Design of customized soft tissue substitutes for anterior single-tooth and posterior double-tooth defects: An in vitro study

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Yue Sun Dr. dent med, PhD1,2 | Malin Strasding Dr. med dent2 | Xinran Liu S.M.D2,3,4 | Birgit Schäfer Dr. med5 | Feng Liu Dr. med dent3,4 | Irena Sailer Dr. med dent2 | Dobrila Nesic PhD2

1Division of Orthodontics, Beijing Stomatological Hospital, Capital Medical University, Beijing, China  
2Division of Fixed Prosthodontics and Biomaterials, University Clinic of Dental Medicine, University of Geneva, Geneva, Switzerland  
3Peking University Hospital of Stomatology First Clinical Division, Beijing, China  
4National Engineering Laboratory for Digital and Material Technology of Stomatology, Beijing Key Laboratory of Digital Stomatology, Beijing, China  
5Geistlich Pharma AG, Wolhusen, Switzerland

Abstract
Objective: This study aims to validate the standardized procedure for designing soft tissue substitutes (STS) adapted to optimally fit single-tooth defects in the anterior jaws and double-tooth defects in the posterior jaw and to compare mathematically modeled average shapes.

Materials and Methods: Casts from 35 patients with 17 single-tooth defects in anterior region and 21 double-tooth defects in posterior region were scanned. STS were designed and sectioned in 3D slices meshes. Thickness values were documented respecting mesial-distal and buccal-lingual orientations. Graphs were embedded into images, and hierarchical clustering was applied to group STS according to shape and thickness.

Results: STS clustered into two groups per defect type. For anterior single defects, STS (n = 4) were either a small and thin oval: 7 mm buccal-lingual, 4–5 mm mesial-distal direction and 1.1–1.5 mm thick or a larger oval (n = 13): 9 mm buccal-lingual, 5–7 mm mesial-distal and 1.6 m thick. For posterior double tooth defects, STS (n = 10) were either narrow, long and thick: 6–7 mm buccal-lingual, 16–20 mm mesial-distal and 2.2 thick or a wide, thinner rectangle (n = 11): 9–11 mm buccal-lingual, 12–14 mm mesial-distal and 1.1–1.5 mm thick.

Conclusions: The study validated the standardized digital method to design grafts for soft tissue volume augmentation and identified four average shapes for anterior single-tooth and posterior double-tooth soft tissue defects.

Clinical Significance: We developed and validated a standardized digital method to design an optimal geometrical shape of a soft tissue substitute for oral volume augmentation and combined it with mathematical modeling to identify average shapes for single-interior, and double-posterior tooth defects. The identified average shapes...
Prior to the placement of implant or tooth-borne restorations, 

offer the possibility to produce better-fitted xenografts or synthetic STS blocks requiring minimal chair-side adaptation leading to reduced clinical time and patient discomfort and potentially improving soft tissue volume augmentation outcomes.

**KEYWORDS**

biomaterial, CAD, gingiva, graft substitutes, personalized medicine, soft tissue augmentation

## 1 | INTRODUCTION

Tooth loss, periodontal or systemic disease, trauma, or congenital disorders may cause various oral soft tissue volume defects and necessitate treatment to maintain functional mastication, speech, and esthetics. Remodeling and resorption of alveolar bone and soft tissue upon tooth extraction still represent a significant problem in restorative dentistry. Prior to the placement of implant or tooth-borne restorations, soft tissue augmentation procedures are often required to improve final treatment outcomes. An increase of soft tissue contours is indicated to stabilize and maintain peri-implant tissue health and improve functional and esthetic results, particularly in the case of a thin gingiva biotype. 

Subepithelial connective tissue graft (CTG) remains the gold standard for soft tissue volume augmentation. Although successful soft tissue regeneration can be achieved with autologous CTG transplantation, several disadvantages still hinder this type of treatment. Infection of the second wound, a limited amount of tissue that can be harvested, and prolonged pain have prompted the quest for alternatives. Soft tissue substitute (STS) requirements for oral soft tissue augmentation comprise biocompatibility, volume and mechanical stability, biodegradability and tissue integration, secure handling, and low cost without compromised efficacy. Different allogenic, xenogenic, and synthetic STS have been developed and produced to date and several have found their application in periodontal and peri-implant soft tissue regeneration. While off-shelf soft tissue substitutes allow unlimited availability, reduce patient morbidity, and shorten intervention time, their clinical use remains limited. The primary issue remains the need for individual STS customization. STS are delivered as rectangular blocks of standardized dimensions and need to be tailored chair-side to fit each soft tissue defect. With the precision of trimming depending on the surgeon, the accuracy of the final shape remains suboptimal. Necessary STS preparation time results in the prolonged exposure of the defect site, thereby increasing the risk of infection, potentially compromising wound healing, and jeopardizing the final outcome. Hence, future STS should be produced in shapes that would better fit individual edentulous defects and be ready for immediate insertion or require minimal chair-side shape customization. The fabrication of STS based on the average shape of single-tooth or double-tooth defects would provide surgeons with an easier STS handling from preparation to subsequent insertion and suturing. 

