Clinical Trial of the Efficacy of Pinhole Surgical Technique Compared to Connective Tissue Graft in Treatment of Gingival Recession

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Complete Research Protocol (HRP-503)

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Template Instructions

Sections that do not apply:

- *In several sections, the addition of checkboxes for **Not Applicable** have been added to the template as responses.*
    - *If an N/A checkbox is present, select the appropriate justification from the list.*
    - *If an N/A checkbox is not present, or if none of the existing checkboxes apply to your study, you must write in your own justification.*
- *In addition:*
    - *For research where the only study procedures are records/chart review: Sections 19, 20, 22, 23, 24, 25, 31, and 32 do not apply.*
    - *For exempt research: Sections 31 and 32 do not apply.*

Studies with multiple participant groups:

- *If this study involves multiple participant groups (e.g. parents and children), provide information in applicable sections for each participant group. Clearly label responses when they differ. For example:*

Response:

Intervention Group:

Control Group:

Formatting:

- *Do not remove template instructions or section headings when they do not apply to your study.*

If you are pasting information from other documents using the "Merge Formatting" Paste option will maintain the formatting of the response boxes.

Amendments:

- *When making modifications or revisions to this and other documents, use the **Track Changes** function in Microsoft Word.*
- *Update the version date or number **on Page 3.***

PROTOCOL TITLE:

Include the full protocol title.

Response: Clinical Trial of the Efficacy of Pinhole Surgical Technique Compared to Connective Tissue Graft in Treatment of Gingival Recession

PRINCIPAL INVESTIGATOR:

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VERSION:

Include the version date or number.

Response: 1/2/2020

GRANT APPLICABILITY:

Indicate whether this protocol is funded by a grant (e.g. NIH, foundation grant). For a grant with multiple aims, indicate which aims are covered by this research proposal.

NOTE: This question does not apply to studies funded by a sponsor contract.

Include a copy of the grant proposal with your submission.

Response: Geistlich Pharma AG, will provide the funding.

RESEARCH REPOSITORY:

Indicate where the research files will be kept, including when the study has been closed. The repository should include, at minimum, copies of IRB correspondence (approval, determination letters) as well as signed consent documents. This documentation should be maintained for 3 years after the study has been closed.

Response:

Location: A locked cabinet at Dr. Othman Shibly's Office with him only and his research assistant who have access to the office or the cabinet.

Address: 3435 Main Street, 250 Squire Hall, Buffalo, NY 14214

Department: Department of Periodontics and Endodontics

1.0 Objectives

1.1 Describe the purpose, specific aims, or objectives of this research.

Response: To compare the efficacy of root coverage achieved by the Pinhole Surgical Technique (PST) technique and the Connective Tissue Graft (CTG) technique in the treatment of Miller class I and II gingival recession defects.

1.2 State the hypotheses to be tested, if applicable.

NOTE: A hypothesis is a specific, testable prediction about what you expect to happen in your study that corresponds with your above listed objectives.

Response: Pinhole Surgical Technique outcomes are not inferior to those of the Connective Tissue Graft surgical technique.

2.0 Scientific Endpoints

2.1 Describe the scientific endpoint(s), the main result or occurrence under study.

NOTE: Scientific endpoints are outcomes defined before the study begins to determine whether the objectives of the study have been met and to draw conclusions from the data. Include primary and secondary endpoints. Some example endpoints are: reduction of symptoms, improvement in quality of life, or survival. Your response should ***not*** *be a date.*

Response:

Primary endpoints: 1) Complete root coverage determined by recession classification, percentage root coverage, and recession depth, 2) Pain Index, 3) Healing Index.

Secondary Endpoints: Improved periodontal parameters; clinical attachment level, probing depth, width of keratinized tissue, gingival thickness, and gingival index.

3.0 Background

3.1 Provide the scientific or scholarly background, rationale, and significance of the research based on the existing literature and how it will contribute to existing knowledge. Describe any gaps in current knowledge. Include relevant preliminary findings or prior research by the investigator.

Response:

Gingival recession is defined as the apical migration of the marginal gingiva and it leads to root surface exposure. It may be localized to a few sites or generalized to several teeth, and the severity may vary within the same person and between different people. A commonly used classification of gingival recession is based on the apical relation of the recession to the mucogingival junction and the level of interproximal bone and gingiva [1].

Data from the third National Health and Nutrition Examination Survey (NHANES III) conducted between 1988 and 1994 show that approximately 24 million U.S. adults had one or more tooth surfaces with ≥3 mm of gingival recession [2]. With an aging population, the number of recession cases in the U.S. is certain to soar. Several etiological factors may cause gingival recessions, including traumatic tooth brushing, malposition teeth, periodontal disease, frenum and bridle insertions, subgingival restorations, maladapted crowns, extraction of adjacent teeth, orthodontic movement, iatrogenic factors, and bone dehiscence [3].

A variety of surgical techniques have been recommended to attain root coverage, including connective tissue graft [4, 5], free gingival graft (FGG) [6, 7], pedicle flaps [8, 9], double papilla grafts [10, 11], coronally positioned flaps [12-15], coronal positioning of previously placed FGG [16], guided tissue regeneration (GTR)[17], and the use of acellular dermal matrix (ADM)[18], or enamel matrix derivatives [19]. A recently developed technique used to attain root coverage is the Pinhole Surgical Technique (PST) described by Chao [20]. This novel approach involves the separation of the gingiva and periosteum from the underlying bone with instruments inserted through a pinhole created in the vestibular area of the involved tooth while filling underneath the undermined interproximal papilla with strips of a bioresorbable membrane, rather than transferring gingival tissue from the palate to the area of recession [20]. The advantage of this technique is the preservation of the gingival tissues and its blood supply, while freeing the flap from its apical attachment for ease of coronal displacement and adequate root coverage. In addition, the lack of a secondary surgical site may eliminate the accompanying pain and discomfort often reported in root coverage procedures.

The connective tissue graft technique was described by Langer and Langer in 1985, in which the patient's own connective tissue is taken mostly from the palate and used to cover the area of recession [5]. The retro-molar pad area (tuberosity) has also been used because of the thickening of the sub-mucosa in that area. This graft material is carefully sutured into place and a coronally advanced flap placed and sutured over it, while part of the graft can be left exposed. Currently the connective tissue graft (CTG) is the most common and predictable treatment for gingival recession, and is considered the gold standard [21]. Key advantages of the connective tissue graft procedure are the availability of two sources of blood supply to the graft: one from the recipient bed, and the other from the overlying flap, the perfect chromatic integration, an optimal esthetic outcome, and excellent color match. In addition, an increase in the thickness of the gingival tissues and the width of keratinized gingiva has been documented with the ability for creeping attachment which is not possible with the use of bioresorbable collagen membranes [18, 22].

3.2 Include complete citations or references.

Response:

1. Miller PD, Jr. A classification of marginal tissue recession. The International journal of periodontics & restorative dentistry 1985;5:8-13.
2. Albandar JM, Kingman A. Gingival recession, gingival bleeding, and dental calculus in adults 30 years of age and older in the United States, 1988-1994. Journal of periodontology 1999;70:30-43.
3. Greenwell H, Fiorellini J, Giannobile W, et al. Oral reconstructive and corrective considerations in periodontal therapy. Journal of periodontology 2005;76:1588-1600.
4. Langer L, Langer B. The subepithelial connective tissue graft for treatment of gingival recession. Dental clinics of North America 1993;37:243-264.
5. Langer B, Langer L. Subepithelial connective tissue graft technique for root coverage. Journal of periodontology 1985;56:715-720.
6. Miller PD, Jr. Root coverage using a free soft tissue autograft following citric acid application. Part 1: Technique. The International journal of periodontics & restorative dentistry 1982;2:65-70.
7. Holbrook T, Ochsenbein C. Complete coverage of the denuded root surface with a one-stage gingival graft. The International journal of periodontics & restorative dentistry 1983;3:8-27.
8. Grupe HE, Warren RF. Repair of Gingival Defects by a Sliding Flap Operation. Journal of periodontology 1956;27:92-95.
9. Pfeifer JS, Heller R. Histologic evaluation of full and partial thickness lateral repositioned flaps: a pilot study. Journal of periodontology 1971;42:331-333.

