# Effects of Er:YAG Photobiomodulation Therapy on Wound Healing of Human Palatal Mucosa After Connective Tissue Graft Harvesting: A Pilot Study

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## STUDY PROTOCOL

### Participants

Patients of the Graduate Periodontics Clinic at the University of Manitoba who require a subepithelial connective tissue graft (SECTG) utilizing autogenous donor tissue harvested from the palate, during the time period from Fall 2018 to Spring 2020, and who sign the consent form will be eligible to participate. Patients will receive initial periodontal examination and treatment if necessary. Patients must be classified as ASA I or ASA II according to the American Society of Anesthesiologists and demonstrate both a Full Mouth Plaque Score (FMPS) and a Full Mouth Bleeding Score (FMBS) <20% to be included in the study. Patients with any contraindications for periodontal surgery, who are currently taking anticoagulants or corticosteroids, or who smoke >10 cigarettes/day will be excluded from the study.

### Clinical Methodology

A computerized randomization program will assign participants to one of two groups. Patients will be block-randomized to ensure a balance between all the operators. Both groups will undergo SECTG surgery for root coverage utilizing an autogenous graft obtained from the patient's palate. Details regarding the preparation of the recipient site and the specific root coverage technique will not be dictated by the experimental protocol as they will have no effect on the outcomes being measured. The palate is anesthetized with 2% lidocaine (1:100000 epinephrine) by greater palatine nerve block, nasopalatine nerve block, and local infiltration as needed, ensuring not to inject anesthetic into the graft tissue. Prior to harvesting the graft, the

thickness of the palatal tissue at the donor site will be measured via transgingival probing (or ultrasound device). Graft tissue will be harvested according to the Single-Incision Technique described by Hurzeler.

**Surgical Technique:** The donor area of the palate is located between the root of the canine and the palatal root of the first molar. Its lateral border is positioned approximately 2 mm from the gingival margin and its medial border is dictated by the position of the palatal neurovascular bundle which can be found 7, 12, or 17 mm from the cementoenamel junction of the correspondent teeth, depending on whether the palatal vault is shallow, average, or high, respectively. A single horizontal incision, whose length corresponds to the required length of the graft, is made at 90° to the underlying bone approximately 2 mm from the gingival margin with a #15 blade. The blade is then angled at approximately 135° to the bone and a split-thickness dissection is started within that first incision, towards the median of the palate. As the incision is advanced, the angle of the scalpel is further flattened until it is nearly parallel to the bone surface. Elevation of the overlying tissue should be avoided to reduce the risk of perforation while making this incision. Split-thickness dissection continues until the necessary dimensions of the graft are obtained, ideally maintaining 1.0-1.5 mm of overlying tissue. The SECTG is separated from the surrounding tissue via incisions to the bone surface at the mesial, distal, and medial borders of the graft. The graft is detached from the bone with a periosteal elevator and placed on a saline-soaked gauze until it is transferred to the recipient site.

The length, width, and thickness of the graft, the thickness of the remaining palatal tissue, and the length of the palatal incision will be measured with digital calipers to the nearest 0.1 mm. Palatal incisions will be closed with cyanoacrylate. Immediately following completion of the

surgical procedure, Group A will receive PBM treatment of the donor site with Er:YAG laser according to the parameters shown to induce maximal proliferation of human gingival fibroblasts (Energy Setting: 80 mJ, Pulse Rate: 25 Hz, Duration: 30 s). Group B will receive sham treatment with the laser unit turned off.

During all sessions of laser treatment, the manufacturer-recommended safety precautions will be stringently adhered to. The clinician, patient, and any other individuals inside the operatory must always wear Laser Safety Glasses designated for use with Er:YAG lasers. Whenever possible, the individuals present within the operatory will be limited to the patient and those directly involved with the procedure (i.e. the clinician and assistant). The activated laser should never be directed anywhere other than the intended site of treatment. If the operator, patient, or anyone else in the operatory suspects they may have incurred damage to their eyes or skin, they should be examined by a dermatologist and/or ophthalmologist. A sign of notification that laser surgery is in progress will be placed at the entrance of the operatory. The Er:YAG laser is not intended for use on patients who have a pacemaker or implantable cardioverter defibrillator, however these patients would not fit the inclusion criteria of ASA I and ASA II classification and thus would already be precluded from participation in the study. The laser unit should not be used in the presence of combustible anesthetic or an elevated concentration of oxygen. If the administration of oxygen is absolutely necessary, it will be ensured that there is no leakage of oxygen and the oxygen delivery tube will be protected with a non-combustible cuff.