In our previous study, a standardized digital method was developed to design an optimal geometrical shape of STS for volume augmentation of the single-tooth posterior soft tissue defects and combined with mathematical modeling to identify average shapes. To further validate this method, the current study aims to apply the same approach to design STS for single-tooth defects in the anterior and double-tooth defects in the posterior region and maxilla and to identify the average STS shapes.

## 2 | MATERIALS AND METHODS

### 2.1 | Defect scans

Conventional stone casts from 35 patients were collected: 17 scans of a single-tooth defect in the anterior region and 21 scans of double-tooth defects in the posterior region. The inclusion criterion was tooth extraction at least 6 months prior to taking the impressions and the presence of neighboring teeth. The exclusion criteria comprised patients suffering from osteoporosis, uncontrolled periodontitis, and uncontrolled diabetes. Ethical approval was not required for this in vitro study. The 35 casts with 37 defect sites were scanned with a laboratory CAD/CAM scanner following a standardized technical approach and software settings (Imetric4D; Courgenay; Switzerland), and STL files were generated (Figure 1A).

### 2.2 | Soft tissue substitute design

Design of an STS for the volume augmentation of single-tooth defects in the anterior region and double-tooth defects in the posterior region followed the previously established steps for single-tooth posterior defects. Briefly, the STL file generated from the scanned cast was imported into the software 3Shape dental designer (Version19, 3Shape; Copenhagen; Denmark). The outline of the STS was designed based on the incision line (Figure 1B). The shape and the thickness of each STS were adapted to optimally fit the defect and in accordance with the desired final clinical outcome. Subsequently, the STL file of each STS (Figure 1C) was imported into GOM inspect (GOM; Braunschweig; Germany) for further analysis.

### 2.3 | Soft tissue substitute thickness measurements and clustering

GOM inspect was used to measure the thickness across each designed STS as described in our previous study. Briefly, the occlusal plane was defined based on the mesial-incisal point of the central incisors (or lateral incisor in case the central incisors are missing) and
the palatal (for maxilla) or buccal (for mandible) cusps of the second premolar in each quadrant. A mesial-distal plane was then drawn through the centers of the adjacent teeth and perpendicular to the occlusal plane, and a buccal-lingual plane was drawn perpendicularly to the occlusal plane and mesial-distal plane (Figure 2A).

The point zero (0,0,0) was defined at the cross of the outer surface of the STS, the mesial-distal plane and buccal-lingual plane. A lingual point was chosen at the cross of the buccal-lingual plane and the buccal margin of the STS, and the same approach was applied to define the buccal point. The top inner point was defined as a point at the cross-curve of the inner surface and buccal-lingual plane, most distant relative to the line connecting the lingual and buccal points. The connection of buccal, lingual and inner top points thus generated a reference circle. Radial sections at a 1 mm distance started from point zero and their number depended on the circumference of the circle (Figure 2B). To measure thickness in the mesial-distal direction, parallel sections were made from point (0,0,0) in the mesial—distal direction at 1 mm distance in the anterior single-tooth defect group and at 2 mm distance in the posterior double-tooth defect group (Figure 2C). Each STS thus resulted in a 3D mesh of slices where \( x = 1 \) mm, \( y = 1 \) or 2 mm and \( z = \) thickness. Thickness values of each STS were documented in an excel chart with a coordinate system where the \( X \)-axis represented the buccal-lingual direction and the \( Y \)-axis the mesial-distal direction (Figure 2D). A scatter/bubble graph was generated for each STS, with the distribution of circles outlining the shape and dimension, and the circle diameter depicting the thickness of each 3D slice (Figure 2E). Scatter graphs were imported as images that were embedded with image embedder VGG-16 (Visual Geometry Group, University of Oxford) to allow image comparison. The complete-linkage hierarchical clustering analysis of STS images was performed to evaluate the similarity of shapes using Orange software (Version 3.24.1, Orange data mining toolbox in Python, Bioinformatics Lab, University of Ljubljana).

### 2.4 | Statistical analysis

Data were analyzed using the IBM SPSS Statistics 26.0 (IBM, New York, USA). To determine data distribution, the thickness values of all 3D slices for each STS were analyzed with the Shapiro–Wilk test. Across each STS, median values and 25% and 75% quartiles of the individual slice thickness were calculated from the excel charts for each shape group and expressed according to the STS orientation.

