

**ORIGINAL ARTICLE**

Reshapable hydrogel tissue expander for ridge augmentation: Results of a series of successive insertions at the same intraoral site

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Abstract

Background: Oral mucosa expansion before ridge augmentation is a procedure to reduce soft tissue exposure and to improve bone graft density and volume after augmentation. This study explored a novel, shapeable hydrogel tissue expander (HTE) in intraoral sites that had undergone previous expansion and surgery.

Methods: Nine beagle dogs had all premolar teeth extracted and adjacent alveolar bone reduced. After at least 3 months healing hydrogels were placed at 4 sites in each dog: maxilla and mandible, right and left. After 6 weeks of expansion, the hydrogels were removed and measured for volume expansion and physical condition. Punch biopsies were taken of the expanded oral mucosa. After 3 months, a second hydrogel insertion was performed at each of the same sites. After this second expansion cycle, volume and hydrogel condition were recorded. Three dogs received ultrasound imaging of the hydrogels during the second expansion. Necropsy specimens were taken of both expanded and non-expanded oral mucosa.

Results: Within 2 weeks after HTE insertion in both first and second insertions, blood flow returned to the pre-insertion level. The first and second insertions resulted in linear oral mucosa gain of 8.13 mm, and 6.44 mm, respectively. First and second insertion hydrogels erupted from 4% of the first expansion sites, and 3% of the second expansion sites. There was no directional migration of the expanding hydrogel at any site. Histology found little inflammatory reaction to any hydrogel implant.

Conclusion: Oral mucosa can be consistently and successfully expanded before bone graft for ridge augmentation even at sites with a history of prior surgeries.

**KEYWORDS**

animal experiments, biomaterials, bone graft, ridge augmentation, soft tissue expanders, surgical techniques

1 | INTRODUCTION

Resorption of alveolar bone is common in patients following tooth extraction. The bone volume loss amounts to 40–60% within the first 3 years, and after 3 years continues at a rate of 0.25% to 0.5% loss per year.¹ Vertical ridge augmentation restores lost alveolar bone but often results in clinical problems and is unpredictable, largely because of problems with soft tissue management.² Surgeons frequently face the challenge of working with poorly vascularized oral mucosa using current “split-thickness” flap techniques.³ This ischemic mucosa causes exposure of grafted bone to microbes of the oral cavity, resulting in reduction or total loss of the susceptible graft. Previous surgery, oral trauma, chronic infections, and history of tobacco use are factors contributing to decline in the mucosal vascularity and ability to heal.^{4–6} In addition, tension introduced by sutures on a fragile mucosal flap further invites necrosis and bone graft exposure.^{7–9} These undesirable outcomes associated with vertical ridge augmentation with an exposed bone graft have a high probability of leading to reduction of up to 6 times final volume as compared with unexposed bone graft.¹⁰ Exposure often leads to reduction or complete loss of the bone graft.^{11–19} It is estimated that up to 45% of attempted ridge augmentations are lost or significantly compromised with the current surgical technique of “split-thickness” mucosa when placing bone grafts,^{14,19} as compared with only 4% bone graft exposure when using a tissue expander before bone grafting.²⁰ There is a significant need for tissue expanders in the dental field.²¹

Tissue expansion, widely used for skin applications, has increasingly been shown to offer promising results also for expansion of oral mucosa.²¹ These devices are commonly used as a means to increase skin surface area under a constant pressure via viscoelastic forces. Application of an optimal expansion rate and force, results in new, fully vascularized tissue,²² which can be applied in a wide variety of surgical procedures such as, breast reconstruction, autologous skin transplantation in burn victims, or vertical ridge augmentation.

Recently we have reported a study assessing tissue perfusion of oral mucosa following insertion of a novel shapeable hydrogel tissue expander (HTE).²² To validate the use of this HTE in an intraoral setting that resembles clinical applications, we used a beagle dog model to simulate the alveolar bone resorption that often occurs in patients following tooth loss.

