

## CASE REPORT

# Reconstruction of intraoral oncologic surgical defects with Integra® bilayer wound matrix

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## Abstract

Utilization of biologic skin substitutes for the management of soft tissue defects as an alternative to autologous skin grafts has expanded over the past 2 decades. The purpose of this case series study was to report our experience with Integra® bilayer wound matrix for reconstruction of intraoral oncologic defects. Case records of 6 patients with intraoral oncologic defects reconstructed with Integra® bilayer wound matrix were retrospectively reviewed. The surgical defect location, size, and time to removal of surgical splint varied. Clinically, normal oral epithelialization was noted for all patients. One patient demonstrated a small area of dehiscence and bone exposure after adjuvant radiation therapy which resolved with minimal intervention. Integra bilayer wound matrix is a viable and versatile option for reconstruction of intraoral oncologic surgical defects. Further exploration of wound healing with Integra® matrix, surgical techniques, and cost-effectiveness is advocated.

## KEYWORDS

biosynthetic skin substitutes, oral cancer, oral reconstruction, wound healing

## 1 | INTRODUCTION

Soft tissue reconstruction of intraoral oncologic surgical defects can be accomplished using a spectrum of wound closure modalities, including primary closure, healing by secondary intention, autologous skin grafts, skin substitutes, and various flaps.<sup>1,2</sup> The goal for a reconstructive surgeon was to implement the simplest technique that will be effective considering the extent and location of the surgical defect and the predicted functional deficit from soft tissue structure loss.<sup>3,4</sup> Primary closure of intraoral defects is often precluded by insufficient tissue availability and concerns for functional morbidities due to restricted movement of mobile tissues such as

the cheeks, lips, tongue, and floor of the mouth.<sup>5</sup> Similarly, healing by secondary intention is known to cause significant scar contractures, intraoral functional deformities of movable structures and extra-oral asymmetry. For large surgical resections, vascularized regional or distant free flap transfers have become a highly successful reconstruction modality; however, these involve complex surgical procedures and are associated with increased costs and concerns for donor site morbidities.<sup>4</sup> For intraoral oncologic defects that do not require a regional or free flap reconstruction, autologous full-thickness or split-thickness skin grafts have been the standard of care.<sup>6</sup> Harvesting skin grafts may be associated with donor site morbidities including, but not limited to, risk of infection,

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scarring, and patient discomfort that may last from days to months.<sup>7,8</sup> Biosynthetic skin substitutes have been increasingly used to overcome the disadvantages of skin grafts and include epidermal substitutes (eg, Apligraf®), dermal substitutes (eg, Alloderm®, Matriderm®), and composite grafts (eg, Integra®, Biobrane®, Dermagraft®).<sup>2,9,10</sup>

Integra® skin regeneration systems (Integra LifeSciences, Plainsboro, New Jersey) have found widespread application for reconstruction of intraoral surgical defects that do not mandate a regional or free flap reconstruction. Integra® bilayer wound matrix is one such regeneration matrix that has found widespread use for intraoral application but is sparsely reported in the literature.<sup>11,12</sup> This bilayer matrix is a composite graft with an inner porous layer made of cross-linked bovine tendon type I collagen and chondroitin-6-sulfate glycosaminoglycan, and an outer layer made of a thin nonresorbable, semi-permeable polysiloxane (silicone sheet). The biodegradable porous bovine collagen layer serves as a scaffold for cellular invasion and capillary growth and is usually replaced within 14–21 days for dermal wounds. The silicone layer provides a flexible adherent covering of the wound surface, controls moisture loss from the wound, and increases tear strength of the matrix. As this layer is nonresorbable, it is removed from the defect allowing epithelial growth by secondary intention in the oral cavity.

The purpose of this article was to report the authors' experience with use of biosynthetic skin substitute Integra® bilayer wound matrix as a one-stage procedure for reconstruction of oral oncologic surgical defects of varying sizes and intraoral location.