10. Cohen DW, Ross SE. The double papillae repositioned flap in periodontal therapy. Journal of periodontology 1968;39:65-70.
11. Ross SE, Crosetti HW, Gargiulo A, Cohen DW. The double papillae repositioned flap--an alternative. I. Fourteen years in retrospect. The International journal of periodontics & restorative dentistry 1986;6:46-59.
12. Bernimoulin JP, Luscher B, Muhlemann HR. Coronally repositioned periodontal flap. Clinical evaluation after one year. Journal of clinical periodontology 1975;2:1-13.
13. Allen EP, Miller PD, Jr. Coronal positioning of existing gingiva: short term results in the treatment of shallow marginal tissue recession. Journal of periodontology 1989;60:316-319.
14. Sorrentino JM, Tarnow DP. The semilunar coronally repositioned flap combined with a frenectomy to obtain root coverage over the maxillary central incisors. Journal of periodontology 2009;80:1013-1017.
15. Tarnow DP. Semilunar coronally repositioned flap. Journal of clinical periodontology 1986;13:182-185.
16. Maynard JG, Jr. Coronal positioning of a previously placed autogenous gingival graft. Journal of periodontology 1977;48:151-155.
17. Al-Hamdan K, Eber R, Sarment D, Kowalski C, Wang HL. Guided tissue regeneration-based root coverage: meta-analysis. Journal of periodontology 2003;74:1520-1533.
18. Harris RJ. A comparative study of root coverage obtained with an acellular dermal matrix versus a connective tissue graft: results of 107 recession defects in 50 consecutively treated patients. The International journal of periodontics & restorative dentistry 2000;20:51-59.
19. Chambrone L, Tatakis DN. Periodontal soft tissue root coverage procedures: a systematic review from the AAP Regeneration Workshop. Journal of periodontology 2015;86:S8-51.
20. Chao JC. A novel approach to root coverage: the pinhole surgical technique. The International journal of periodontics & restorative dentistry 2012;32:521-531.
21. Chambrone L, Chambrone D, Pustiglioni FE, Chambrone LA, Lima LA. Can subepithelial connective tissue grafts be considered the gold standard procedure in the treatment of Miller Class I and II recession-type defects? Journal of dentistry 2008;36:659-671.
22. Henderson RD, Greenwell H, Drisko C, et al. Predictable multiple site root coverage using an acellular dermal matrix allograft. Journal of periodontology 2001;72:571-582.

4.0 Study Design

4.1 Describe and explain the study design (e.g. case-control, cross-sectional, ethnographic, experimental, interventional, longitudinal, observational).

Response: Randomized, split-mouth, double blinded design clinical trial.

5.0 Local Number of Subjects

5.1 Indicate the total number of subjects that will be enrolled or records that will be reviewed locally.

Response:

52 subjects

5.2 If applicable, indicate how many subjects you expect to screen to reach your target sample (i.e. your screen failure rate).

Response:

100 subjects

5.3 Justify the feasibility of recruiting the proposed number of eligible subjects within the anticipated recruitment period. For example, how many potential subjects do you have access to? What percentage of those potential subjects do you need to recruit?

Response:

The school of dental medicine at SUNY at Buffalo is a large center with a tremendous number of patients that get dental care every year, recruiting will be solely from the patients of the school through flyers near every entrance, exit, stairs, and elevator.

6.0 Inclusion and Exclusion Criteria

*6.1 Describe the criteria that define who will be **included** in your final study sample.*

NOTE: This may be done in bullet point fashion.

Response:

1- The patients should be above 18 years old.

2- The presence of Miller's class I or II gingival recession on at least two matching bilateral or contralateral gingival recession defects (≥ 2 mm).

3- Recession defect on maxillary incisors, maxillary and mandibular canines, or premolars.

4- Absence of a history of periodontal surgery at the involved sites in the last 12 months.

5- History of compliance with oral hygiene instructions and periodontal recall.

6- Sufficient palatal or tuberosity donor tissue thickness (> 2mm).

*6.2 Describe the criteria that define who will be **excluded** from your final study sample.*

NOTE: This may be done in bullet point fashion.

Response:

1- Patients with systemic illness known to affect the outcome of periodontal therapy, including diabetes, immune deficiencies, etc.

2- Pregnant and lactating women

3- History of allergic reactions to drugs or materials used in the surgery including collagen.

4- Current use of any form of tobacco.

6.3 Indicate specifically whether you will include any of the following special populations in your study using the checkboxes below.

NOTE: Members of special populations may not be targeted for enrollment in your study unless you indicate this in your inclusion criteria.

Response: none

☐ Adults unable to consent

☐ Individuals who are not yet adults (infants, children, teenagers)

☐ Pregnant women

☐ Prisoners

*6.4 Indicate whether you will include non-English speaking individuals in your study. **Provide justification if you will exclude non-English speaking individuals.***

*In order to meet one of the primary ethical principles of equitable selection of subjects, non-English speaking individuals may **not** be routinely excluded from research as a matter of convenience.*

In cases where the research is of therapeutic intent or is designed to investigate areas that would necessarily require certain populations who may not speak English, the researcher is required to make efforts to recruit and include non-English speaking individuals. However, there are studies in which it would be reasonable to limit subjects to those who speak English. Some examples include pilot studies, small unfunded studies with validated instruments not available in other languages, studies with

numerous questionnaires, and some non-therapeutic studies which offer no direct benefit.

Response:

English speaking individuals only, Due to the small size of the study, we do not expect to encounter non-English speakers. There are also a large number of questionnaires involved in this study. Therefore it is reasonable to limit subjects to those who speak English.

7.0 Vulnerable Populations

If the research involves special populations that are considered vulnerable, ***describe the safeguards included to protect their rights and welfare.***

NOTE: You should refer to the appropriate checklists, referenced below, to ensure you have provided adequate detail regarding safeguards and protections. You do not, however, need to provide these checklists to the IRB.

7.1 For research that involves ***pregnant women,*** *safeguards include:*
NOTE CHECKLIST: Pregnant Women (HRP-412)

Response:

☐ **N/A**: This research does not involve pregnant women.

7.2 For research that involves ***neonates of uncertain viability or non-viable neonates,*** *safeguards include:*
NOTE CHECKLISTS: Non-Viable Neonates (HRP-413), or Neonates of Uncertain Viability (HRP-414)

Response:

☐ **N/A:** This research does not involve non-viable neonates or neonates of uncertain viability.

7.3 For research that involves ***prisoners****, safeguards include:*
NOTE CHECKLIST: Prisoners (HRP-415)

Response:

☐ **N/A:** This research does not involve prisoners.

7.4 For research that involves ***persons who have not attained the legal age for consent to treatments or procedures involved in the research ("children")****, safeguards include:*
NOTE CHECKLIST: Children (HRP-416)

Response:

☐ **N/A:** This research does not involve persons who have not attained the legal age for consent to treatments or procedures ("children").

7.5 For research that involves ***cognitively impaired adults****, safeguards include:*
NOTE CHECKLIST: Cognitively Impaired Adults (HRP-417)

Response:

☒ **N/A:** This research does not involve cognitively impaired adults.

7.6 Consider if other specifically targeted populations such as students, employees of a specific firm, or educationally or economically disadvantaged persons are vulnerable. ***Provide information regarding their safeguards and protections, including safeguards to eliminate coercion or undue influence.***

Response:

No specifically targeted populations will be included.