### 3 | RESULTS

Based on the defect region, 17 grafts were designed to fit into the anterior single-tooth defects and 21 designs into posterior double-tooth defects. A set of objective landmarks and standardized steps, established in our previous study, were applied during the design and analysis processes.

In the anterior single-tooth group, 14 defects were in the maxilla and three in the mandible. The hierarchical clustering analysis of
FIGURE 2  Standardized procedure to measure soft tissue substitute (STS) thickness. To section the STS into 3D slices where \( x = 1 \) mm, \( y = 1 \) mm and \( z = \) thickness, three planes were defined in GOM Inspect: occlusal, mesial-distal and buccal-lingual plane (A). The circle was drawn to fit the inner side of the STS (B) and the radial sections were obtained at 1 mm distance (C). Parallel slicing in mesial-distal and buccal-lingual directions allowed partitioning of the entire STS into a mesh (D). In the mesial-distal direction, parallel sections were made from point (0,0,0) at 1 mm distance in the anterior single-tooth defect group and at 2 mm distance in the posterior double-tooth defect group.

FIGURE 3  Scatter graph outlining the shape, median (50%), Q1 (25%) and Q3 (75%) values depicting thickness across graphs for anterior single-tooth group 1, \( n = 4 \) (A) and group 2, \( n = 13 \) (B). The intensity of red color corresponds to the thickness ranging from 0.001 mm (lightest shade) to 2.2 mm (darkest shade).
scatter graph images separated the STS shapes into two groups of 4 and 13. All designed STS had the highest thickness on the buccal side. The analysis of the median STS shape for group 1 \( (n = 4; 2 \text{ in mandible and two in maxilla}) \) revealed an oval shape, with a length of 7 mm in buccal-lingual and 5 mm in mesial-distal direction (Figure 3A). The four thickest points resided in the center of the STS and ranged from 1.06 to 1.46 mm. The thickness gradually decreased from the center toward the edges until 0.005 mm. The highest 25% and 75% values in the center were 1.07 mm (1 point) and 1.52–1.86 mm (4 points), respectively. The median shape of group 2 \( (n = 13, 1 \text{ in mandible, 12 in maxilla}) \) was also an oval, yet larger in both directions and thicker compared to group 1. The maximum length was 9 mm in a buccal-lingual and 7 mm in a mesial-distal direction (Figure 3B). The three thickest points of around 1.6 mm resided in the center of the STS and then gradually decreased toward the edges. The thickness gradually decreased toward the edges until 0.04 mm. The highest 25% and 75% values in the center were 1–1.3 mm (11 points) and 2.0–2.2 mm (3 points), respectively.

In the posterior double-tooth group, 8 defects were in the maxilla and 13 in the mandible. The hierarchical clustering analysis of scatter graph images separated the STS shapes into two groups of 10 and 11. All designed STS had the highest thickness on the buccal side. The median shape of group 1 \( (n = 10, \text{ all in maxilla}) \) was a long and narrow rectangle of 7 mm in the buccal-lingual...
direction and extending to 20 mm in the mesial-distal direction (Figure 4A). The six median STS highest thickness points were around 2.15 mm in the center and then gradually decreased to the edges until 0.02 mm. The highest 25% and 75% quartile values in the center were 1.57–1.80 mm (8 points) and 2.02–2.15 mm (8 points), respectively. The median shape of group 2 ($n = 11$; 3 in mandible and 8 in maxilla) was a thin and wide square, with 11 mm in buccal-lingual direction and 14 mm in mesial distal direction (Figure 5B). The median STS thickest points (21) ranged from 1.05–1.45 mm gradually decreasing toward the edges until 0.05 mm. The highest 25% and 75% values in the center were 1.02–1.29 mm (13 points) and 1.52–1.73 mm (6 points), respectively.

4 | DISCUSSION

A consensus on the best treatment modality for soft tissue volume augmentation with satisfactory long-term outcomes has not been reached. In the era of personalized medicine, soft tissue volume augmentation procedure still relies on tedious and inaccurate hand-shaping of subepithelial CTG or a xenogeneic matrix block. In our previous proof-of-concept study, a standardized procedure to digitally design individual STS and a mathematical modeling tool to obtain average STS adapted to optimally fit single-tooth soft tissue defects in the posterior jaw were developed. In this study, the approach was validated by designing individual STS for single-tooth anterior and double-tooth posterior defects necessitating soft tissue volume augmentation. Based on the clustering of individual design images, the average shapes obtained for each defect type identified two distinct STS geometries in each group.