The rate and force of expansion of soft tissue must match not only the anatomic site²³ but also accommodate any tissue alterations incurred by previous surgery or trauma. A common clinical scenario requires ridge augmentation at a site with a history of multiple surgeries or injury. This study uniquely explores the ability to expand tissues comparing two successive surgical insertions of HTE at the same sites to better understand the clinical challenges associated with intraoral scarred tissue expansion in preparation for ridge augmentation. Our model relied on two successive expander insertions at the same site. In our previous publication, we reported on only the second insertion results representing the common clinical situation of a previous surgical procedure or trauma.²²

2 | MATERIALS AND METHODS

2.1 | Canine model of oral mucosa expansion using hydrogel tissue expander

All animal studies were approved by the Indiana University Institutional Animal Care and Use Committee. Nine adult female Beagle dogs (Marshall BioResources, North Rose, NY), 13 months old, were subject to premolar tooth extraction and reduction of alveolar bone. Each animal was allowed to recover for at least 3 months before the insertion of the first, shapeable hydrophilic polymer: hydrogel tissue expander (HTE) (Restiex, Akina, Inc., West Lafayette, IN). The hydrogel in this study is comprised of chemically crosslinked poly(ethylene glycol) (PEG) and poly(lactide-co-glycolide) (PLGA) polymers connected by acrylate linkages. PLGA is a biodegradable and biocompatible polymer with a well-established history of clinical safety.²⁴

Four HTEs were implanted in four oral mucosa sites for each dog: right and left maxilla and mandible. During the first insertion, five variations of HTEs were tested in 36 sites. Each expander (initial dimensions: approximately 5 mm wide × 20 mm long × 3 mm thick end-tapered semi-cylinder) was comprised of an acrylate-crosslinked mixture of polyester and polyethylene glycol that varied based on percent compositions and molecular weight of each component to achieve varying expansion properties as previously described.²⁴ For example, the type C and type E expanders were both comprised of 65% (w/w) PLGA-PEG-PLGA-diacrylate, 22% (w/w) PEG (600 Da)-diacrylate, 9% (w/w) ethylene glycol-diacrylate, and 4% (w/w) Polylactide (Mw ~30 kDa)-diacrylate. For type “C” the PLGA-PEG-PLGA

**TABLE 1** Expansion metrics

Animals	Insertions	Number of sites	Volume and mechanical strength	Migration	Perfusion	Histology
9 dogs	1st insertion	24 (“E” hydrogel)	Photographs	Laser surface scan	Laser speckle imaging	3 punch biopsies per site
	2nd insertion	32 (“C” hydrogel)	Photographs, ultrasound	Laser surface scan	Laser speckle imaging	7 punch biopsies per site

diacrylate was 5000-1000-5000 Da for each block whereas the more hydrophilic type “E” was 3500-1000-3500 Da for each block. Initial screening with 4 sites was performed with expander types “A” to “E.” This screening identified type E as a promising candidate for initial implantation and, as such, an additional 20 sites were performed for first insertion using type “E”. After 6 weeks of expansion and monitoring, the hydrogels were removed, biopsies were collected, and all sites were allowed to heal for another 3 months. Following the recovery period, a second insertion of HTEs was completed. Formulation “E” was used for the second insertion in the initial dog, but was lost 3 days after insertion because of the force and rate of expansion. These properties of the HTE did not match the physical requirements of the scarred mucosa for re-implantation. By design, the “C” formulation expanded at a slower rate than the “E” formulation and was used for the remainder of the test animals after this loss. The second implantations were performed at the exact same sites as the first implantations. After 6 weeks of hydrogel assessment, the devices were removed, tissue biopsies were collected and the animals were euthanized. Table 1 is an overview of our study.

2.2 | Surgical technique

Surgical placement of the HTEs was achieved via “C”-shaped full-thickness incision characterized by a convex arc directed toward the vestibule. A full-thickness pouch created in this manner allowed for insertion of the device, and closure of the incision was performed with interrupted horizontal mattress sutures.

2.3 | Volume expansion and movement assessment

A digital camera (Nikon D90 camera, Nikon Corporation, Shinagawa, Tokyo, Japan) with a 105 mm f/2.8 lens (Nikon AF-S VR Micro-Nikkor 105 mm f/2.8G IF-ED lens, Nikon Corporation, Shinagawa, Tokyo, Japan) was used to photograph each of the HTE before insertion and immediately after removal, with a ruler in the frame of the photograph to aid in measurement calibration, as previously described. Image software (MicroSuite FIVE, B & B Microscopes Ltd, Pittsburgh, PA), was used to assess the dimensional change. The physical condition of the expanded hydrogels was recorded and judged as either “whole,” “fragmented,” or “crumbled.”