8.0 Eligibility Screening

8.1 Describe ***screening procedures*** *for determining subjects' eligibility. Screening refers to determining if prospective participants meet inclusion and exclusion criteria.*

📎 *Include all relevant screening documents with your submission (e.g. screening protocol, script, questionnaire).*

Response: Subjects who contacted the clinics over the phone will be assessed for their willingness to participate in the study and upon their approval they will be scheduled for a screening visit and will be evaluated according to the inclusion and exclusion criteria. Also, comprehensive patient evaluation including eligibility questionnaire, complete medical and dental history, full mouth examination, periodontal charting, and full-mouth radiographic x-rays and photos will be taken for affected and non-affected sites. Urine pregnancy test will be performed when needed to assure eligibility of interested women.

☐ **N/A:** There is no screening as part of this protocol.

9.0 Recruitment Methods

☐ **N/A:** This is a records review only, and subjects will not be recruited. NOTE: If you select this option, please make sure that all records review procedures and inclusion/exclusion screening are adequately described in other sections.

9.1 Describe when, where, and how potential subjects will be recruited.

NOTE: Recruitment refers to how you are identifying potential participants and introducing them to the study. Include specific methods you will use (e.g. searching charts for specific ICD code numbers, Research Participant Groups, posted advertisements, etc.).

Response:

Posted advertisements that contain the clinics contact name and number will be distributed throughout the three floors of the School of Dental Medicine- SUNY at Buffalo near the entrances, exits, stairs, and elevators. And throughout the SUNY at

Buffalo campus. Also, advertisement will be posted on PST Doctor's forum, PST social media (facebook and instagram) directed towards potential participant and doctors, Dental Town, American Academy of Periodontology Forum, Dentistry Today Magazine, Compendium Dental Journal, Email list of PST certified doctors in the NY state area, DentMat emailing list to doctors in the NY state area, Geistlich emailing list to doctors in a 100 miles radius around Buffalo including Ontario, Canada, and any posted media including craigslist. Also the study will be advertised through radio and TV interviews with the PI and/or study members. We will also utilize the services of The CTSI Community Engagement Team (CET) to assist in subject recruitment. The CET hosts the Buffalo Research Registry (BRR) that can connect us to community members who have completed a health profile and have agreed to be contacted about potential research opportunities that they may be an interested in based on their self-reported information. The CET also goes out and tables at many events in the community throughout the year and they have agreed to have the IRB approved flyer for this project at the table. They attend events such as Good for the Neighborhood hosted by Independent Health Foundation, UB on the Green, Juneteenth, Elmwood Arts Festival and many others. The CET also hosts a standing table at Conventus on the 4th floor of UBMD where the IRB approved flyer can be spotlighted as well. Newspaper ad will be posted directed towards participants.

Upon calling the clinics, the subjects will be asked some questions over the phone about their willingness to participate in the study and if they agree, they will be scheduled for screening visit.

9.2 Describe how you will protect the privacy interests of prospective subjects during the recruitment process.

NOTE: Privacy refers to an individual's right to control access to him or herself.

Response:

Patients will be informed about the study in the dental clinic in private. The subject controls their own privacy interests, as they will contact the study team if they are willing to participate in the research.

9.3 Identify any materials that will be used to recruit subjects.

NOTE: Examples include scripts for telephone calls, in person announcements / presentations, email invitations.

For advertisements, include the final copy of printed advertisements with your submission. When advertisements are taped for broadcast, attach the final audio/video tape. NOTE: You may submit the wording of the advertisement prior to taping to ensure there will be no IRB-required revisions, provided the IRB also reviews and approves the final version.

Response:

Posted advertisement will be posted that include some information about the study.

10.0 Procedures Involved

*10.1 Provide a description of **all research procedures or activities** being performed and when they are performed once a subject is screened and determined to be eligible. Provide as much detail as possible.*

NOTE: This should serve as a blueprint for your study and include enough detail so that another investigator could pick up your protocol and replicate the research. For studies that have multiple or complex visits or procedures, consider the addition of a schedule of events table in in your response.

Response:

Pre-surgical treatment:

Upon recruitment of eligible candidates, at-least two matching bilateral or contralateral gingival recession defects are assigned as one tooth will receive the test (PST) technique and one tooth will receive the control (CTG) technique. The first tooth will be randomly assigned to one of the two techniques by opening a prepared randomization schedule letter for each patient that would include which quadrant will be treated first with the Pinhole technique. This will assure that there is equal distribution of whether the PST technique or the CTG technique is performed first. The patients will be blinded of which technique is applied to each of their teeth, and the independent clinical examiner, who will only perform the pre-operative and the 6 weeks, 3, 6, 12, 18, and 24 months evaluations and measurements visits, will be blinded on which technique was used.

The initial therapy will consist of oral hygiene instructions, correction of the recession etiological factor(s), and dental prophylaxis as needed. Two weeks evaluation of adequate oral hygiene and control of gingival inflammation (PI and GI<15%)[27] is carried out, and if adequate the first surgical procedure will be performed the same visit after reviewing the surgical consent with the subjects. While, the second surgical procedure for the other sites receiving the comparative technique will be performed 3 weeks later by the same surgeon.

Surgical treatment:

All teeth with recession defects will be treated upon patient's needs, and only two matching bilateral or contralateral gingival recession defects will be included in the statistical analysis. All surgeries are performed by the same expert periodontist.

At the beginning of each surgery a timer will be started to compare operator's time for each technique, and another timer will be used at the suturing stage of the CTG Technique. Both surgical techniques will require achieving local anesthesia using 2% Lidocaine with 1:100,000 epinephrine, all recession defects are thoroughly scaled using curettes (Gracey Curettes, Hu-Friedy, Chicago, IL, USA) and any root surface deposit, soft cementum, root prominence, or irregularities are eliminated to allow for proper graft adaptation and adequate blood supply. For the sites receiving the control technique (Connective Tissue Graft), the technique

described by Langer B. and Langer L. will be performed starting with a sulcular incision followed by a partial thickness flap with two vertical incisions to the mucogingival junction placed at least one-half to one tooth wider mesiodistally than the area of gingival recession. The interproximal papillae are left intact [5]. A CTG is then harvested according to the technique described by Bruno,[29] the first incision is perpendicular to the 2nd premolar and 1st molar and is 2-3 mm apical to their gingival margin and as wide as the recipient site, followed by a second incision parallel to the for mentioned teeth and is 1-2 mm apical to the first incision, then the CTG is raised by periosteal elevator and released from apical and lateral attachments by sharp incision when needed. The graft is then prepared to have a homogenous thickness of 1.5-2 mm. The donor CTG is stabilized to the underlying connective tissue interproximally using 4-0 Vicryl sutures. The recipient flap is re-positioned coronally, to cover as much as possible of the graft with no tension, 2 mm coronal to the CEJ, then sutured with 4-0 Vicryl sutures. For the sites receiving the test technique (Chao Pinhole Surgical Technique)[20] the surgery starts with a small pinhole opening in the alveolar mucosa apical to the mucogingival junction of the affected tooth, the flap is then undermined using special instruments to create a full thickness pouch, followed by extending the pouch horizontally and coronally to undermined the adjacent papilla without incising it and free the flap for its coronal displacement. Then multiple 2x12mm strips of collagen resorbable membrane material (Bio-Gide, Geistlich Pharma AG) are packed under the papilla to secure the flap in a coronal direction. Gentle pressure is applied for 5 minutes to minimize the thickness of the blood clot after each of the procedures. The patients are advised to brush all teeth and sites except the buccal surfaces of the operated-on teeth, which are to be cleaned with 0.12% Chlorhexidine mouth rinse. Patients will be seen at day 1 and 2 weeks for follow-up, healing and pain index will be recorded and a checklist will be used to assess the patient's post-operative condition, also at 2 weeks follow-up prophylaxis will be performed away from gingival margins of operated on teeth. Sutures to be removed two weeks after the surgery for the CTG sites. Six weeks after the surgery, the patients can resume mechanical tooth cleaning in the operated areas using a post-operative ultra soft-bristle brush and will receive prophylaxis teeth cleaning at the clinics. Patients will be asked to record the name of the pain medications taken, frequency, and dosage while also recording the pain index on daily basis for the first 3 weeks after the surgery. All measurements will be recorded at 6 weeks, 3, 6, 12, 18, and 24 months post-operatively for each procedure and oral hygiene reinforced. Six and 12 months prophylaxis will be performed.