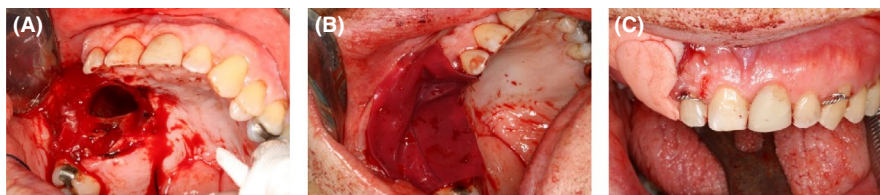
## 2 | CASE SERIES

Six patients treated by a single maxillofacial prosthodontist who underwent surgical resection of malignant oral tumors and Integra® bilayer wound matrix grafting between September 2018 and April 2019 were retrospectively assessed. Institutional review board approval (Protocol: PA19-0035) was obtained for assessing patients' photographs and demographic, medical, surgical, and prosthodontic treatment details. The included malignant tumors varied in intraoral location and surgical defect sizes.

After tumor resection, the final surgical defect was measured for appropriate sizing of the Integra® bilayer wound matrix (Figure 1A). For defects involving the maxilla or mandible, a preoperative irreversible hydrocolloid impression was made in order to fabricate a polymethyl methacrylate surgical stent made of heat-polymerized acrylic resin that is used to adapt the matrix against the underlying bone. Alternatively, a surgical stent was immediately fabricated in the operating room using light-polymerized Triad® VLC Denture Base Material (Patterson Dental Supply, Inc, Saint Paul, MN). The stent was placed over the defect to optimize the fit prior to grafting procedures. Integra® bilayer wound matrix was sutured to the surrounding oral mucosa using either 3-0 chromic gut (Gut Chromic™, Ethicon, Somerville, NJ) or 3-0 polyglactin (Vicryl™, Ethicon, Somerville, NJ) interrupted sutures (Figure 1B). The surgical stent was relined with Trusoft™ Resilient Denture Acrylic Relining Material, (Keystone Industries, Gibbstown, NJ), in order to closely adapt the matrix to the surgical defect. The stent was secured using 24-gauge ligature wires on two or three teeth for stability (Figure 1C). For defects involving highly movable oral tissues including buccal mucosa, floor of the mouth, and lateral/ventral tongue, the Integra matrix was supported with a Trusoft™ bolster sutured to surrounding oral mucosa with a 3-0 silk suture. In areas where a bolster was not possible, the matrix was stabilized using 4-0 silk or 3-0 polyglactin sutures.

The oral surgical splints and bolsters were removed 1–3 weeks postoperatively. The silicone sheet of the Integra matrix was removed when it was easily detached from the underlying granulation tissue, commonly between 2–3 weeks postoperatively. Satisfactory granulation tissue coverage was noted for all patients on removal of the Integra® silicone sheet.

For maxillectomy and mandibulectomy defects, interim prostheses were relined with Trusoft™ and inserted for continuous wear. Patients were instructed to remove the interim obturator only for oral hygiene and prosthesis care. Interim prostheses were adjusted and relined with Trusoft™ at subsequent visits to improve adaptation to the healing defect. Adjuvant radiation therapy was required for case 3 and was scheduled 6 weeks postoperatively.



**FIGURE 1** (Case 1): A, Surgical defect following infrastructure maxillectomy, B, Integra® bilayer wound matrix sutured to surrounding oral mucosa, and C, relined surgical stent with ligature wires

## 2.1 | Case 1

A 75-year-old man, never smoker, with a T1N0M0 squamous cell carcinoma of the right maxillary gingiva with gingival leukoplakia underwent an infrastructure maxillectomy, and extractions of the right maxillary canine, first premolar, and first molar. The final surgical defect measured 3 × 2.5 cm with a 1.5 cm diameter oroantral communication (Figure 1A).

Following suturing of the matrix to surrounding oral tissues, a previously fabricated oral surgical stent was ligated to the right maxillary second molar, lateral incisor, and left maxillary canine (Figure 1C). The stent was removed 9 days later, and an interim obturator was inserted to protect the immature healing tissues and support the attached silicone sheet (Figure 2A,B). The patient returned for a follow-up visit 3 weeks postoperatively when the silicone sheet of the Integra® bilayer wound matrix was removed, and early granulation of the surgical defect was noted. Notably, the oroantral communication was lined by granulating tissue and appeared to be very small, approximately 1mm diameter, compared with the original surgical defect. At a subsequent 2-month postoperative follow-up, well healed oral mucosa lined the surgical defect with complete closure of the oroantral defect (Figure 2C).