Migration of the expanding hydrogel was assessed by a laser surface scan (660 nm V2 laser probe, Class 2 M) (FaroArm, FARO Technologies, Lake Mary, FL). This technique allows precise 3-dimensional time-delineated assessment of the implanted expander in relation to a fixed point. The analysis was performed on oral mucosa for each of the first insertion sites and for all sites in six of the nine dogs undergoing the second insertion. The chronological sequence at each predetermined scanning time point was sensitive to any migration of the HTE. Migration was assayed using 3D analysis software (Geomagic Qualify, 3D Systems, Rock Hill, SC). The “measure distance” feature in the software was used to determine the distance between the anterior edge of the expander bulge and the base of the dog's canine tooth. This distance was determined for the same implantation in the same animal at each scanned time point and measured in millimeters. Because the tooth is a static point, a consistent change in distance over time would represent migration.

2.4 | Tissue perfusion assessment using laser speckle contrast imager

To assess blood perfusion of oral mucosa we employed a laser speckle contrast imager (LSI), Class 1 laser (moorFLPI-2 blood flow image, Moor Instruments, UK) at low resolution/high speed image acquisition rate (25 Hz). The scans were performed once a week, under sedation. Each of the two tissue regions of interest (ROI) were assessed for a duration of 1 minute. ROI-1 represents area of mucosa in contact with hydrogel, whereas ROI-2 represents an adjacent area that had not been surgically manipulated. Details of the tissue perfusion assessment are found in our previous publication.²²

2.5 | Histologic tissue analysis

The expanders were allowed to expand in the mucosa tissue for 6 weeks or until secondary endpoint of tissue expander self-removal (i.e., eruption through the expanding mucosa). After the 6-week expansion, the expanded hydrogel was removed, biopsies were taken, and the mucosa was resutured.

Immediately after hydrogel removal on Day 42 of the first and second insertions, biopsies were taken using a round 2 mm dermatology punch biopsy knife. It was presupposed that after 90 days of healing these small biopsies would have minimal influence on the second hydrogel implant expansion parameters. For both first and second insertions,