The following measurements will be recorded at baseline, 6 weeks, 3, 6, 12, 18, and 24 months post-surgically:

I. Complete root coverage (CRC): The number of sites that resulted in 100% root coverage.

II. Recession Depth (RD): Measured in millimeters from the gingival margin at the mid-buccal aspect of the root, to the CEJ or relative CEJ.

III. Percentage root coverage (%RC): calculated as ([RD preoperative - RD postoperative]/RD preoperative) × 100%.

IV. Recession classification: The recession type will be classified according to the criteria suggested by Miller.

V. Probing depth (PD): Measured in millimeters from the gingival margin to the base of the periodontal sulcus at 6 sites per tooth.

VI. Clinical attachment level (CAL): Measured in millimeters from CEJ or relative CEJ to the base of the periodontal sulcus at 6 sites per tooth.

VII. Width of the keratinized tissue (KTW): Measured in millimeters at mid-buccal aspect of the tooth from the gingival margin to the mucogingival junction.

VIII. Gingival Thickness: Measured in millimeters at the mid-buccal of the gingiva and 2 mm apical the gingival margin at the attached gingiva or the alveolar mucosa using a #15 endodontic reamer with a silicon disk stop.

IX. Plaque index (PI): Is used for estimating the status of oral hygiene by measuring dental plaque that occurs in the areas adjacent to the gingival margin.

X. Gingival index (GI): GI is measured according to Loe and Sillness and scored on a scale of 0 to 3.

More measurements include:

- ❖ Healing index (HI): A horizontal scale from 1-5 evaluating tissue color, response to palpation, granulation tissue, incision margin, suppuration, adopted from Aleksic[25]. To be assessed at day 1 and 2 weeks post-surgically as follows:
- 1 (very poor)= ≥50% of the gingiva is red, bleeding on palpation, presence of granulation tissues, incision margin not epithelialized (loss of epithelium beyond incision margin), and presence of suppuration.
- 2 (poor)= ≥50% of the gingiva is red, bleeding on palpation, presence of granulation tissues, incision line not epithelialized (connective tissue exposed), and no suppuration.
- 3 (good)= 25-50% of the gingiva is red, no bleeding on palpation, no granulation tissues, no connective tissue exposed, and no suppuration.
- 4 (very good)= <25% of the gingiva is red, no bleeding on palpation, no granulation tissues, no connective tissue exposed, and no suppuration.

- 5 (excellent)= all tissues are pink, no bleeding on palpation, no granulation tissues, no connective tissue exposed, and no suppuration.

❖ Pain index (PN): Pain is recorded on a horizontal pain scale of 0-10, Pain index to be recorded by the patients at 9 am, 3pm, and 9 pm from the day of the surgery and for 3 weeks post-treatment. Also, the patients will be asked to record the name of pain medications taken, dosage, and frequency for the 3 weeks after the surgery. Pain index as follows; Mild for ‘‘0 to 3,’’ moderate for ‘‘4 to 6,’’ and severe for ‘‘7 to 10.’’ None to minimal pain meant little or no discomfort; moderate was any pain that bothers the patient and mildly affects normal daily functions and activities; and severe is considered any pain that could not be tolerated and even disrupts the patient’s daily functions or activities [26].

❖ Patient’s Condition Checklist: the patient’s condition will be assessed Patient’s Condition Checklist: the patient’s condition will be assessed according to a pre-set checklist at day 1 and 2 weeks post-surgically, as follows:

- Clinical appearance of the face: Swelling: severity (mild, moderate, severe), location, lymph nodes, hard or fluctuant, hot or normal temperature; coloration.
- Bleeding: if yes, location, nature (persistent, intermittent, stops with pressure).
- Infection or sloughing: if yes, location, extent in mm vertically and horizontally, probable cause of infection.
- Patient temperature.
- Pain medications taken: name, dosage, quantity.
- Photos will be taken.

❖ Time: surgical time will be calculated for each surgical procedure from the time of surgical incision or pinhole creation to the conclusion of the surgery; also the time of suturing will be calculated for CTG.

10.2 Describe what data will be collected.

NOTE: For studies with multiple data collection points or long-term follow up, consider the addition of a schedule or table in your response.

Response: recession depth, recession classification, percentage root coverage, percentage complete root coverage, probing depth, clinical attachment level, width of keratinized tissue, gingival thickness, plaque index, and gingival index at baseline, 6 weeks, 3, 6, 12, 18, and 24 months post-surgically. Also, pain index and the name of post-operative pain medication taken, dosage, and frequency will be recorded for the 3 weeks following the surgery and healing index at 1 day and 2 weeks following the surgery with patient's condition checklist. Additionally, Surgical time for each surgical procedure and suturing time for CTG will be calculated at the surgical visit.

10.3 List any instruments or measurement tools used to collect data (e.g. questionnaire, interview guide, validated instrument, data collection form).

Include copies of these documents with your submission.

Response: Standardized periodontal probe 12 UNC (Hu-Friedy, Chicago, IL) for periodontal measurements

Telephone screening script, periodontal charting form, medical and dental history form, eligibility questionnaire, patient's condition checklist, data collection forms, pain index, and healing index.

10.4 Describe any source records that will be used to collect data about subjects (e.g. school records, electronic medical records).

Response:

Patient's chart for full dental and medical history, radiographic x-rays to identify the extent of disease.

*10.5 Indicate whether or not **individual** subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings will be shared with subjects or others (e.g., the subject's primary care physician) and if so, describe how these will be shared.*

Response:

Any finding that might lead us to suspect an underlying medical condition, the patient will be notified and advised to follow with primary care physician at the same time. Recommendation for treatment of other teeth or sites will be made when needed as a full mouth periodontal exam will be performed for all initially illegible patients, the findings and the results of the study will be included in a report and will be shared with the patients at the end of the study.

*10.6 Indicate whether or not **study** results will be shared with subjects or others, and if so, describe how these will be shared.*

Response:

The study results are to be published in a respected specialized journal. Also, the study results will be shared with the subjects and any future treatment recommendations will be given to all subjects if needed.

11.0 Study Timelines

11.1 Describe the anticipated duration needed to enroll all study subjects.

Response:

12 months

11.2 Describe the duration of an individual subject's participation in the study. Include length of study visits, and overall study follow-up time.

Response:

The overall subject's participation time is 12 - 24 months

After the 2 hours screening visit, eligible patients will be scheduled for 3 visits including the two visits of surgical therapy, followed by one day and 2 weeks follow-up visits and 6 weeks, 3, 6, 12, 18, and 24 months evaluations visits for a total of 15 visits distributed over 12-24 months. Each appointment is expected to be 30 minutes to 3 hours except surgical therapy visit is 3-4 hours.

11.3 Describe the estimated duration for the investigators to complete this study (i.e. all data is collected and all analyses have been completed).

Response:

24 months

12.0 Setting

12.1 Describe all facilities/sites where you will be conducting research procedures. Include a description of the security and privacy of the facilities (e.g. locked facility, limited access, privacy barriers). Facility, department, and type of room are relevant. Do not abbreviate facility names.

NOTE: Examples of acceptable response may be: "A classroom setting in the Department of Psychology equipped with a computer with relevant survey administration software," "The angiogram suite at Buffalo General Medical Center, a fully accredited tertiary care institution within New York State with badge access," or, "Community Center meeting hall."

