

## **Cover Page**

### **Official Title of the Study:**

The Use of Temporary Anchorage Devices for Ridge Preservation after Tooth Extraction

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## Research Team Members

### 1) Se-Lim Oh: PI

- Developing the research protocol
- Obtaining the IRB approval and the approval of continuing review
- Confirming the subject eligibility and supervising research procedures
- Data analysis

### 2) Dianna (Hyun San) Lee: a research team member

- Performing the research procedures

## Abstract

The remodeling of the alveolar bone following tooth extraction results in significant bone loss at the extraction site. An excessive bone loss hampers the implementation of treatment plans, prediction of esthetic outcomes, and patient satisfaction. Placing bone substitute materials in an extraction socket may reduce the alveolar bone resorption. However, postoperative infection and inflammation are common side effects following bone graft surgeries. Finding a less invasive approach to preserve the alveolar ridge would be amenable to dental clinic. An animal study reported that bone density significantly increased in the extraction site with transcortical mini-screw placements, exhibiting markedly less atrophied alveolar ridge. In addition, the side effects from a mini-screw placement are minimal and no antibiotics are required. Therefore, we propose the placement of a transcortical mini-screw at the buccal plate of an extraction socket as a minimally invasive approach to preserve the alveolar ridge. The objective of this study is to determine the effects of transcortical mini-screws placed at the buccal plates of the extraction sockets in humans. We hypothesize that placement of a transcortical mini-screw at the buccal plate will significantly reduce bone loss at the site. To test this hypothesis, we are performing a prospective split-mouth design study. We are recruiting patients who need extraction of two maxillary premolars for orthodontic treatments. Cone beam computed tomography (CBCT) is exposed after the extraction of two premolars and before a transcortical mini-screw placement ( $T_0$ ). One 8-mm length mini-screw is placed at the buccal plate of the extraction socket on one side. The contralateral extraction socket is untreated. The mini-screw is removed at 6 months and the follow-up CBCT is obtained ( $T_6$ ). We will compare changes in the alveolar bone width at both extraction sides using the CBCTs. We predict that the placement of a transcortical mini-screw at the buccal plate of the extraction socket significantly reduces bone loss at the extraction site. Results of this study will offer a useful measure to sustain an edentulous alveolar ridge for a lengthy period without losing bone proper.