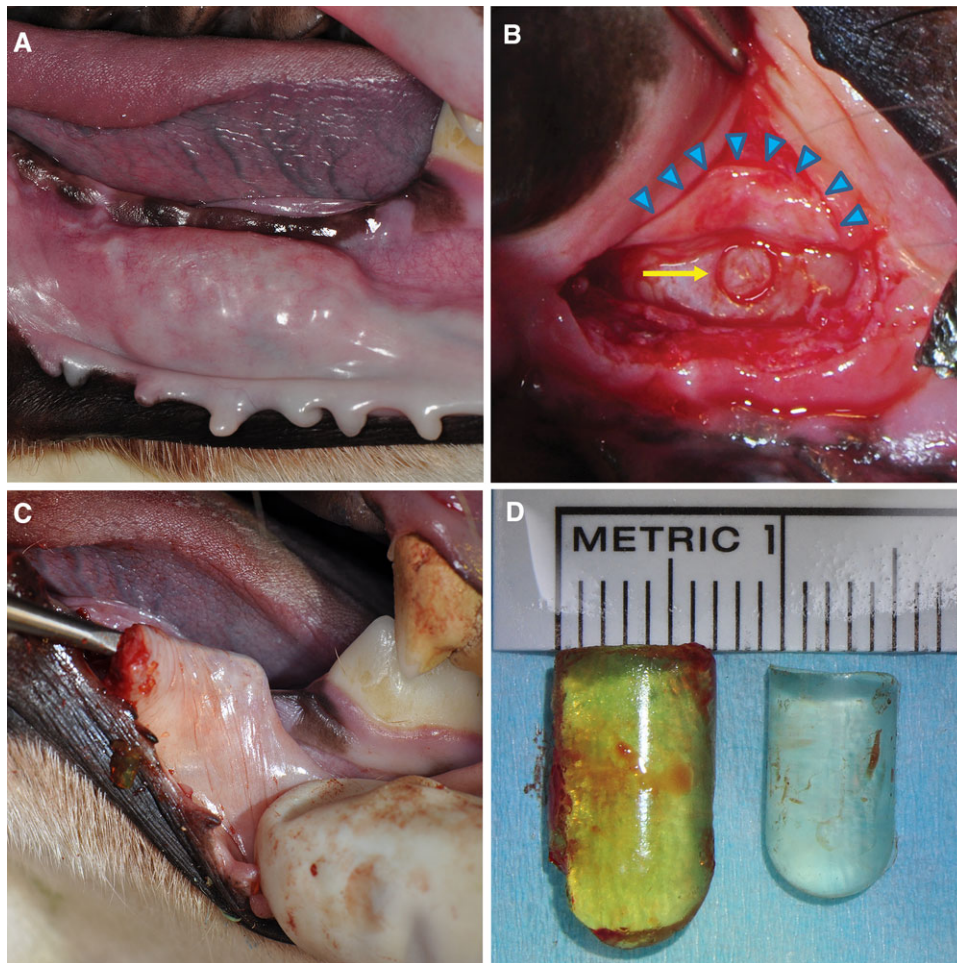


FIGURE 1 Removal of expanded hydrogel. **A**, HTE, after 6 weeks of expansion. **B**, Just after removal of expanded HTE, maxillary site. Blue arrows point to a thin fibrous capsule that covered the expanded HTE. Yellow arrow points to punch biopsy of very thin, uniform fibrous capsule that formed between bone and inserted HTE. **C**, Marked increase in new, vascular soft tissue for vertical ridge augmentation. **D**, Expanded compared with unexpanded HTE

two-millimeter punch biopsies were taken through the anterior (rostral) and posterior (caudal) zones of the hydrogel expansion site, and into the periosteum at the deepest internal extent of the expanded hydrogel. These biopsies demonstrated the fibrous capsule that enclosed each expanded hydrogel. The second insertion took the same biopsy sites as the first insertion, but added 4 additional biopsy sites of unexpanded mucosa next to the expanded oral mucosa. Each biopsy was performed in a manner that included the submucosal connective tissue close to the hydrogel to reveal any possible inflammatory reaction, fibrosis, neovascularization, or retained hydrogel particles resulting from the hydrogel insertion, expansion, and removal. Each biopsy was placed in neutral buffered formalin and fixed for at least 24 hours. Fixed biopsy cores were embedded in paraffin oriented so that sections included both surface and deep tissues of the cores. Histologic sections 4 microns in thickness were stained with hematoxylin and eosin, and with Masson's trichrome stain. Each section was graded for vascularity of the mucosal flap, extent of histiocytic infiltration around the gel, and thickness

of the fibrous capsule. In addition, each section was examined for the presence or absence of retained hydrogel, chronic inflammatory cells, acute inflammatory cells, and proper orientation of the biopsy core to permit full thickness evaluation. These data were recorded in an Excel spreadsheet for statistical evaluation.

2.6 | Statistical analysis

Mixed-model ANOVA tests were used to analyze data points obtained for each dog and for each of the surgical sites. A *P* value of 0.05 was considered statistically significant. Standard error of the mean (SEM) is shown in the graphs.

3 | RESULTS

3.1 | Hydrogel expansion and migration

Each of the sites receiving HTE tolerated the material well, allowing for creation of a clinically relevant amount of

TABLE 2 Expansion results

Insertion		1st	2nd
Hydrogel tested		“E”	“C”
Number sites tested		24	32
Eruption rate		4%	3%
Hydrogel expansion	Linear	50%	32%
	Volume	135%	107%
Mucosa gain	Linear	8.13 mm	6.44 mm

additional tissue. Figure 1A illustrates typical results of expanded oral mucosa. The capsule was incised with a sharp dissection and the expander was easily removed in entirety with no apparent attachment to the surrounding tissue, as shown in Figure 1B. A large amount of mucosa was created, as demonstrated in Figure 1C. This method was used for all second HTE insertions. Figure 1D compares an unexpanded with an expanded HTE, where at the time of insertion the expanded HTE was at the same dimension and volume as the unexpanded HTE.

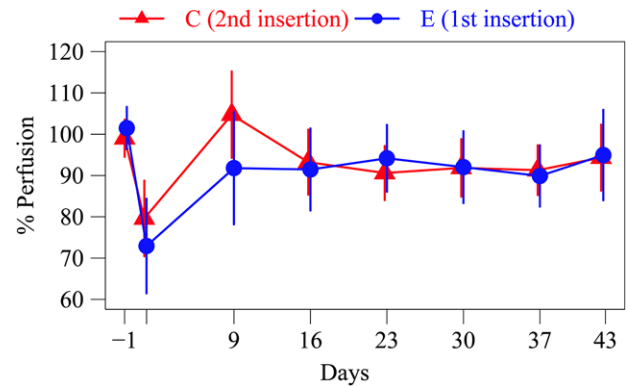
To assess the extent of HTE migration, we used the laser surface scanner to record topographic parameters relative to a constant point of reference (canine tooth). The type “E” first insertion measurements matched the type “C” second insertion measurements. No specific migratory trend was observed, that is, the HTE was not consistently drifting towards one direction over time, despite significant hydrogel expansion. Statistical analysis of the data points confirmed the null hypothesis of no hydrogel migration.