Response:

The periodontal clinics at the university at Buffalo/ School of Dental Medicine. The dental school has card access for personnel, with security cameras in the hallways leading to/from clinics. Clinics are fully locked after working hours with no access to any staff/personnel. The subjects' data will be stored at Dr. Othman Shibly's office locked cabinets in the Department of Periodontics and Endodontics at the university at Buffalo which is a locked office with access to only him and his research assistant.

12.2 For research conducted outside of UB and its affiliates, describe:

- *Site-specific regulations or customs affecting the research*
- *Local scientific and ethical review structure*

NOTE: This question is referring to UB affiliated research taking place outside UB, i.e. research conducted in the community, school-based research, international research, etc. It is not referring to multi-site research. UB affiliated institutions include Kaleida Health, ECMC, and Roswell Park Cancer Institute.

Response:

☐ **N/A:** This study is not conducted outside of UB or its affiliates.

13.0 Community-Based Participatory Research

13.1 Describe involvement of the community in the design and conduct of the research.

NOTE: Community-Based Participatory Research (CBPR) is a collaborative approach to research that equitably involves all partners in the research process and recognizes the unique strengths that each brings. CBPR begins with a research topic of importance to the community, has the aim of combining knowledge with action and achieving social change to improve health outcomes and eliminate health disparities.

Response:

☐ **N/A:** This study does not utilize CBPR.

13.2 Describe the composition and involvement of a community advisory board.

Response:

☐ **N/A:** This study does not have a community advisory board.

14.0 Resources and Qualifications

*14.1 Describe the qualifications (e.g., education, training, experience, expertise, or certifications) of the Principal Investigator **and** staff to perform the*

research. When applicable describe their knowledge of the local study sites, culture, and society. Provide enough information to convince the IRB that you have qualified staff for the proposed research.

NOTE: If you specify a person by name, a change to that person will require prior approval by the IRB. If you specify a person by role (e.g., coordinator, research assistant, co-investigator, or pharmacist), a change to that person will not usually require prior approval by the IRB, provided that the person meets the qualifications described to fulfill their roles.

Response:

Principle investigator is a diplomate of the American Board of Periodontology, a clinical assistant professor, and the director of the post-graduate periodontal program at the university at Buffalo with years of experience in teaching and research, where he performed multiple retrospective and prospective clinical studies other than reviews and non–clinical studies. The co-investigator is an external study team member whom might be involved in supervising the Pinhole surgical procedure, clinical examiner and research coordinator will be Periodontists and/or periodontal resident. His staff will consist of an experienced dental assistant and hygienists that are well trained to conduct clinical research with experience in patient's privacy maintenance and following IRB guidelines. Lastly, the consulting statistician and epidemiologist is an external team member whom will be overlooking the study raw data without any identifiable patient information.

Describe other resources available to conduct the research.

14.2 Describe the time and effort that the Principal Investigator and research staff will devote to conducting and completing the research.

NOTE: Examples include the percentage of Full Time Equivalents (FTE), hours per week. The question will elicit whether there are appropriate resources to conduct the research.

Response:

0.2 FTE

14.3 Describe the availability of medical or psychological resources that subjects might need as a result of anticipated consequences of the human research, if applicable.

NOTE: One example includes: on-call availability of a counselor or psychologist for a study that screens subjects for depression.

Response:

The patients will be provided with the phone number of the research assistant, whom has direct contact with the surgeon and principle investigators, to call in case of dental adverse events or emergencies, and patients can be seen on emergency basis any day of the week if needed. In case of medical emergency, patients will be instructed to call 911. And in case of medical emergencies during the dental visit or treatment, a code team is always available during working

hours, which are trained in medical emergencies and patient's condition stabilization.

14.4 Describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions.

Response:

All persons assisting will be gathered in a meeting at the beginning of the study to explain to them the protocol of the study, copies of the protocol will be given to them and all questions will be answered then responsibilities and duties will be assigned to each member. Also, The principle investigator and research assistant will be available, on the phone and email address, to answer any question or concern from the staff throughout the study. GCP principles will be closely adhered and the research staff will be trained accordingly.

15.0 Other Approvals

15.1 Describe any approvals that will be obtained prior to commencing the research (e.g., school, external site, funding agency, laboratory, radiation safety, or biosafety).

Response:

IRB approval, organization sponsor approval, funding agency approval.

☐ **N/A:** This study does not require any other approvals.

16.0 Provisions to Protect the Privacy Interests of Subjects

16.1 Describe how you will protect subjects' privacy interests during the course of this research.

NOTE: Privacy refers to an individual's right to control access to him or herself. Privacy applies to the person. Confidentiality refers to how data collected about individuals for the research will be protected by the researcher from release. Confidentiality applies to the data.

Examples of appropriate responses include: "participant only meets with a study coordinator in a classroom setting where no one can overhear", or "the participant is reminded that they are free to refuse to answer any questions that they do not feel comfortable answering."

Response: The subjects will be interviewed and their information will be reviewed with them in the clinic that has closed doors with no other people other than the research staff around. Also, all subjects will be reminded that they have the right to refuse to answer any questions that they do not feel comfortable answering. And they can withdraw from the study at any time.

16.2 Indicate how the research team is permitted to access any sources of information about the subjects.

*NOTE: Examples of appropriate responses include: school permission for review of records, consent of the subject, HIPAA waiver. This question **does apply** to records reviews.*

Response:

HIPPA authorization and consent will be approved by the included subjects before the beginning of the study. The research staff will have access to the information provided by the patients.

17.0 Data Management and Analysis

17.1 Describe the data analysis plan, including any statistical procedures. This section applies to both quantitative and qualitative analysis.

Response: The main aim of this study is to assess the efficacy of the pinhole surgical technique in treating gingival recession compared to an established surgical treatment method. We therefore will focus in this clinical trial on one primary endpoint, namely recession depth. The change in recession depth during the study observation period will therefore be used for the calculation of sample size.

We previously have calculated the sample size based on parameter estimates gathered from published studies. We now have recalculated the sample size and used parameters estimates generated from 28 cases already treated in this clinical trial. This should give more accurate parameters to calculate the sample size needed. We also used the 80% power. Accordingly, we used the following assumptions to calculate the sample size:

Standard deviation in the group A: 0.91

Standard deviation in the group B: 0.95

Correlation: 0.46

Effect size (the difference in the reduction in recession depth between the test and control groups): 0.4 mm

Level of significance: 0.05

Power: 80%

Type of test: 2-sided

Based on these assumptions, the sample size is 48. In addition, we anticipate a drop out of 4 subjects. Hence, the total number of participants needed for this study is 52.

17.2 If applicable, provide a power analysis.

NOTE: This may not apply to certain types of studies, including chart/records reviews, survey studies, or observational studies. This question is asked to elicit whether the investigator has an adequate sample size to achieve the study objectives and justify a conclusion.

Response: Please see item 17.1

17.3 Describe any procedures that will be used for quality control of collected data.

Response:

Standardization of measurement and radiographs and assurance of intraoperator reproducibility will be performed.

18.0 Confidentiality

A. Confidentiality of Study Data

*Describe the local procedures for maintenance of confidentiality of **study data and any records that will be reviewed for data collection**.*

*18.1 A. Where and how will all data and records be stored? Include information about: password protection, encryption, physical controls, authorization of access, and separation of identifiers and data, as applicable. Include physical (e.g. paper) **and** electronic files.*

Response:

All charts, data and materials for the study are held with the principle investigator, and are kept together in a file for each individual subject, while electronic data will be kept on a password protected disc, all materials are stored in a locked cabinet and access is limited to the principal investigator, and the research assistant. A password locked computer of the University that is further secured by a personal account is used for data analysis. All the data related to the results will be retained for 5 years after the completion of the study for long-term follow-up if needed. GCP (by ISO14155) principles will be followed in close adherence. Patient information will be stored under a code assigned for each patient only and no names will be stored to protect patient's confidentiality. Medical and dental history information will be saved until the 12 months follow-up is completed, as they are important in the clinical management of patients during the course of the study, and then will be safely discarded and not used in any data analysis.