## 2.2 | Case 2

A 63-year-old man, former tobacco user, underwent a marginal mandibulectomy for a well-differentiated verrucoid squamous cell carcinoma of the anterior mandibular gingiva, and wide local excision of right buccal mucosa for a moderately differentiated invasive squamous cell carcinoma. The resulting surgical defect measured approximately 1.5cm in the anterior mandible and 3 cm over the buccal mucosa (Figure 3A). Integra® matrix was secured to the right buccal mucosa using 3.0 chromic gut sutures (Figure 3B). An oral bolster was created using Trusoft™ and secured with silk sutures (Figure 3C). The bolster was removed as was the silicone sheet, 1-week and 2-week postsurgery, respectively.

For the anterior mandibular site, matrix was secured to the anterior mandible, lip, and floor of mouth. An oral surgical stent was relined with Trusoft™ and ligated to teeth for applying pressure toward the bone and lip. Normal oral epithelization was noted for the anterior mandible and buccal mucosa defect (Figure 3D) at a 3-month postoperative

follow-up visit, with minimal reduction in maximum mouth opening.

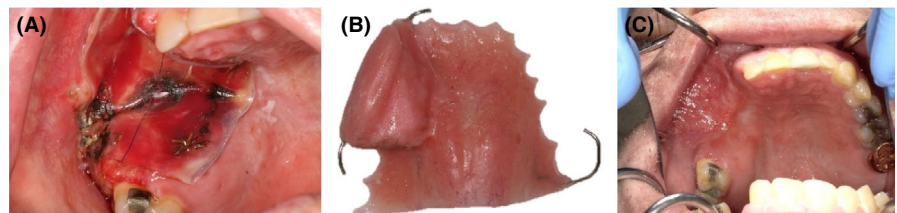
## 2.3 | Case 3

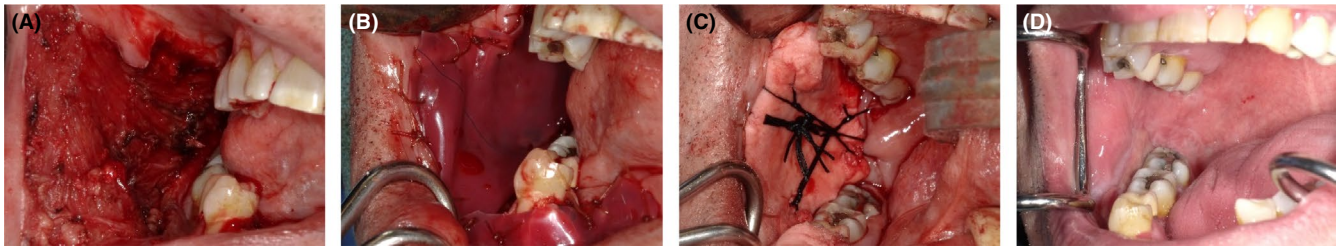
A 55-year-old woman, never smoker, with a well-differentiated squamous cell carcinoma of the right maxillary gingiva underwent a wide local excision of the right maxillary gingiva and buccal mucosa; hence, resulting in a surgical defect that extended from the distal aspect of the right maxillary canine to the maxillary tuberosity (Figure 4A). After frozen section analysis, the right maxillary canine was extracted, and gingival excision was extended distal to the right maxillary lateral incisor. The Integra® matrix was sutured into the defect, which measured approximately 5 x 3 cm (Figure 4B). An immediately fabricated surgical stent was relined with Trusoft™ with buccal extension for formation of an adequate vestibule. The stent was ligated to the right maxillary central incisor and left first premolar, with good stability. The stent and silicone sheet of the Integra® matrix were removed 2 weeks postoperatively with granulation noted over all aspects of the bone and majority of the buccal mucosa defect. Early signs of epithelization were noted over the surgical defect four weeks postoperatively. The patient underwent adjuvant radiation therapy. Three weeks after completion of radiation therapy a small area of exposed bone was noted (Figure 4C), which was removed with underlying granulation tissue noted. Complete epithelization of the wound was confirmed at a subsequent 8-month postradiation (11-month postoperative) visit. Scar contracture of the buccal mucosa and loss of vestibule were noted postradiation.