Restoration of partially or fully edentulous areas often requires bone and soft tissue augmentation. The stability of bone level has been correlated with the sufficient amount of soft tissue around implants, and an influence on the final esthetic outcomes was demonstrated. An ideally restored soft tissue should consist of a harmonious gingival margin, adequate papillae and follow a convex contour of the alveolar bone. The optimal fit and rigid immobilization of any STS are essential for the initial oxygenation and nutrient supply through plasmatic diffusion until vascularization ensues. Due to disadvantages the application of CTG presents, different allograft and xenograft substitutes have been developed and used in clinics, including collagen xenograft (porcine) matrices (Mucograft, Geistlich; Mucoderm, botiss biomaterials), collagen allograft matrix (AlloDerm, BioHorizon), and reconstituted collagen matrix (Fibro-Gide, Geistlich). Comparative reviews identified similar outcomes between AlloDerm or Fibro-Gide and CTG yet the better performance of CTG compared to Mucograft. Recent studies demonstrated similar buccal mucosal thickness between Fibro-Gide and subepithelial CTG after 3 and 5 years as well as between Mucoderm and subepithelial CTG after 6 months. Another recent study however reported inferior increase in the soft tissue profile in Fibro-Gide compared to subepithelial CTG after 1 year. Despite promising performance of different STS, the circumvention of the second wound site, decreased surgical time, risk of infections and patient morbidity, these prefabricated STS blocks require time-consuming manual shape adaptation without possibility for standardization. Therefore, the production of individualized optimally fitting STS and/or—at the least—blocks corresponding to average defect shapes requiring minimal on-site customization and material waste would bring considerable clinical benefits.

A standardized approach to design individual STS and to mathe-matically define average shapes for the posterior mandible and maxilla defects has been developed. Three different STS shapes have been identified, corresponding to the single-tooth defects in the posterior region. In the current study, to validate the approach, the procedure was applied to design STS for the defects resulting from single-tooth loss in the anterior region and double-tooth loss in the posterior region. All designs were made respecting the irregular defect shape, with the inner surface perfectly filling the lost volume and the outer surface corresponding to the desired ridge contour. Hierarchical clustering of the embedded individual STS images revealed two different shapes in each group. The anterior single-tooth defects in group 1 were an equal mixture of mandible and maxilla, while maxilla defect predominated in group 2 (92%). The posterior double-tooth defects in group 1 comprised solely mandibular defects while maxilla defects (73%) predominated in group 2. Thus, the application of image clustering demonstrated an efficient separation of shapes corresponding to the defect mainly in one jaw, that is, in accordance with their particular anatomical characteristics.

Similar to the single-tooth posterior defects and regardless of the size or position of the defects, the required main volume augmentation was always on the buccal side, in line with the more pronounced loss of the buccal tissues after tooth removal. The thickest points corresponded to the standard thickness of subepithelial CTG (1–3 mm) but not to the thick volume-stable yet highly porous substitute collagen block (6–8 mm). Comparison of these shapes and their thicknesses with those identified for single-tooth posterior STS revealed four main average shape types (Figure 5): a small and thin STS (anterior single-tooth defect, group 1), large STS with the thickness of 1.5–1.9 mm (anterior single-tooth defect, group 2, and all posterior single-tooth defects), narrow and thick rectangle up to 2.2 mm (posterior single-tooth defects group 1), very large yet thinner rectangle of 1.1–1.5 mm (posterior single-tooth defects group 1). These data suggest that for the majority of single-tooth defects, one large STS could be produced and if necessary, minimally shaped to achieve most tissue volume augmentation on the buccal side where the major loss occurred.

The main limitation of the study is a limited number of samples. A larger number of STS for all types of defects should be analyzed to further validate the approach and to achieve a more reliable normalized data distribution. With the establishment of an entirely digital workflow, our method could be easily combined with intraoral scanning and further accelerate soft tissue volume augmentation procedures. Additionally, for defects comprising alveolar bone and soft tissue, CBCT and intraoral scans could be combined, leading to a personalized augmentation of both hard and soft tissue volumes. Finally, the identified average shapes may lead to the production of better-
fitted xenograft or synthetic STS blocks requiring minimal chair-side adaptation to reduce clinical time and patient discomfort and potentially improve soft tissue volume augmentation outcomes. The currently ongoing laboratory study on animal jaws will test the easiness and the time needed for STS application and pave the way for a clinical trial.

5 | CONCLUSIONS

This study validated the standardized digital method to design the geometrical shape of STS to augment volume in anterior single-tooth and posterior double-tooth soft tissue defects. The STS design procedure together with mathematical modeling and the clustering algorithm is robust and reliable to be applied to different types of defects with the clustering results accurately differentiating the defect shapes.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Yue Sun https://orcid.org/0000-0001-8452-5944
Malin Strasding https://orcid.org/0000-0003-1679-6202
Irena Sailer https://orcid.org/0000-0002-4537-7624
Dobrila Nesic https://orcid.org/0000-0003-1609-9255

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