 × 5	2	0	No

the hospital for postoperative observation for multiple nights. Postoperative instructions included using a straw when drinking liquids to minimize contact with the surgery site, swish and spit oral cavity Peridex rinse daily, and refrain from brushing their teeth on the affected area for 1 week. In cases where a bolster was used, it was kept in place for 5-7 days and removed at an outpatient clinic visit. Tongue mobility exercises were recommended to the patients if reconstruction of the tongue or floor of the mouth was done once the bolster was removed. Follow-up visits were made at 1-2 weeks postoperatively, and at 2 months postoperatively.

3 | RESULTS

All patients had a current or past diagnosis of oral cancer, or a diagnosis of a benign lesion of either the oral cavity or oropharynx that required reconstruction with more than primary closure (Table 1). None of the patients have previously undergone radiation therapy. The defect was located on the oral tongue (n = 6) (Figures 1-3), floor of the mouth (n = 2), buccal mucosa (n = 1), and soft palate (n = 1). One patient had a lesion involving both the oral tongue and floor of the mouth (n = 1). Tumor histopathology included squamous cell carcinoma (SCC) (n = 9), lichen planus (n = 1), and pleomorphic adenoma (n = 1). Out of the nine cases of SCC, most were primary reconstruction after resection of the tumor (n = 7), one was secondary reconstruction for a SCC after a failed free flap (n = 1), and one was a revision of a postoperative scar causing significant tongue tethering and pain (n = 1). The decision to use the Biodesign graft was carefully weighed against other options, such as microvascular free flap, local rotational flap and split-thickness skin graft, and different commercial biomaterials.

In all cases, the surgery was uneventful. Mean operative time was 149 minutes (range 66 and 312 minutes). Mean defect size was 22 cm^2, the smallest defect measured 3 × 2.5 cm and the largest 8 × 4 cm. A bolster was used in five patients and waived in six others. Postoperative courses were uneventful and immediate revision surgery was not needed in any of the cases. Mean hospital stay was 2 days: three patients were discharged on the same day of the procedure, two stayed at the hospital overnight, five required a 2-day

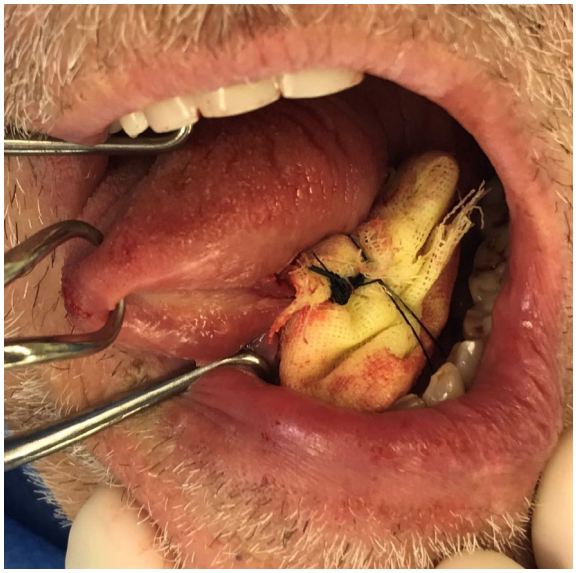

FIGURE 2 Gauze bolster attached on top of the Biodesign Sinonasal Repair Graft after removal of pT1N0 lesion of oral tongue and floor of the mouth