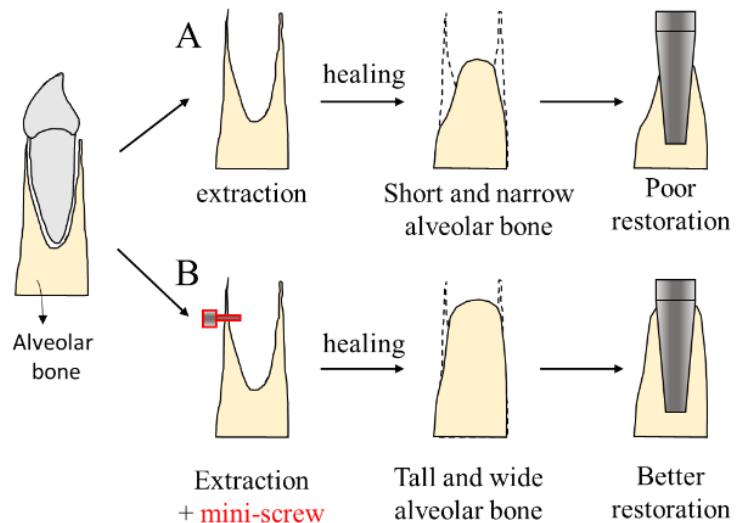
## Research Plan

### SIGNIFICANCE AND INNOVATION

**Bone loss following tooth extraction is inevitable but current available procedures for preserving bone after tooth extraction are not satisfactory.** Teeth develop from tooth buds in the jaw bone, known as alveolar bone. The alveolar bone undergoes constant remodeling process throughout the life of teeth. When teeth are extracted, the surrounding alveolar bone remodels and undergoes atrophy, resulting in reduced alveolar ridge in width and height,<sup>1-3</sup> most of which takes place in the first 3 months after tooth extraction (Fig 1).<sup>4</sup> Within six to eight weeks, the total ridge thickness was reduced by 15% of the original value in average.<sup>5</sup> The ridge width was reduced from 12 mm at baseline to 6 mm at 12 months.<sup>3</sup> Such bone reduction hampers the success of treatments such as implant placements, esthetics for ideal fixed dental restorations, and orthodontic teeth treatment through the edentulous space.<sup>6,7</sup> To modify bone remodeling after tooth extraction, various surgical ridge preservation procedures were proposed using bone substitute materials in conjunction with barrier membranes.<sup>8</sup>

However, extractions often occur without planning. Bone graft/ridge preservation surgeries may not be feasible at the time of extraction due to a lack of finance, insufficient time, and/or a lack of treatment plan. In addition, inflammation and postoperative swellings commonly occur after ridge preservation surgeries, thus, antibiotics are prescribed after the surgeries.<sup>8</sup> A minimally invasive and cost-effective approach to preserve the alveolar ridge following tooth extraction is desirable.

**We propose a transcortical mini-screw insertion in order to preserve edentulous ridge as a minimally invasive (no antibiotics prescription requiring) and cost-effective (\$180) approach.** Transcortical mini-screws are widely used in orthodontic treatments for temporary anchorage purposes. Transcortical orthodontic mini-screws are not fully integrated but maintain contact with alveolar bone ranged from 10% to 58% of surface,<sup>9</sup> which makes it easy to be removed after orthodontic treatments. In addition, the side effects of transcortical mini-screws such as per-implant inflammation are extremely low.<sup>9</sup> One of the premises of our proposal is an animal study showing that a placement of transcortical mini-screw at the buccal plate of an extraction socket significantly increased bone density in the extraction site, which resulted in markedly less atrophy of alveolar ridge.<sup>10</sup> Furthermore, a case report<sup>11</sup> indicates that insertion of transcortical mini-screws in the alveolar plate may result in increased bone density in the region. However, clinical studies determining the effects of a transcortical mini-screw placement on ridge preservation is lacking. The objective of our study is to investigate effects of a transcortical mini-screw placement on alveolar ridge preservation after tooth extraction. Successful outcomes will suggest the potential novel clinical application of the mini-screw for ridge preservation after tooth extraction, which can greatly enhance dental practice.



**Figure 1. Schematic of alveolar bone changes following tooth extraction.** A. Bone loss following tooth extraction is problematic for functional and esthetic restoration. B. In this study, we predict that mini-screw placement in the buccal plate of extraction socket will reduce the bone loss (lower), which should enhance prognosis of the restoration.

## **THE OBJECTIVE**

The objective of our study is to investigate effects of a transcortical mini-screw placement on alveolar ridge preservation after tooth extraction.

## **SPECIFIC AIMS**

Specific Aim 1: To evaluate the clinical outcomes between the treated sites with a transcortical screw (the experimental group) and the non-treated sites (the control group)

*Null Hypothesis:* There will be no differences in clinical parameters between the two groups.

*Approach:* The investigators will conduct a prospective split-mouth design clinical study. The investigators will compare the clinical changes in the vertical ridge height and the horizontal ridge width at 3 months and 6 months from baseline (tooth extraction).

Specific Aim 2: To evaluate the radiographic outcome between the experimental and the control group

*Null Hypothesis:* There will be no difference in alveolar bone height and width between the two groups.

*Approach:* The study will measure the alveolar bone heights and widths using cone beam computed tomographies (CBCTs) at baseline and 6 months.

## **APPROACH**

This is an on-going prospective clinical study under a protocol approved by the IRB (HP-00076020). Six subjects completed the study protocol. Interim data analysis was performed from these six subjects.