18.2 A. How long will the data be stored?

Response:

5 years after the study is completed.

18.3 A. Who will have access to the data?

Response:

The principle investigator and his research assistant upon the approval of the principle investigator.

18.4 A. Who is responsible for receipt or transmission of the data?

Response:

Principle investigator and research assistant.

18.5 A. How will the data be transported?

Response:

Paper files and the electronic data disc are transported in large dark plastic boxes on the department's cart from/to the principle's investigator's office to/from the clinics where the study will be taking place by the principle investigator and/or research assistant. Electronic files will be accessed on the department and clinics computers that are password locked computers of the University that are further secured by a personal account user name and password.

B. Confidentiality of Study Specimens

*Describe the local procedures for maintenance of confidentiality of **study specimens**.*

☐ **N/A:** No specimens will be collected or analyzed in this research. *(Skip to Section 19.0)*

18.6 B. Where and how will all specimens be stored? Include information about: physical controls, authorization of access, and labeling of specimens, as applicable.

Response:

18.7 B. How long will the specimens be stored?

Response:

18.8 B. Who will have access to the specimens?

Response:

18.9 B. Who is responsible for receipt or transmission of the specimens?

Response:

18.10 B. How will the specimens be transported?

Response:

19.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

☐ **N/A:** This study is not enrolling subjects, or is limited to records review procedures only. This section does not apply.

NOTE: Minimal risk studies may be required to monitor subject safety if the research procedures include procedures that present unique risks to subjects that require monitoring. Some examples include: exercising to exertion, or instruments that elicit suicidality or substance abuse behavior. In such cases, N/A is not an acceptable response.

19.1 Describe the plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe.

Response:

The medical monitor person will periodically evaluate the collected data to assure patient's safety and well-being. A full periodontal exam will be performed at each evaluation visit to insure the overall maintenance of oral health throughout the study. Oral hygiene will be evaluated each visit. Patients will be closely monitored, as they will be seen for follow-up at day 1 and 2 weeks post-surgically. Patient's post-operative condition will be assessed according to a pre-set checklist to assure patient's safety. Suture removal will be done 2 weeks following the surgery and then evaluations and measurements at 6 weeks, 3, 6, 12, 18, and 24 months after the surgery. At the 2 weeks, 6 weeks, 6, 12, 18, and 24 months follow-ups full mouth prophylaxis will be performed. Pain index and healing index will be recorded and if patients developed any treatment complications, they are instructed to call the research staff for an additional evaluation and treatment if needed. If any other medical or dental treatment is needed, the patients will be referred to appropriate specialties.

19.2 Describe what data are reviewed, including safety data, untoward events, and efficacy data.

Response:

Updated medical and dental history, plaque index, patient's condition checklist, gingival index, recession depth, percentage root coverage, probing depth, clinical attachment level, width of keratinized tissues, gingival thickness, pain index, and healing index.

19.3 Describe any safety endpoints.

Response:

Maintenance of the overall oral health.

19.4 Describe how the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with participants).

Response:

Clinical measurements will be collected during the study visit at 6 weeks, 3, 6, 12, 18, and 24 months post-surgical treatment, healing and patient's condition will be assessed at day 1 and 2 weeks post-surgically. The medical monitor will assure patient's safety is maintained upon evaluation of all measurements. If patients developed any treatment complications, they will be informed and treated accordingly.

19.5 Describe the frequency of safety data collection.

Response:

All outcomes will be recorded at 6 weeks, 3, 6, 12, 18, and 24 months after the surgery. Healing index and patient's condition checklist at day 1 and 2 weeks post-surgically, and pain index the first 3 weeks after the surgery. Surgical time for each surgical procedure and suturing time for CTG will be calculated at the surgical visit.

19.6 Describe who will review the safety data.

Response:

Medical monitor is assigned by the organization sponsor to review the data periodically and make sure all patients are still eligible for treatment and that all the study criteria are met. The medical monitor is a certified dentist who is not involved in the patient treatment.

19.7 Describe the frequency or periodicity of review of cumulative safety data.

Response:

Monthly.

19.8 Describe the statistical tests for analyzing the safety data to determine whether harm is occurring.

Response:

Pre and post comparison through paired t-test of the measurements

19.9 Describe any conditions that trigger an immediate suspension of the research.

Response:

Developing diabetes, pregnancy, periodontal disease, immune deficiency, smoking, uncontrolled medical condition, or persistent non-compliance with study

appointments, instructions or oral hygiene instructions will result in immediate suspension from the study.

20.0 Withdrawal of Subjects

☐ **N/A:** This study is not enrolling subjects. This section does not apply.

*20.1 Describe **anticipated** circumstances under which subjects may be withdrawn from the research without their consent.*

Response:

Lack of compliance with oral hygiene, post-operative instructions, or follow-up appointments. Also, if any changes occurred in the medical history or medications taken that might affect the treatment, healing, or outcomes e.g. some blood pressure or epilepsy medications, pregnancy, antibiotics, diabetis, smoking. Lastly, if any other oral condition occurred on the teeth of interest e.g. cavity, root canal, loosening of the teeth or pockets. All subjects will be informed of any new information that may affect their health, welfare, or choice to stay in the research.

20.2 Describe any procedures for orderly termination.

NOTE: Examples may include return of study drug, exit interview with clinician. Include whether additional follow up is recommended for safety reasons for physical or emotional health.

Response:

At the end of the study, the patients will be given a report of the study and the results, and they will be informed if any further procedure is needed for the site maintenance and the future recommendations will be explained.

20.3 Describe procedures that will be followed when subjects withdraw from the research, including retention of already collected data, and partial withdrawal from procedures with continued data collection, as applicable.

Response:

Upon withdrawal from the study before the one-month follow-up after the surgery, all measurements and data collected will be discarded and will not be used in any research publication. If withdrawal occurred after the 6 weeks follow-up, the patient will be asked if they would agree on using their data in the study analysis and publication. If they agreed, data will be retained, and if not will be discarded.

21.0 Risks to Subjects

21.1 List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related to their participation in the research. Consider physical, psychological, social, legal, and economic risks. Include a description of the probability, magnitude, duration, and reversibility of the risks.

NOTE: Breach of confidentiality is always a risk for identifiable subject data.

Response:

Some forms of gingival recession will benefit from soft tissue graft procedure and will be recommended to be done for the subjects whether they are in a study or not as standard of care. All soft tissue grafting surgeries might posses the same surgical risks including; pain, discomfort, bleeding, failure and redo of procedure, swelling, bruising, infection, tooth sensitivity, temporary or permanent numbness in surgical area, inflammation.

Risks related to the anesthetics might include but are not limited to allergic reactions, accidental swallowing of foreign matter, facial swelling or bruising, pain, soreness or discoloration at the site of injection of the anesthetics.

Finally, Breach of confidentiality is always a risk for identifiable subject data.

21.2 Describe procedures performed to lessen the probability or magnitude of risks, including procedures being performed to monitor subjects for safety.

Response:

Review of medical history and medications of the patient, patients will be instructed to use over the counter pain medications including ibuprofen and/or acetaminophen as needed. Also, maintenance of good oral hygiene will decrease the chance of infection or inflammation of the surgical site. Day one and 2 weeks follow-up will be performed and a patient's condition checklist will be followed. Also, the patients will record their pain throughout the first 3 weeks after the surgery.

*21.3 If applicable, indicate **which procedures** may have risks to the subjects that are currently unforeseeable.*

Response:

All soft tissue surgeries will have similar risks whether in the study or outside the study.

21.4 If applicable, indicate which research procedures may have risks to an embryo or fetus should the subject be or become pregnant.

Response:

Upon pregnancy the subject will be withdrawn from the study.