Table 2 summarizes the outcomes of the first and second insertion in respect to the physical condition of the retrieved hydrogel. During the process of first insertion, the majority of sites received the “E” HTE. Other formulae were tried early during the study, however, type “E” appeared to have optimal clinical characteristics of strength and degree of expansion without premature eruption of the mucosa by the expanding hydrogel. Only one out of 24 hydrogels was lost (accounting for 4% rate of HTE loss). For the second insertion we opted for the more slowly expanding “C” formulation. From 32 sites that received hydrogel “C,” only one was lost (accounting for a 3% rate of HTE loss).

Table 2 also summarizes the linear and volume expansion data for both insertions. HTE “E” has a higher gain of volume (135% vs. 107%) and linear expansion (50% vs 32%), and as a result produces a larger mucosal gain than type “C” (8.13 mm vs. 6.44 mm).

3.2 | Tissue perfusion in the primary and secondary insertion of HTE

Blood perfusion of oral mucosa during the first two weeks following HTE insertion, has been characterized by hypo- and subsequent hyper-perfusion, as the manipulated tissue

**FIGURE 2** Perfusion of oral mucosa during 6 weeks of expansion, comparison of first and second insertions

recovers from the incision and insertion of a foreign body. Following the initial two weeks, we observed the blood flow returning to baseline. Our previous study concentrated in depth on perfusion of expanding oral mucosa following the 2nd insertion.²² The tissue perfusion during the first HTE insertion was indistinguishable from oral mucosa perfusion following the second tissue expansion. Figure 2 compares the oral mucosa perfusion during 6 weeks of expansion for both the first and second insertions.

3.3 | Dimensional ratio of HTE during expansion

Figure 3 shows the ultrasound measured dimensional changes from the second insertion's last 3 dogs. These data indicate no trend for dimensional ratios (ratio of length/height, height/width, length/width) over 6 weeks of expansion. The symmetry of the hydrogel expansion during swelling in vivo preserved the initial shape of the HTE as it enlarged. The swelling was unisotropic, a necessary feature for a reshapable expander to maintain proper contours regardless of how it is cut.

3.4 | Tissue histology of the primary and secondary insertion of HTE

Histologic assessment of expanded oral mucosa showed a thin, uniform capsule located in the submucosal tissue above the nerves and muscle. The capsule appeared to be thin with slightly compact fibrous connective tissue and absence of histiocytic or granulomatous inflammation of the cavity lining. Inflammation was rarely found in the biopsies.

At euthanasia, no dog had palpable lymphadenopathy in the head or neck. Histology found no sign of fibrous capsule thickening or inflammatory response to micro-particles of hydrogel adjacent to the HTE in some biopsies. These acellular fragments shrunk during processing and dehydration, leaving connective tissue spaces no larger than 50 μ m. These micro-particles, apparently in the process of gradual

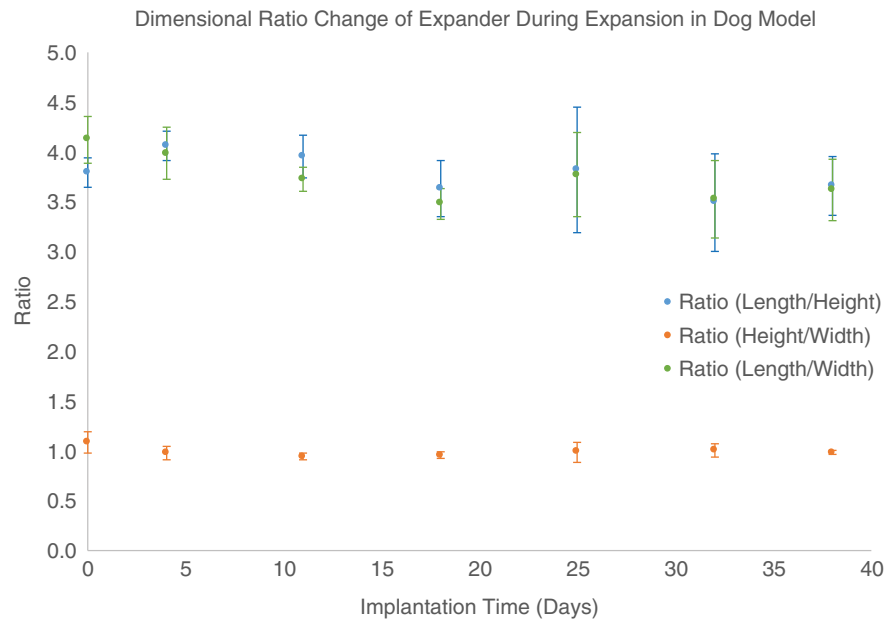


FIGURE 3 Dimensional ratio change during 6 weeks of expansion

absorption by the surrounding tissue were found in 19% of the sites (Figure 4A–D). As reported in our previous publication, no hydrogel micro-particles were found in tissues of unexpanded mucosa apart from the HTE cavity, indicating no spread of hydrogel from the site of primary insertion.²²