Both groups will receive 2 g of Amoxicillin (or 600 mg of Clindamycin in cases of penicillin allergy) and 400 mg of Ibuprofen immediately following surgery, in addition to the standard post-operative instructions given to patients at the U of M Graduate Periodontics Clinic. This includes

application of an ice pack for the first 24 hours, BID rinsing with 0.12% Chlorhexidine, avoiding the surgical sites during oral hygiene, avoiding hot foods and liquids, avoiding hard and crunchy foods for 24 hours after surgery, refraining from smoking for two weeks and avoiding sucking on straws or spitting. Patients will also be provided with a bag of 30 200-mg Ibuprofen tablets. They will be given a Visual Analogue Scale (VAS) questionnaire to rate their post-operative pain from 0 to 10 for each night of the first post-operative week.

At the one-week post-operative appointment, the participants will return their VAS questionnaires and any remaining Ibuprofen tablets. They will be asked to fill out a modified Oral Impacts on Daily Performance (OIDP) questionnaire to assess the effect of the palatal wound on their oral-health related quality of life during the first post-operative week. A clinician who did not perform the surgery and is blinded to which treatment group the patient belongs will assess the donor site at the one- and two-week post-operative appointments according to a modified early-wound healing index (MEHI) proposed by Fickl (a variation of the EHI originally conceived by Wachtel) as well as the healing index (HI) of Landry, Turnbull and Howley. Participants will return for a six-week post-operative appointment, during which tissue thickness at the donor site will be measured via bone sounding and a histological specimen will be harvested with a tissue punch. Tissue samples will immediately be submerged in a solution of 10% neutral buffered formalin. Clinical photographs will be taken at all appointments.

**Risks**

There is the risk in both the test and control groups of post-operative complications that are associated with any periodontal surgery including intraoral pain or discomfort, bleeding,

infection, swelling and bruising. There is also a risk that the desired outcome, either partial or complete root coverage (depending on the severity and classification of the initial recession defect), may not be achieved by the surgical procedure.

**Potential Benefits**

If Er:YAG photobiomodulation of the palatal donor site results in improved and/or faster healing of the tissue or less post-operative discomfort, then patients requiring SETGs will benefit from a shorter and more pleasant healing period following their surgery. Also, as the effects of Er:YAG PBM on healing have never been investigated in human studies, the information gained from this study would help direct future research on this topic.

**Consent Process**

Patients of the Graduate Periodontics Clinic at the University of Manitoba who require SECTG and who meet the eligibility requirements will be asked personally if they would like to be a part of the project. After being given a brief description of the research, if the patient is interested, they will be provided a written summary of the study and a consent form to sign if they would like to take part.

**Data Security**

All data will be recorded based on the subject's assigned number after they have agreed to participate and have signed the consent form. Their names and contact information will be stored in a secure, locked location at the U of M Graduate Periodontics Clinic. Findings from the

study may be published or presented in a public forum. Participants' names will not be used and no identifying details revealed.

**STATISTICAL ANALYSIS PLAN**

The study will be blinded at the level of data collection and data assessment. The primary outcome for this study is the patients' post-operative discomfort from the palatal donor site during the first week following surgery. This is assessed by VAS scores and analgesic consumption. Friedman's two-way ANOVA test will compare the change in VAS scores over time within each treatment group. Mann-Whitney U test will compare the difference in VAS scores between the two groups at each time point as well as the differences in total analgesic use between the two groups. The secondary outcomes are healing of the donor site and the palatal wound's effect on the patients' OHQoL. Healing is assessed by MEHI and HI scores and by tissue thickness. Wilcoxon Signed Ranks test will compare the change in MEHI and HI scores from week one to week two within each treatment group. Mann-Whitney U test will compare the differences in MEHI and HI scores between the treatment groups as well as the differences in tissue thickness at six weeks post-operatively between the groups. OHQoL is assessed by OIDP scores. The differences in OIDP scores between treatment groups is compared with Mann-Whitney U test. The level of significance is $p \leq 0.05$. IBM SPSS Statistics for Windows (Version 25.0) is used for analysis.