## 2.4 | Case 4

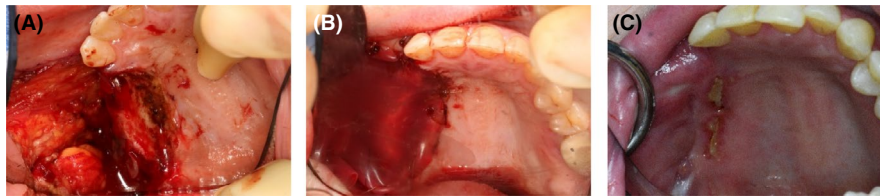
An 85-year-old man, active tobacco smoker, 102 pack-years (1.5 packs/day for 68 years), with a history of adenocarcinoma of the right hard palate and squamous cell carcinoma of the right oral tongue developed a high-grade dysplasia lesion of the anterior floor of mouth. He underwent wide local excision of the anterior floor of mouth, marginal mandibulectomy, extractions, and re-implantation of the salivary ducts (Figure 5A). Integra matrix was sutured to the lower labial mucosa, floor of the mouth, and ventral tongue (Figure 5B).

**FIGURE 2** (Case 1): A, Silicone sheet of Integra® matrix after removal of surgical stent 1 wk postoperatively, B, relined interim obturator, and C, 2-mo postoperative healing with complete closure of oroantral fistula

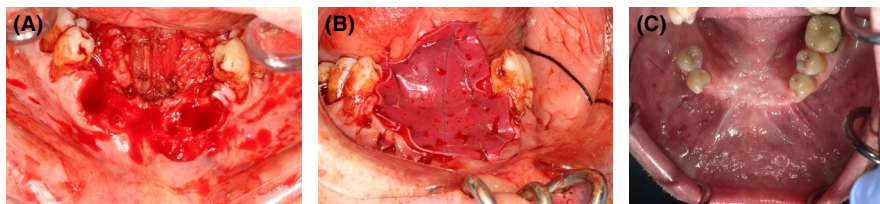




**FIGURE 3** (Case 2): A, Surgical defect following wide local excision of buccal mucosa, B, Integra® bilayer wound matrix sutured to surrounding oral mucosa, C, oral bolster secured to underlying tissues, and D, 3 mo postoperative healing with maximum mouth opening within normal limits



**FIGURE 4** (Case 3): A, Surgical defect following wide local excision of the right maxillary gingiva and buccal mucosa, B, Integra® bilayer wound matrix sutured to surrounding oral mucosa, and C, exposed bony sequestrum after radiation therapy



**FIGURE 5** (Case 4): A, Surgical defect following marginal mandibulectomy and wide local excision of anterior floor of the mouth, B, Integra® bilayer wound matrix sutured to surrounding oral mucosa, and C, 2-mo postoperative healing with normal movable mucosa

The Integra matrix was supported by a prefabricated oral surgical stent relined by Trusoft™. A Trusoft™ bolster was extended posteriorly to the floor of the mouth and anteriorly to the labial mucosa to stabilize the matrix on movable tissues. The stent and silicone sheet of the matrix were removed 2.5 weeks postoperatively, and good granulation tissue was noted covering the entire surgical defect. At a subsequent follow-up visit 2 month postoperatively, keratinized soft tissue covered the alveolar ridge and normal oral movable mucosa lined the floor of the mouth and labial mucosa, with no functional morbidities (Figure 5C).

## 2.5 | Case 5

A 70-year-old woman, former tobacco smoker, with a history of multiple recurrences of oral cavity squamous cell and verrucous carcinomas underwent wide local excision of left maxillary gingiva with a final diagnosis of well-differentiated squamous cell carcinoma with verrucous features. The patient is edentulous and wears a maxillary implant-retained

overdenture with locator abutments. The resulting surgical defect involved 3 out of 4 implants and measured 4x2cm (Figure 6A). Integra® matrix was sutured to the surrounding gingiva and upper lip with perforations for implant locator abutments (Figure 6B). The overdenture was relined with Trusoft™ and secured to the implants. The patient was instructed not to remove the overdenture herself, and this was removed 7 days postoperatively with good granulation tissue covering the surgical defect. Complete epithelization was noted at her subsequent 1-month follow-up visit.