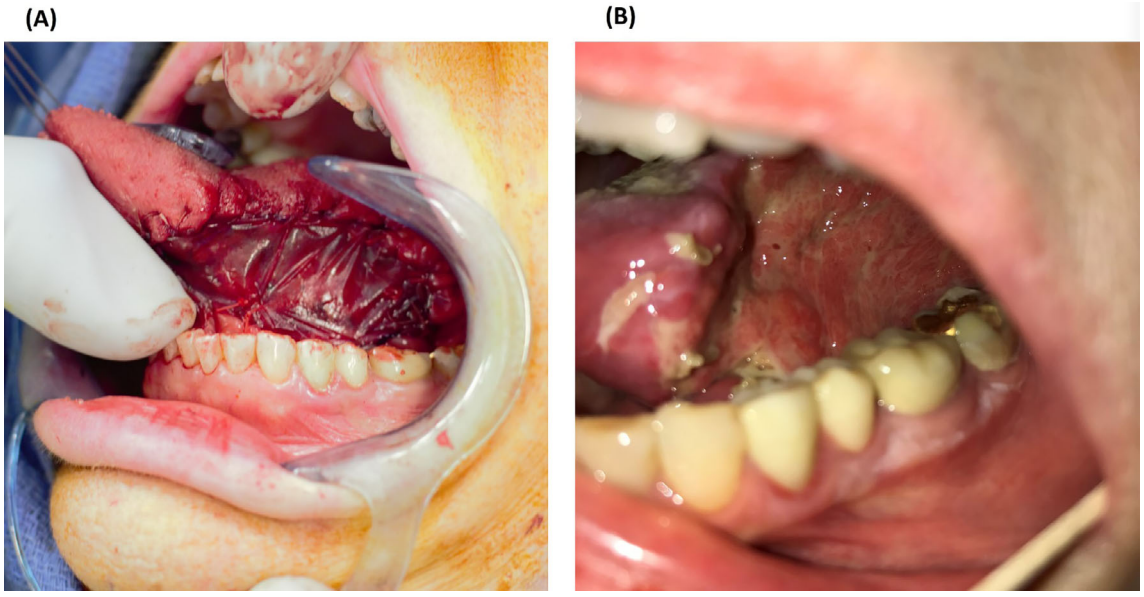

FIGURE 1 75-year old women with pT2N2b oral tongue squamous cell carcinoma after surgical resection and reconstruction. A, Biodesign Sinonasal Repair Graft sewn on to the tissue defect. B, The lesion at 7 days after graft placement with bolster

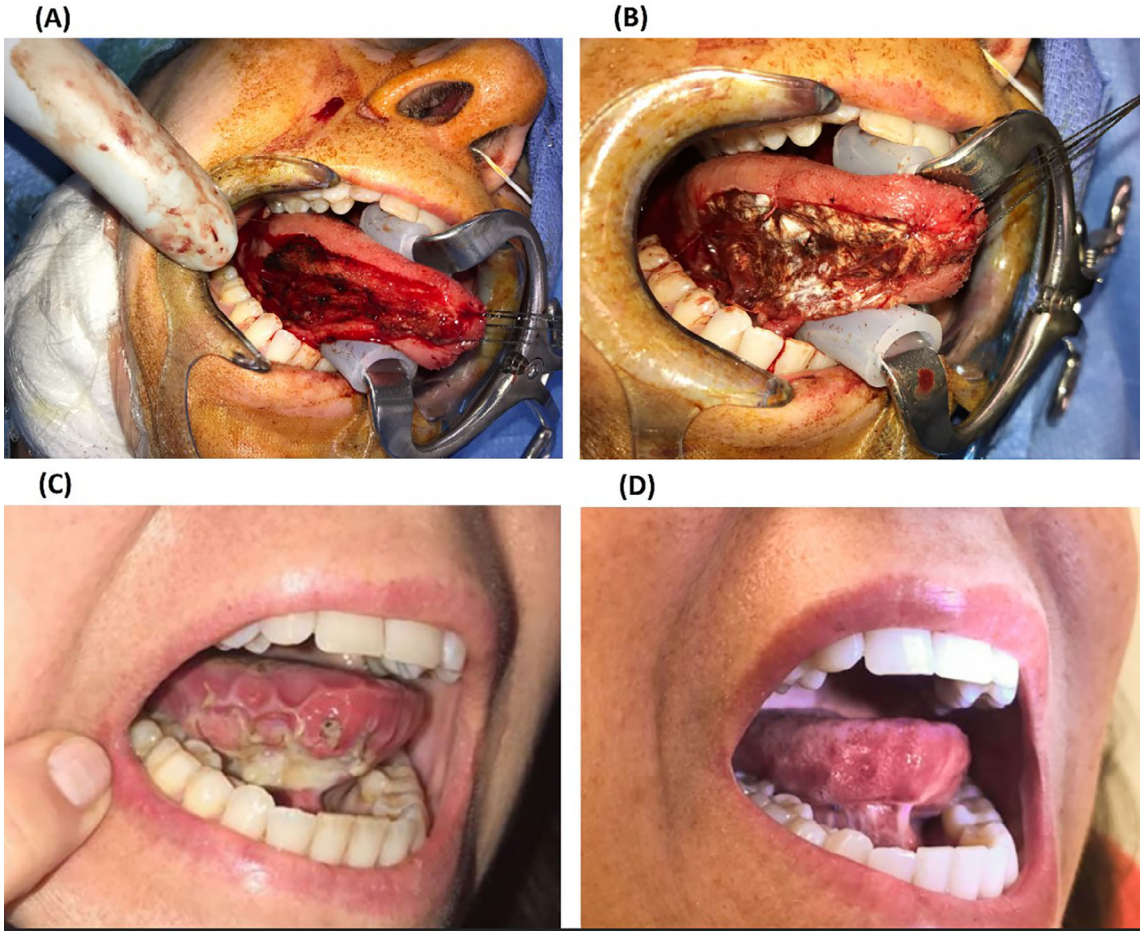

FIGURE 3 48-years old female with pT1N0 oral cancer admitted for revision resection of tissue and tongue reconstruction. A, Surgical defect; B, Biodesign graft in place; C, follow-up at 2 weeks; D, follow-up at 2 months