4 | DISCUSSION

Expansion of oral mucosa continues to be a challenging, but necessary, surgical procedure to assist with vertical ridge augmentation and other dental procedures requiring mucosal flaps. In this study, we have shown that a shapeable hydrogel tissue expander is effective for flap generation both in tissue with minimal surgical manipulation or previous trauma, as well as in tissue previously subjected to surgery.

Initial studies of HTE insertion revealed what we believe to be the optimal approach to hydrogel placement in oral mucosa. It is best to insert a self-enlarging expansion device via creation of a pouch beneath the full-thickness oral mucosa. It appeared preferable to have the convexity of the incision pointing toward the vestibule. As a result, the HTE expanded toward the vestibule instead of erupting into the mouth. Although the HTE used in this study may be shaped by trimming into almost any configuration, we limited the scope to adjusting only the length of the hydrogel cylinder at the time of insertion. The slow, continuous, symmetrical expansion of HTE used in this study, when compared to episodic bolus expansion with a silicone rubber balloon tissue expander, caused no disruption of the incision, compromise of the circulation, or pronounced fibro-inflammatory response.

Initially, an incision for HTE removal was made in the same location as the insertion incision. However, this nar-

row opening led to “crushing” and “crumbling” of some expanded hydrogels during removal. To better simulate a clinical application of the expander and to avoid possible incomplete removal of the HTE, the technique was modified. A crestal incision similar to the one used for bone grafting not only allowed retrieval of the intact hydrogel but also exposed a strong mucosal flap supported by the HTE-associated thin fibrous capsule as shown in Figure 1B.

The study was designed to closely simulate clinical situations faced in dental practice. On removal of the expanded HTE there was a 45% symmetrical gain in volume. The optimal swelling kinetics were characterized by initial 70% swelling during the first few days relative to the original volume, followed by slow 30% increase in volume over the next 4–6 weeks. The physicochemical properties of the HTE resulted in formation of a fibrous capsule thinner than the capsules typically surrounding silicone implants. The fibrous capsule in our study had no adverse impact on the surrounding tissue and showed no inclination to contract as it matured. We postulate that formation of the thin fibrous capsule, possibly within the first two weeks post insertion,²⁵ may have secured the expanding hydrogel and prevented it from migrating. The lack of migration, supported by FaroArm laser surface scanner (FaroArm, FARO Technologies, Lake Mary, FL) data, would permit precise localization of the expanded mucosa in clinical applications.

Implanting foreign material into the human body elicits an immune response. However, hydrophobic materials elicit a stronger immune response than hydrophilic materials.²⁶ Hydrophilic PEG-based hydrogels were previously found to encourage early-stage inflammation/healing but have very limited foreign-body reaction or chronic inflammation.²⁷ The hydrophilic PEG polymers are known to prohibit protein