1. Sample size determination: The original sample size was determined to provide 80% power to recognize a significant difference of 1 mm between the two sides with a 95% confidence interval ( $\alpha=0.05$ ) and standard deviation of 1.0 mm, considering the difference in the mean width of the edentulous alveolar ridge as the primary outcome variable. Based on the power analysis reperformed by following the formula described by Faul et al<sup>12</sup> using the interim data from the 6 subjects, 14 subjects will provide 80% power to recognize a significant difference of 0.5 mm in the width of the alveolar ridge between the two sides.

2. The Study Population: Patients with the following conditions are included: a) age  $\geq 18$  years, and b) two maxillary premolars (one from the left side and the other from the right side) required to be extracted in accordance with recommended dental treatment plans. Exclusion criteria are as follows: a) hyper-/hypothyroid dysfunctions, b) diabetes mellitus, c) subjects with a history of a chronic use of corticosteroid ( $> 6$  months), d) subjects with a history of taking oral/IV bisphosphonates within the past 2 years, e) smokers, and f) other systemic conditions influencing bone integrity.

### 3. Research Procedures (Figure 2)

1) Obtaining signatures on the consent form at screening visit.

The PI and the POC will follow the protocol in the approved IRB application while we are obtaining signatures from the potential subject. The information will be given to the potential subject in the separate room. The potential subject will be encouraged to ask the PI and the POC any questions regarding this protocol. (Approximately 40 to 60 minutes)

2) Placement of a mini-screw at the buccal plate of the extraction socket in one side (left or right) one week after the atraumatic extraction of maxillary premolars

- Limited volume CBCT with high resolution will be exposed before the mini-screw placement; this is standard of care.
- Clinical photographs and intraoral images will be obtained for both sites.
- One mini-screw (8 mm length) will be placed at the buccal plate of one extraction site. After bone sounding, a mini screw will be placed at the position 3 mm from the alveolar crest. The other extraction site will be untreated. (Approximately 30 minutes)
  - The PI and the POC will monitor subjects closely.
  - Local anesthesia with lidocaine will be administered to minimize patients' discomfort.
  - Postoperative instruction will be given to subjects.

3) 3 months follow-up (30 minutes); Clinical photographs and intraoral images will be obtained for both sites.

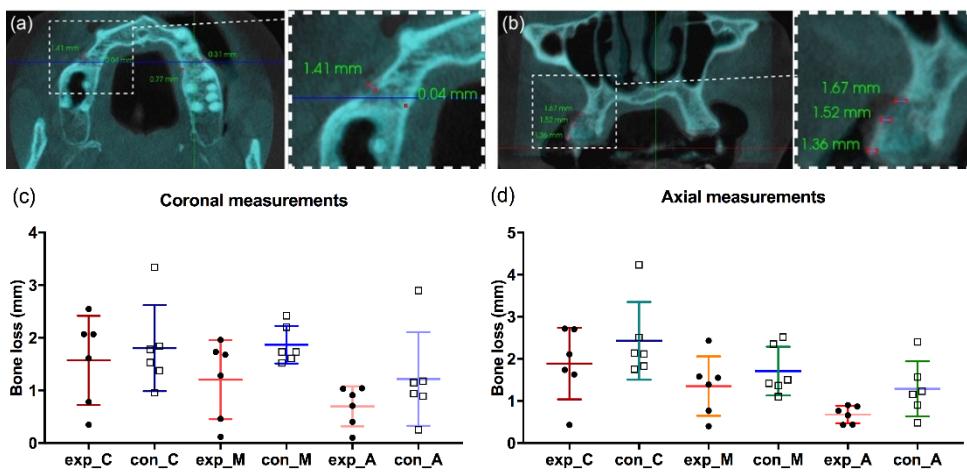
4) 6 months follow-up (40 minutes)

- The mini-screws will be removed.
- Clinical photographs and intraoral images will be obtained for both sites.
- Limited volume CBCT with high resolution will be exposed; this is a study procedure.



**Figure 2.** Intraoperative photographs from one of subjects. (a) Mini-screw (arrow) placed 1 week after extraction. (b) 3-month follow up. (c) 6-month follow up after removal of screw.