hospitalization and one stayed for 8 days (mainly due to ongoing recovery from a previous failed free flap surgery). Dobhoff feeding tube was used in half of the cases (n = 5), four of those required it for 2 days, and one patient for 6 days. In all cases, Biodesign grafts have healed well and provided a functional coverage of the surgical wound in the initial postoperative course. One patient presented with a late complication of obstruction of Wharton's duct by the graft resulting in obstructive sialadenitis. He underwent diversion sialodochoplasty with resolution of salivary obstruction. Two patients reported tongue tethering postoperatively: one patient had self-limited tethering that resolved within 2 months following the procedure, and the second patient had a persistent mild tethering, but with good mobility of the tongue in all directions including protrusion. A patient who had preoperative tethering due to a scar continued to have dysarthria; however, it had improved considerably compared to the preoperative quality of speech. No other complications related to the graft have been noted. At the 2-month follow-up, all patients reported normalcy of diet. The material was well tolerated with fair results of contour, feeling, and integration with the native tissue. The graft did not have a visible tendency to contract, tear, slough or stiffen. In all cases, no further intervention was required.

4 | DISCUSSION

The current study demonstrates the safety and effectiveness of porcine SIS grafting for repair of oral and oropharyngeal defects of various etiologies. The authors had extensive prior experience with the product for on-label wound locations (sinonasal cavity) and considered these wounds similar in defect size and character to the off-label wound location (oral cavity, oropharynx). The use of porcine SIS in head and neck area has been underreported in the otolaryngology literature to date compared to its well-documented use for other surgical disciplines, for example, cardiovascular surgery, or abdominal surgery.[22,23]

The porcine SIS has characteristics that allow its integration into the tissue. It provides an acellular matrix that is composed of collagen (types I, III, VI), glycosaminoglycans (hyaluronic acid, chondroitin sulfate A and B, heparin, and heparan sulfate), proteoglycans, growth factors (TGF-2, TGF-β) and fibronectin.[10,12] Yang et al previously published an in vitro study on bladder regeneration after repair with SIS xenograft.[24] The study found evidence that SIS components stimulated attachment, proliferation, and migration of the bladder cells. The study results imply that SIS may have preserved bioactive factors

inducing cell regrowth and healing through cell adhesion factors, mitogenic factors, chemotactic cytokines, and angiogenic factors.

A recent prospective randomized trial illustrated Biodesign SRG as a reconstructive option for the exposed nasoseptal flap donor site in skull base reconstruction.[21] Subjects were randomized to intervention (graft) and control (no graft), and remucosalization of the nasal cavity was reported in endoscopic recordings. Remucosalization proved to be significantly faster in the treatment group. Another study tested the porcine SIS's ability to withstand loading pressure, reporting on complete retaining of its strength, which would support its use in locations exposing the graft to pressure (eg, hernia repair or skull base repair during Valsalva maneuver by the patient).[15]

Advantages of using a xenograft include reduced operative time, no need for second surgery site, customizability of the size of the graft, and relative ease of implantation to the defect. Disadvantages of this technique may include risks inherent to xenograft origin,[25] inability to provide bulk equivalent to a soft tissue flap, inability to find local infection, and expense (although the expense may be put into perspective of the potential savings from decreased operative time and postoperative stay).

The size of the oral and oropharyngeal defect often dictated the decision for the optimal reconstruction.[1,26] In small defects which can be closed without creating significant tension, primary closure is the simplest and most effective method. For moderate and large defects, primary closure does not restore lost volume and may alter anatomical proportions. Maintaining or reproducing original volume is critically important for satisfactory postoperative tongue function. Thus, in large defects, regional pedicle flap or microvascular free flap reconstructions are better suited to restore volume.