21.5 If applicable, describe risks to others who are not subjects.

Response:

None

22.0 Potential Benefits to Subjects

22.1 Describe the potential benefits that individual subjects may experience by taking part in the research. Include the probability, magnitude, and duration of the potential benefits. Indicate if there is no direct benefit.

*NOTE: Compensation **cannot** be stated as a benefit.*

Response:

Possible benefits include covering the exposed roots and increase the amount of gingival tissue covering the tooth to help prevent further gingival recession, to maintain oral health, improve tooth prognosis, and help decrease tooth sensitivity and improve esthetics. This research will also help Periodontist make a sound decision on which technique carries the most successful results, the best course of healing, with the least amount of pain and post-operative discomfort, which will help other patients choose the most comfortable procedure for them in the future.

23.0 Compensation for Research-Related Injury

☐ **N/A:** The research procedures for this study do not present risk of research related injury (e.g. survey studies, records review studies). This section does not apply.

*23.1 **If the research procedures carry a risk of research related injury,** describe the available compensation to subjects in the event that such injury should occur.*

Response:

The *subjects will get medical treatment if they are injured as a result of taking part in this study. The study doctor will explain the treatment options and tell the subject where they can get treatment.*

However, the sponsor will pay for the reasonable costs of medical care for any physical injury that specifically results from the study, to the extent that:

- The injury resulted from the study and not from a pre-existing medical condition
- The costs are not paid for by the subject's medical insurance or other third party
- The injury did not result from a failure to follow study protocol or instructions, or from the negligence or misconduct of the study personnel

23.2 Provide a copy of contract language, if any, relevant to compensation for research related injury.

*NOTE: If the contract is not yet approved at the time of this submission, submit the current version here. If the contract is later approved with **different language regarding research related injury**, you must modify your response here and submit an amendment to the IRB for review and approval.*

Response:

Should any Study subject suffer a Protocol-induced injury, Sponsor will pay for reasonable and necessary costs of diagnosis, therapy and/or medical treatment including

hospitalization costs ("Treatment Costs") for such Protocol-induced injuries. Sponsor will reimburse Institution and/or subjects for such Treatment Costs dependent upon by whom the Treatment Costs were incurred. Sponsor will not be responsible for paying for Treatment Costs associated with the treatment of normal progression of the subject's disease, nor for injuries resulting from interventions that the subjects would have incurred had they not participated in the Study. Additionally Sponsor will not be responsible for Treatment Costs to the extent such Protocol-induced injury is caused by the malpractice, negligence, error or omission ("Negligence") by the Investigator, Study Staff or Institution, except to the extent such Negligence is caused by Sponsor or Sponsor's employees, agents or affiliates. The obligation of Sponsor under this section shall survive termination of this Agreement.

24.0 Economic Burden to Subjects

24.1 Describe any costs that subjects may be responsible for because of participation in the research.

NOTE: Some examples include transportation or parking.

Response:

The treatment will be provided at no cost, but the subjects will not be compensated for their time and their transportation method.

☐ **N/A:** This study is not enrolling subjects, or is limited to records review procedures only. This section does not apply.

25.0 Compensation for Participation

25.1 Describe the amount and timing of any compensation to subjects, including monetary, course credit, or gift card compensation.

Response:

The subjects will receive all the treatment at no cost.

☐ **N/A:** This study is not enrolling subjects, or is limited to records review procedures only. This section does not apply.

☒ **N/A:** There is no compensation for participation. This section does not apply.

26.0 Consent Process

26.1 Indicate whether you will be obtaining consent.

NOTE: This does not refer to consent documentation, but rather whether you will be obtaining permission from subjects to participate in a research study. Consent documentation is addressed in Section 27.0.

☒ ***Yes*** *(If yes, Provide responses to each question in this Section)*

☐ ***No*** *(If no, Skip to Section 27.0)*

26.2 Describe where the consent process will take place. Include steps to maximize subjects' privacy.

Response:

In the periodontal clinic which is a private quiet room with no one present other than the principle investigator or research assistant or dental assistant. The study details, time involvement, adverse events, and benefits will be explained to the patients, and all their questions will be addressed. The patients will be given at least one week to decide if they want to enroll in the study, if needed.

26.3 Describe how you will ensure that subjects are provided with a sufficient period of time to consider taking part in the research study.

NOTE: It is always a requirement that a prospective subject is given sufficient time to have their questions answered and consider their participation. See "SOP: Informed Consent Process for Research (HRP-090)" Sections 5.5 and 5.6.

Response:

The patients will be given at least one week to decide if they want to enroll in the study, if needed.

26.4 Describe any process to ensure ongoing consent, defined as a subject's willingness to continue participation for the duration of the research study.

Response:

The patient will be provided a copy of the consent for their reference and records. The consent at the beginning of each visit will be reviewed with the patient to ensure the patient still agrees to receive the treatment before performing any procedure.

26.5 Indicate whether you will be following "SOP: Informed Consent Process for Research (HRP-090)." If not, or if there are any exceptions or additional details to what is covered in the SOP, describe:

- *The role of the individuals listed in the application who are involved in the consent process*
- *The time that will be devoted to the consent discussion*
- *Steps that will be taken to minimize the possibility of coercion or undue influence*
- *Steps that will be taken to ensure the subjects' understanding*

Response:

☐ We have reviewed and will be following "SOP: Informed Consent Process for Research (HRP-090)."

Non-English Speaking Subjects

☐ **N/A:** This study will not enroll Non-English speaking subjects. *(Skip to Section 26.8)*

26.6 Indicate which language(s) other than English are likely to be spoken/understood by your prospective study population or their legally authorized representatives.

NOTE: The response to this Section should correspond with your response to Section 6.4 of this protocol.

Response:

26.7 If subjects who do not speak English will be enrolled, describe the process to ensure that the oral and written information provided to those subjects will be in that language. Indicate the language that will be used by those obtaining consent.

NOTE: Guidance is provided on "SOP: Informed Consent Process for Research (HRP-090)."

Response:

Cognitively Impaired Adults

☐ **N/A**: This study will not enroll cognitively impaired adults. *(Skip to Section 26.9)*

26.8 Describe the process to determine whether an individual is capable of consent.

Response:

Adults Unable to Consent

☐ **N/A**: This study will not enroll adults unable to consent. (*Skip to Section 26.13)*

When a person is not capable of consent due to cognitive impairment, a legally authorized representative should be used to provide consent (Sections 26.9 and 26.10) ***and, where possible, assent of the individual should also be solicited*** *(Sections 26.11 and 26.12).*

26.9 Describe how you will identify a Legally Authorized Representative (LAR). Indicate that you have reviewed the "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" for research in New York State.

NOTE: Examples of acceptable response includes: verifying the electronic medical record to determine if an LAR is recorded.

Response:

☐ We have reviewed and will be following "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."

26.10 ***For research conducted outside of New York State****, provide information that describes which individuals are authorized under applicable law to consent on behalf of a prospective subject to their participation in the research. One method of obtaining this information is to have a legal counsel or authority review your protocol along with the definition of "legally authorized representative" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."*

Response:

26.11 Describe the process for ***assent of the adults****:*

- *Indicate whether assent will be obtained from all, some, or none of the subjects. If some, indicate which adults will be required to assent and which will not.*

Response:

- *If assent will not be obtained from some or all subjects, provide an explanation of why not.*

Response:

26.12 Describe whether ***assent of the adult*** *subjects will be documented and the process to document assent.*

NOTE: The IRB allows the person obtaining assent to document assent on the consent document using the "Template Consent Document (HRP-502)" Signature Block for Assent of Adults who are Legally Unable to Consent.