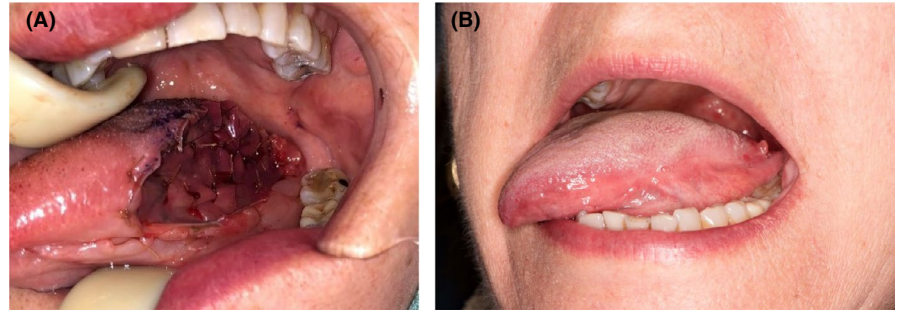
## 2.6 | Case 6

A 67-year-old woman, former smoker with a 15 pack-year history of smoking, was diagnosed with invasive squamous cell carcinoma of the left ventral tongue. She underwent a left partial glossectomy with a resulting surgical defect that was 1.5 cm x 1cm. Integra was sutured at the periphery as well as the center of the defect to allow for intimate contact with the underlying tissues, as a supporting bolster was not feasible



**FIGURE 6** (Case 5): A, Surgical defect following wide local excision of left maxillary gingiva, B, Integra® bilayer wound matrix sutured to surrounding gingiva and upper lip with perforations for locator abutments, and C, 2-mo postoperative healing

**FIGURE 7** (Case 6): A, Surgical defect following partial glossectomy, B, 2-month postoperative healing with excellent contralateral and protrusive tongue movement



(Figure 7A). The silicone sheet of the Integra matrix was dislodged prior to her 2 weeks postoperative visit as chronic gut sutures resorbed. At a subsequent 2-month postoperative follow-up visit, complete epithelization of the lateral wall of the tongue was observed (Figure 7B).

### 3 | DISCUSSION

This case series illustrates the great utility of Integra® bilayer wound matrix for reconstruction of small to large intraoral oncologic surgical defects as well as its versatility on movable and nonmovable mucosa. Despite its widespread clinical usage, a literature search revealed only 2 published clinical reports on intraoral application of Integra® skin substitutes.<sup>11,12</sup> Beech and Farrier (2016) described a case of mandibular osteoradionecrosis defect that was reconstructed using an Integra® regeneration system.<sup>12</sup> Rua González et al (2018) described its successful use in small intraoral oncologic defects.<sup>11</sup> In contrast, cases included in this series varied in intraoral location and surgical defect sizes, ranging from 1 to 5cm, as well as one case with an oroantral fistula. Some surgical defects were confined to keratinized tissues overlying alveolar ridges that could be easily immobilized, while others were located on highly movable oral tissues including buccal mucosa, floor of the mouth and tongue. In all cases, the patients underwent surgical excision for a malignant tumor and were reconstructed with Integra® bilayer wound matrix with placement of a bolster, surgical splint, and/or stabilizing sutures. Successful early granulation tissue was noted in all cases when the silicone sheet of Integra® matrix was removed. Oral epithelialization was noted in all cases; one case healed successfully but showed small areas of

dehiscence and bone exposure following adjuvant radiation (case 3). On conservative management with sequestrectomy and chlorhexidine 0.12% topical rinses, adequate recovery was seen for this patient. As depicted by these cases, Integra® bilayer wound matrix can be a successful alternative for soft tissue reconstructions of small to large size defects that do not mandate a vascularized regional or free flap transfer.

Remarkably, the Integra® bilayer wound matrix also allowed for complete closure of an oroantral communication in case 1. Previous clinical reports on the use of skin substitute or allogeneic grafts for oroantral fistula closure have depicted their success in small defects resulting from tooth extractions<sup>13</sup>; however, the oroantral communication established in case 1, subsequent to an infrastructural maxillectomy, was sizable and measured nearly 1.5cm in diameter. Complete closure of the oroantral defect without any persistent fistula suggest that Integra® wound matrix may also find application in oral surgical procedures for closure of oroantral communications and should be explored further for clinical- and cost-effectiveness.

For decades, autologous skin grafts have been the gold standard for reconstruction of intraoral oncologic surgical defects where vascularized tissue is not required. However, harvesting skin grafts leaves an uncovered donor site wound with an inherent risk of acute morbidities, including pain, infection, and pruritis, as well as chronic cosmetic complications resulting from hypertrophic scarring and pigmentation irregularities.<sup>14-16</sup> The donor site wounds are often reported to cause much higher postoperative pain than the primary recipient sites. Even in large intraoral oncologic resections, patients report higher discomfort with the donor site imitating a painful “road rash” sensation that may persist for months postoperatively in some cases.