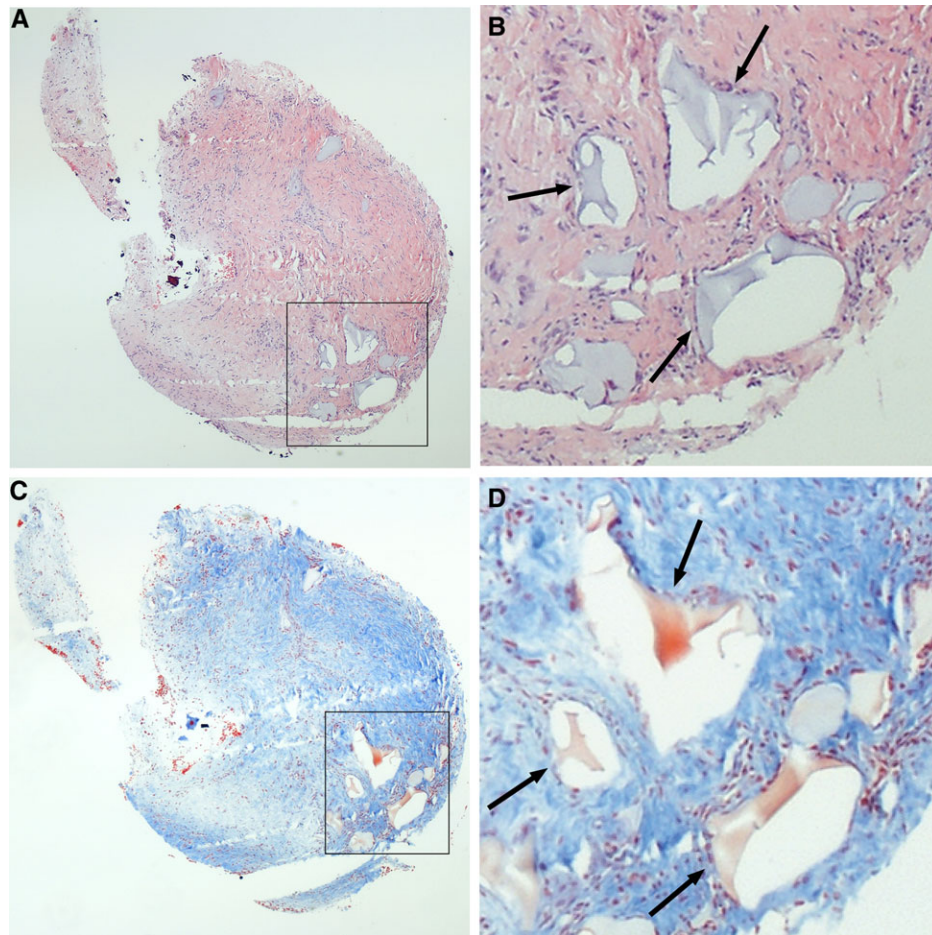


FIGURE 4 Histology of possible particles of HTE in the fibrous capsule. All particles identified were less than 50 μm in length. **A**, Overview of specimen. Square is area enlarged in panel B. H&E stain. **B**, Possible particles of hydrogel shown with black arrows. H&E stain. **C**, Overview of specimen. Masson's Trichrome stain. **D**, Possible particles of hydrogel with black arrows. Trichrome stain

attachment and activation, thereby reducing clotting²⁸ and immune response.²⁹ This protein non-attachment property is more pronounced with copolymers such as poloxamers³⁰ and PEG-PLGA.³¹ Similarly PEG-fumarate biodegradable hydrogels have a mild foreign-body reaction, and form a thin fibrous capsule with minimal inflammation. It has been suggested that this fibrous capsule reduces access of the hydrogel breakdown products to the rest of the tissue.³² As long as the fibrous capsule is intact, hydrogel migration will be minimal, as discovered in our study. Further, symmetrical expansion of HTE should invite applications of this expansion method in clinical circumstances where an unusual shape or configuration of the flap is required.

Inadequate tissue perfusion is an important cause for hydrogel eruption that may be as significant as the type of incision and HTE placement. Expansion that is too rapid results in ischemia, followed by necrosis of the expanding oral mucosa. Oral mucosa with a history of previous surgeries or injury, poses significant challenges for expansion because of irreversible changes in the tissue affecting its elasticity. Although oral mucosa forms less scar than skin, the healing process does

show histologic fibrosis.^{5,6} Oral mucosa split-thickness flaps with fenestration result in scars lasting at least 140 days, even when there is no exposure of the alveolar bone.³³ An immunohistochemical assessment of human oral mucosa comparing smokers and non-smokers found the same vascular density in both, but smaller and less abundant larger blood vessels nourished the mucosa of smokers.³⁴ Smoking status of the patient, age, and any history of previous surgery affects the quality and elasticity of oral mucosa. Changes in mucosal physiologic properties pose an additional challenge for hydrophilic saltatory balloon type expanders. We have previously described in more detail successful outcomes of oral tissue expansion following secondary HTE insertion.²² Assessment of tissue perfusion following the insertion of both type "E" and type "C" HTE revealed no significant difference between them, despite different characteristics of volume and rate of expansion, and prior tissue manipulation for each of the devices.