**4. Radiographic Measurements:** CBCT will be exposed after teeth extraction and before the mini-screw placement ( $T_0$ ). One mini-screw will be placed at the buccal plate of the extraction socket one week following the extraction of maxillary premolars in one side. The other extraction socket site will be untreated. At 6 months, the follow-up CBCT will be exposed for the maxilla after removal of the mini-screws. A blinded evaluator will measure the width of alveolar ridge on the CBCTs made at  $T_0$  and  $T_6$ . Changes in the width of alveolar ridge were measured from the outer wall at  $T_0$  to the outer wall at  $T_6$ . A positive value indicates bone loss. In the sagittal section, three levels will be determined by measuring from the crest to the apex and dividing the socket length into thirds. The measurements will be performed in coronal and axial sections (Figs 3a and 3b).



**Figure 3.** Measurements of bone loss after tooth extraction on CBCTs. (a-b) Examples of coronal (a) or axial (b) measurements. Changes of bone level from  $T_0$  to  $T_6$  was measured. Superimposition of two CBCT images ( $T_6$ , blue;  $T_0$ , grey) was performed using Invivo 6.0 software. Right side images present magnification of insets in left panels. (c-d) Changes in the width of alveolar ridge (mean  $\pm$  SD) in the experimental (exp) and the control (con) side at the crestal (C), middle (M), and apex (A) level in coronal or axial sections.

**5. Interim data and statistical analysis:** No inflammation and infection related to the mini-screw placements were observed in all 6 subjects. Miniscrews were removed at 6 months from 3 subjects and at 8 months from 3 subjects (the mean of 7-month) in keeping with planned dental treatments. Overall, the experimental side with the miniscrew placement showed less bone loss than the control side at the crestal, middle, and apex level in both coronal and axial measurements (Figs 3c and 3d). Upon completion of the study, a paired t-test will be performed to compare the changes in the width of alveolar ridge from the two sides. We will also measure mineral density distribution at the extraction sites from the two sides using CBCTs.

**6. Expected outcomes:** We predict that the experimental side with mini-screw placements will exhibit a significantly less bone loss than the control side. Bone density in the experimental side will be significantly greater than the control side.

## **7. Research Related Risks**

Clinical risks for mini-screw are low. Overall failure rate of mini-screws is about 10% with orthodontic loading. Four to five weeks after the mini screw placement, failure rate dropped to 5%. Failures of mini-screw are mainly from loosen screws, which mean the mini-screws are mobile and are not firmly attached (or engaged) to the bone. Our incidence of loosen screws will be very low because the mini-screw will not be loaded for 6 months.

Some of the potential risks are as follows:

- Participants may experience inflammation, mild pain, or discomfort at the mini-screw site for about 2 days. Pain medication (Tylenol or Ibuprofen) will be enough to solve this problem.
- Infection rarely develops. If it occurs, antibiotics will be prescribed.
- The screw could become loose. If this occurs, the participant should contact the clinic immediately. We will remove the loosen screw and replace with a new one.
- The incidence of broken screws is very rare although a screw breaks might occur during the removal of a screw. A broken screw can be easily removed with an instrument.
- The mini-screw may not prevent bone loss.
- As with any study, there is a risk that the study data may not be kept confidential. We will minimize this risk by storing data in a secure location, such as a locked cabinet in a locked office. Electronic data will be password-protected.

**8. Potential limitation:** Not all measurements at the three levels may be significantly different. Preserving bone at the crestal and the middle level is critical in implant dentistry. Preserving bone at the apex level is clinically meaningful in orthodontics. It is difficult to measure bone loss in the palatal side with coronal sections of CBCTs. Therefore, we will also measure bone loss using axial sections of CBCTs. CT based bone density measurement may not be as accurate as direct measurement using bone biopsy. However, it is a very powerful non-invasive tool to measure mineral density.<sup>13</sup>

## **9. Study period-time table for completion of the project**

<b>Research procedures</b>	<b>5 months</b>	<b>6 months</b>	<b>1 month</b>
<b>Recruitments</b>	X		
<b>Research procedures</b>	X	X	
<b>Data analysis and preparing manuscript</b>			X

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