Solanki et al reported that even in burn surgery cases, the skin graft donor wounds represent the most painful aspect of care.<sup>17</sup> Furthermore, donor site wounds produce hemorrhous exudates that may require repeated dressings until complete epithelization has been achieved.<sup>17</sup> Patients report persistent pain while the dressings are in place and during dressing changes for several days to weeks postoperatively.<sup>18</sup> Donor sites are also prone to infection if the exudates are not contained by dressings, which can prolong the healing time, require more frequent dressing changes, and the use of oral and topical antibiotics, further adding to the patient's discomfort.<sup>19,20</sup> The primary advantages of using skin substitutes such as Integra<sup>®</sup> bilayer wound matrix for intraoral oncologic surgical defects is optimization of patients' comfort and quality of life postoperatively by preventing a donor site wound.

Although, costs of an Integra<sup>®</sup> bilayer wound matrix per unit is substantially higher than an autologous skin graft, these costs may be offset by reduced intraoperative times and equipment required for autograft harvesting, as well as foregone time and resources required for postoperative donor site wound management.<sup>21,22</sup>

Split-thickness skin grafts are usually fragile and may easily tear while suturing to adjacent oral mucosa, whereas the silicone layer of the Integra<sup>®</sup> bilayer wound matrix increases its tear strength and permits easier handling. Furthermore, Integra<sup>®</sup> skin substitute allows granulation of native fibroblasts into the biodegradable collagen layer and epithelization through secondary intention, which leads to normal epithelialization of the recipient site. Conversely, autologous skin grafts may retain their original epidermal architecture with atypical texture within the oral cavity. In all included cases, clinically normal appearance of keratinized and nonkeratinized oral mucosa was noted in the recipient sites.

Our documentation of the six cases indicates that, similar to autologous skin grafts, reconstruction of surgical defects with Integra<sup>®</sup> skin substitutes was successful where adequate immobilization of the matrix against a vascular recipient bed was achieved by using a surgical splint, bolster, and/or stabilizing sutures. It is also crucial to protect the Integra<sup>®</sup> matrix from shearing forces and detachment. In addition, repositioning of the matrix is best carried out by lifting it away from the graft bed instead of moving or "floating" the sheet to avoid damage to the porous collagen layer. Based on manufacturer's recommendations, we also avoided contamination of Integra<sup>®</sup> matrix with petroleum-based products such as xeroform gauze, which are commonly used with autologous skin grafts.

In the two prior reports on intraoral use of Integra<sup>®</sup> skin substitutes, the time to removal of silicone sheets was reported between 2 weeks (González et al, 2018) and 3 weeks

(Beech and Farrier 2016). The postoperative follow-up visits of the patients reported in this series were not consistent due to several factors, such as length of hospital stay, out-of-state travel, and other scheduled appointments. This also led to variations in the postoperative time to removal of surgical splints and silicone sheets of Integra<sup>®</sup> bilayer wound matrix. The authors observed favorable granulation tissue covering the surgical defect at one week (cases 1 and 4) and two weeks (cases 2,3,5,6). The current recommendation for removal of the silicone layer is 21 days postoperatively is for dermal wounds. Intraoral postoperative time to removal of surgical splints and silicone sheets of Integra<sup>®</sup> bilayer wound matrix requires further investigation.

Furthermore, these 6 cases illustrated minimal graft shrinkage in patients who did not undergo adjuvant radiation therapy. In contrast, autologous skin grafts are expected to undergo considerable shrinking.<sup>23</sup> Integra<sup>(R)</sup> bilayer wound matrix may result in less contracture of the recipient site. Further exploration of wound healing with Integra<sup>(R)</sup> matrix, surgical techniques, histological analysis, patients' quality of life, and cost-effectiveness is advocated.

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## CONFLICT OF INTEREST

None declared.

## AUTHOR CONTRIBUTIONS

AS and AM: wrote the manuscript. AS, AM, and RC: were responsible for data collection. AS, AM, JM, and RC: contributed to primary treatment providers; MC and RC: contributed to critical revision during protocol and manuscript development. All authors: read and approved the final version of the manuscript.

## ETHICAL APPROVAL

University of Texas MD Anderson Cancer Center Institutional Review Board approved Protocol ID PA19-0035 on 02/11/2019 and determined that it is not human subjects research and does not require IRB approval. The Waivers of Informed Consent and Authorization were granted.

## DATA AVAILABILITY STATEMENT

Not applicable.

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