There is no clear consensus, however, on the ideal type of reconstructive method for mid-sized defects. A recent publication by Ji et al. on long-term functional outcomes of tongue reconstruction after partial glossectomy concluded that healing by secondary intention had the best results in tongue mobility, articulation, and speech intelligibility, compared with primary closure or flap reconstructions.[27] Despite the conclusion of the publication, complications of secondary intention for oral cavity defects (e.g. postoperative hemorrhage, excessive deep scarring, ankyloglossia, and postoperative pain), make this approach unfavorable, especially if the defect is larger than 2 cm or is in non-tongue locations such as floor of the mouth.[26] Another reconstructive option for mid-sized defects is split thickness skin graft; however, the main drawback is scar contracture and risk of donor site morbidity.[26] There are certain instances where although the surgeon may feel that microvascular free flap reconstruction would be the preferred reconstructive method, either the patient declines it or is deemed medically unfit to endure extended time in the operating room. In these specific situations, xenografts may provide a satisfactory degree of coverage, despite not providing the equivalent restoration of volume. Compared with primary closure, reconstruction with xenograft allows better maintenance of the spatial anatomical parameters of the oral or oropharyngeal sites because the defect margins remain in their original position. Compared to local and free flap reconstructions, non-autologous grafts do not carry the additional risk of morbidity of the donor site.

Location and anatomy likewise dictate the reconstructive approach. For example, the smallest defect in our series was 3×2.5 cm—for a defect of this size located on lateral tongue, primary closure is simple and appropriate; however, on the ventral tongue or floor of mouth, primary closure could result in excessive tissue contraction. The challenge for the reconstructive surgeon is to decide which technique is best suited for each individual case, considering not only functional outcomes but also overall aesthetics and the patient's personal preference.

There are alternatives to porcine SIS among biomaterials. One commonly used product is AlloDerm allograft but it is significantly thicker (0.9-1.6 mm compared with 0.2 mm for SRG) and has the tendency to integrate less and slough off in the oral cavity location.[28] Compared to this AlloDerm allograft, Biodesign SRG provides more consistent thickness, no sidedness (no need to orientate for proper placement) and is about 40% less expensive.

Limitations of this study include the data being largely collected in retrospective nature, the use of subjective instead of objective tools to assess dysphagia, dysarthria, and quality of healing. The outcomes were extracted from clinic notes and verified by follow-up discussions with surgeons. Another limitation is the lack of a specific surgical protocol; multiple surgeons used this product and treatment was thus nonuniform, varying based on our center's developing experience with the product. Our surgeon with the most experience using the product initially used a bolster on every application, then attempted a few without a bolster, and ultimately went back to using a bolster. This is in large part due to the appearance of the wound at the first follow-up visits and the development of scarring in patients who did not receive a bolster. However, none of the scarring seemed to be clinically relevant at the 3-month follow-up visit. At the end of our study, Dobhoff tubes were no longer placed routinely. All our surgeons agree to elect the autologous flap reconstructions if there is a bone exposure in the wound.

Although the scenario of previously irradiated patients has not occurred in this case series, future research should ascertain the quality of healing of Biodesign SRG in irradiated oral cavity and oropharynx sites. It can be expected that the healing will be poorer compared to non-irradiated patients, since past research has shown reduced chances of graft intake even with use of vascularized autografts.[29] It should also be noted that, unlike mucus-producing grafts (jejunal patches and colon autologous flap patches), Biodesign SRG does not offer any advantage concerning post-irradiation xerostomia.[6-8]

In this case series, the one complication related to the reconstruction with Biodesign graft was the obstruction of Wharton's duct. This occurred 1 month after a floor of mouth reconstructive procedure for SCC. The graft was sewn near the papilla of the duct and the resulting granulation and edema led to submandibular gland swelling. Conservative management with antibiotics and steroids was attempted, but ultimately the obstruction was managed with a diversion sialodochoplasty. It is worth noting that after this study

was already closed for enrollment, our center had another case where Biodesign SRG was used in which the papillae of both submandibular ducts were involved with tumor. To avoid this complication, bilateral sialodochoplasties were prophylactically performed prior to the graft placement. At the time of this writing—5 weeks following the procedure—the patient showed no signs of salivary obstruction.

5 | CONCLUSION

The current study reports the safety and effectiveness of Biodesign Sinonasal Repair Graft in oral cavity and oropharyngeal reconstruction in a series of 11 patients. The material appears to be an additional tool that can be used for mid-sized defects in the oral cavity and oropharynx without bone exposure.

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Corresponding author reached out to the Director of Medical Sciences at Cook Biotech Incorporated, Mr. Jason Hodde, ATC, RAC, CCRP (jason.hodde@cookbiotech.com) with question about the date when Biodesign Sinonasal Repair Graft was approved by the FDA. This information was provided by Mr. Hodde at no cost.

CONFLICT OF INTEREST

None of the authors declare any financial interest in this article. Dr. M. Boyd Gillespie, MSc declares having consulted with Cook Biomedical on sleep surgery devices from September 2017 till February 2020, none since.

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