A critical histologic assessment of the oral mucosa revealed possible "shedding" of micro-hydrogel particles, which would result in residual hydrogel fragments in the fibrous capsule. This process has also been shown to occur



with silicone.³⁵ The micro-particles of hydrogel underwent shrinkage during processing and dehydration. Nevertheless, the original size *in vivo* could be seen by microscopic cavities in the fibrous capsule, which were usually less than 50 μm in the maximum dimension. No histologic inflammatory reaction was seen near these lacunae. Neither lacunae, nor the dehydrated hydrogel particles in them, were found in control histology specimens of oral mucosa taken from unexpanded tissue. The control biopsies were near, but not in contact with the HTE, indicating that hydrogel micro-particles do not migrate.²² Such “shed” hydrogel particles are more prevalent and larger in rodents, indicating that species differences as well as the more rapidly expanding formulations used in the rat study may be a factor in this phenomenon.²⁴

Throughout the current study with dogs, all the hydrogel expanders removed through crestal incisions were intact and easily removed with no apparent attachment to the consistently thin, uniform fibrous capsule. The final metabolites of HTE (by cleavage of all alky-ester bonds) are lactic acid, glycolic acid, PEG (~700–1000 Da), ethylene glycol, and poly(acrylic acid). Lactic acid enters the tricarboxylic acid cycle and is metabolized to carbon dioxide. Glycolic acid is either excreted unchanged in the kidney or it enters the tricarboxylic acid cycle.³⁶ Ethylene glycol (very small quantity) is metabolized to glycolic acid. PEG in HTE is well below the molecular weight threshold of urinary clearance.³⁷ The excretion of poly(acrylic acid) is slow, through the liver and spleen, but has been reported to be well tolerated in doses above those encountered in practical HTE applications.³⁸ Time to absolute degradation may be extensive, but in the absence of biocompatibility issues, as shown in this study, excretion may not represent a clinical problem. The hydrogel in HTE not only can be reshaped by the surgeon, but also appears to have fewer biocompatibility and pharmacologic concerns than silicone surfaces used with other tissue expanders.³⁹

4.1 | Summary

The thin, uniform fibrous capsule found in our study, when compared with other implants such as silicone rubber, appears to result from expansile pressure and continuous swelling of the hydrogel, without toxic or inflammatory influences. The HTE fibrous capsule did not become thicker or denser over time, as often found with silicone rubber implants. A thickened capsule may limit expansion of mucosa and affect the formation of new tissue. Based on this observation, we used an HTE with modified swelling kinetics showing delayed and slowed expansion for the second implant because of anticipated stiffness of the previously surgically manipulated tissues.

Tissue expanders increase available tissue in a region due to the biological processes of tissue “creep” (or “biological

stretch”) that allow epithelia to increase in surface area under a constant pressure due to viscoelastic forces. However, the body reacts to different expander devices in a variety of ways, including foreign-body reaction, temporary hyperpigmentation, and neo-vascularization. Nevertheless, regardless of the device, with appropriate expansion force and timing, there is generation of new, fully vascular tissue.⁴⁰

Oral mucosa is more delicate and difficult to expand than skin. In our experience, excessively rapid expansion of hydrogels erupted through the mucosa and were removed or lost. The process involved steps of ischemia, necrosis, and finally eruption and loss of the device. This occurred both with early HTE prototypes and with another, commercially obtained hydrogel tissue expander (Osmed, Ilmenau, Germany). Understanding the relationship between hydrogel properties, tissue biomechanical properties and surgical technique are critical for obtaining excellent *in vivo* results. The hydrogel formula and surgical design described here have been used successfully with uneventful and successful healing for gingival mucosa expansion in dogs.

5 | CONCLUSION

We present a comparison of oral mucosa expansion during the first and second insertion at the same sites, using HTE tissue expanders with 2 different specifications in the rate and force of expansion. Tissue perfusion was well preserved, the device did not migrate within tissue, there was no apparent toxicity or bio-incompatibility, and the result was adequate additional tissue surface area suitable for ridge augmentation. The accrued tissue would be suitable to cover a bone graft during ridge augmentation without split-thickness flaps. We report a shapeable, self-contained hydrogel tissue expander with a success rate of about 96% for first insertion and near 97% for re-operative second insertions at the same sites.

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AUTHOR CONTRIBUTIONS

JG and KP manufactured the hydrogel, performed analysis, assisted in data collection, and participated in planning of the experiments. DDD conducted histological staining and



design of histological criteria. DB conducted collection of data, data analysis, interpretation of findings, and manuscript writing. GJE performed statistical analysis. SST participated in manuscript writing. CTB performed surgery, conducted collection of data, data analysis, interpretation of findings, planning of the experiments, and manuscript writing.

CONFLICTS OF INTEREST

DB, DDD, GJE, and SST report no conflicts of interest. JG is General Manager and KP is President of Akina, Inc., the institution developing the Restiex® expander. JG, KP, and CTB are listed on a patent application for the hydrogel tissue expander studied.

DISCLAIMERS

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health, the U.S. Department of Veterans Affairs, or the United States Government.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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