Response:

Subjects who are not yet Adults (Infants, Children, and Teenagers)

☐ **N/A**: This study will not enroll subjects who are not yet adults. *(Skip to Section 27.0)*

*26.13 Describe the criteria that will be used to determine **whether a prospective subject has not attained the legal age for consent to treatments or procedures involved in the research** under the applicable law of the jurisdiction in which the research will be conducted **(e.g., individuals under the age of 18 years)**. For research conducted in NYS, review "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" to be aware of which individuals in the state meet the definition of "children."*

NOTE: Examples of acceptable responses include: verification via electronic medical record, driver's license or state-issued ID, screening questionnaire.

Response:

*26.14**For research conducted outside of New York State**, provide information that describes which persons have not attained the legal age for consent to treatments or procedures involved the research, under the applicable law of the jurisdiction in which research will be conducted. One method of obtaining this information is to have a legal counsel or authority review your protocol along the definition of "children" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."*

Response:

26.15 Describe whether parental permission will be obtained from:

Response:

☐ One parent even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child.

☐ Both parents unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

☐ Parent permission will not be obtained. A waiver of parent permission is being requested.

NOTE: The requirement for parent permission is a protocol-specific determination made by the IRB based on the risk level of the research. For guidance, review the "CHECKLIST: Children (HRP-416)."

*26.16Describe whether permission will be obtained from individuals **other than parents**, and if so, who will be allowed to provide permission. Describe your procedure for determining an individual's authority to consent to the child's general medical care.*

Response:

*26.17 Indicate whether assent will be obtained from all, some, or none of the **children**. If assent will be obtained from some children, indicate which children will be required to assent.*

Response:

26.18 When assent of children is obtained, describe how it will be documented.

Response:

27.0 Waiver or Alteration of Consent Process

Consent will not be obtained, required information will not be disclosed, or the research involves deception.

☐ **N/A:** A waiver or alteration of consent is not being requested.

27.1 If the research involves a waiver or alteration of the consent process, please review the "CHECKLIST: Waiver or Alteration of Consent Process (HRP-410)" to ensure that you have provided sufficient information for the IRB to make the determination that a waiver or alteration can be granted.

NOTE: For records review studies, the first set of criteria on the "CHECKLIST: Waiver or Alteration of Consent Process (HRP-410)" applies.

Response:

27.2 If the research involves a waiver of the consent process for planned emergency research, please review the "CHECKLIST: Waiver of Consent for Emergency Research (HRP-419)" to ensure you have provided sufficient information for the IRB to make these determinations. Provide any additional information necessary here:

Response:

28.0 Process to Document Consent

☐ **N/A:** A Waiver of Consent is being requested.
(Skip to Section 29.0)

28.1 Indicate whether you will be following "SOP: Written Documentation of Consent (HRP-091)." If not or if there are any exceptions, describe whether and how consent of the subject will be obtained including whether or not it will be documented in writing.

NOTE: If your research presents no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of the research context, the IRB will generally waive the

requirement to obtain written documentation of consent. This is sometimes referred to as 'verbal consent.' Review "CHECKLIST: Waiver of Written Documentation of Consent (HRP-411)" to ensure that you have provided sufficient information.

If you will document consent in writing, attach a consent document with your submission. You may use "TEMPLATE CONSENT DOCUMENT (HRP-502)". If you will obtain consent, but not document consent in writing, attach the script of the information to be provided orally or in writing (i.e. consent script or Information Sheet).

Response: Written consent will be used.

☐ We will be following "SOP: Written Documentation of Consent" (HRP-091).

29.0 Multi-Site Research (Multisite/Multicenter Only)

☐ **N/A:** This study is not an investigator-initiated multi-site study. This section does not apply.

*29.1 If this is a multi-site study **where you are the lead investigator**, describe the processes to ensure communication among sites, such as:*

- *All sites have the most current version of the IRB documents, including the protocol, consent document, and HIPAA authorization.*
- *All required approvals have been obtained at each site (including approval by the site's IRB of record).*
- *All modifications have been communicated to sites, and approved (including approval by the site's IRB of record) before the modification is implemented.*
- *All engaged participating sites will safeguard data as required by local information security policies.*
- *All local site investigators conduct the study appropriately.*
- *All non-compliance with the study protocol or applicable requirements will be reported in accordance with local policy.*

Response:

29.2 Describe the method for communicating to engaged participating sites:

- *Problems*
- *Interim results*
- *Study closure*

Response:

29.3 Indicate the total number of subjects that will be enrolled or records that will be reviewed across all sites.

Response:

29.4 If this is a multicenter study for which UB will serve as the IRB of record, and subjects will be recruited by methods not under the control of the local site (e.g., call centers, national advertisements) describe those methods.

Response:

30.0 Banking Data or Specimens for Future Use

☐ **N/A:** This study is not banking data or specimens for future use or research outside the scope of the present protocol. This section does not apply.

*30.1 If data or specimens will be banked (stored) for **future use, that is, use or research outside of the scope of the present protocol**, describe where the data/specimens will be stored, how long they will be stored, how the data/specimens will be accessed, and who will have access to the data/specimens.*

NOTE: Your response here must be consistent with your response at the "What happens if I say yes, I want to be in this research?" Section of the Template Consent Document (HRP-502).

Response:

30.2 List the data to be stored or associated with each specimen.

Response:

30.3 Describe the procedures to release banked data or specimens for future uses, including: the process to request a release, approvals required for release, who can obtain data or specimens, and the data to be provided with specimens.

Response:

31.0 Drugs or Devices

☐ **N/A:** This study does not involve drugs or devices. This section does not apply.

31.1 If the research involves drugs or devices, list and describe all drugs and devices used in the research, the purpose of their use, and their regulatory approval status.

Response:

Trade name: BIO-GIDE Bioresorbable Bilayer Collagen Membrane (Geistlich Pharma AG) (K042197)

FDA approved, regulation number: 872.3930, regulation class: 2, product code: NPL, Dated: August 12, 2004

The bioresorbable collagen membrane strips will be used to stabilize the gingival flap coronal to the area of cemento-enamel Junction without the use of suture materials according to the novel technique described by "Chao J. A Novel Approach to Root Coverage: The Pinhole Surgical Technique. Int J Periodontics Restorative Dent. 2012;32:521–531". Which also has an advantage of being a native collagen membrane that is not reconstituted or subjected to cross-linking agents and is harvested and purified in a manner which allows it to retain the native fibrillar and fiber bundle structure as well as the native bilayer structure seen in its tissue source.

31.2 Describe your plans to store, handle, and administer those drugs or devices so that they will be used only on subjects and be used only by authorized investigators.

Response:

52 packages will be ordered by the grant and those will be stored in the same cabinet with the information about the subjects, with each package labeled with a number corresponding to the subject to insure that each package will be used for each patient. The membrane will be used by the study surgeon at the specific site that was chosen randomly

If the drug is investigational (has an IND) or the device has an IDE or a claim of abbreviated IDE (non-significant risk device), include the following information:

31.3 Identify the holder of the IND/IDE/Abbreviated IDE.

Response:

The device status is post market approval, on-label study and the FDA 510k K042197 and updated by K050446 (attached).

31.4 Explain procedures followed to comply with FDA sponsor requirements for the following:

	Applicable to:		
FDA Regulation	***IND Studies***	***IDE studies***	***Abbreviated IDE studies***
21 CFR 11	***X***	***X***	
21 CFR 54	***X***	***X***	
21 CFR 210	***X***		
21 CFR 211	***X***		
21 CFR 312	***X***		
21 CFR 812		***X***	***X***
21 CFR 820		***X***	

Response:

The device status is post market approval, on-label study and the FDA 510k K042197 and updated by K050446 (attached).

32.0 Humanitarian Use Devices

☐ **N/A:** This study does not involve humanitarian use devices. This does not apply.

32.1 For Humanitarian Use Device (HUD) uses provide a description of the device, a summary of how you propose to use the device, including a description of any screening procedures, the HUD procedure, and any patient follow-up visits, tests or procedures.

Response:

32.2 For HUD uses provide a description of how the patient will be informed of the potential risks and benefits of the HUD and any procedures associated with its use.

Response: