COVER PAGE: Study Informed consent and HIPPA Informed Consent

IRB PROTOCOL APPROVAL: 14 August 2024 (most recent amendment eIRB Version 1.8); original document (eIRB Version 1.7) approved 06 March 2024.

Study Title: Characterizing the effects of Leukocyte-platelet-rich fibrin on sleep and perceived quality of life on mucogingival periodontal surgery healing.

NCT #: NA

DEFENSE HEALTH AGENCY
BROOKE ARMY MEDICAL CENTER
3551 ROGER BROOKE DRIVE
JBSA FORT SAM HOUSTON, TEXAS 78234-4504

MCHE-ZQ

14 August 2024

MEMORANDUM FOR: David Seiler, Capt, USAF, DC
FROM: San Antonio Institutional Review Board

PROJECT TITLE:
REFERENCE #: C.2024.040/ eIRB Reference #971422
SUBMISSION TYPE: AMENDMENT
REVIEW TYPE: EXPEDITED

ACTION: APPROVED
APPROVAL DATE: 14 August 2024

1. Thank you for submitting this amendment for the above research study. The San Antonio Institutional Review Board (SA-IRB) has reviewed and APPROVED your submission under the Expedited Pathway, IAW 32CFR219.110 (b) [and 21CFR56.110 (b) if applicable. No further action on this submission is required at this time.

2. The following items were reviewed and approved in this submission based on the applicable federal regulation(s):

- EIRB Modification Form v1.2
- Data Collection Sheet v1.3
- Total Data collection v1.1

3. No changes were made in the approval criteria, risk category or continuing review cycle.

4. If you have any questions, the POC is Elizabeth Suvias at elizabeth.suvias.ctr@health.mil. Please include your project title and reference number in all correspondence.

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Date: 2024.08.14 13:55:05 -05'00'

Sandra M. Escolas, PhD, CIP
Designated Expedited Review IRB Member

DEFENSE HEALTH AGENCY
BROOKE ARMY MEDICAL CENTER
3551 ROGER BROOKE DRIVE
JBSA FORT SAM HOUSTON, TEXAS 78234-4504

MCHE-ZQ

07 March 2024

MEMORANDUM FOR:	David Seiler, Capt, USAF, DC
FROM:	San Antonio Institutional Review Board
PROJECT TITLE:	Characterizing the Effects of Leukocyte-Platelet-Rich Fibrin on Sleep and Perceived Quality of Life on Mucogingival Periodontal Surgery Healing
REFERENCE #:	C.2024.040 / eIRB Reference #965309
SUBMISSION TYPE:	NEW PROJECT
REVIEW TYPE:	CONVENED IRB
ACTION:	ACTION
IRB APPROVAL DATE:	06 March 2024
EXPIRATION DATE:	06 March 2025

1. Congratulations! The San Antonio Institutional Review Board (SA-IRB) reviewed and APPROVED your aforementioned protocol and supporting documents. The research is judged to constitute greater than minimal risk. The protocol has been assigned control number C.2024.040. Please refer to this designation in all correspondence. Your protocol was reviewed for regulatory compliance under Full Committee Review, in accordance with 32CFR219.111. Applicable OHRP (under 45CFR46), FDA (under 21CFR50 and 56) and HIPAA (45CFR160 and 164) regulations were also consulted, as appropriate.

2. As part of this approval, the following determinations were made:

a. The protocol, eIRB Version 1.7, is approved to enroll 80 subjects.

b. An informed consent process has been approved in accordance with (IAW) 32CFR219.116 (a). Use of a written, informed consent document, eIRB Version 1.5, is approved which encompasses all of the required elements of informed consent. The signature of each subject on the informed consent document is required IAW 32CFR219.117 (a). Federal regulations also require each participant receive a copy of the consent document. The stamped, IRB-approved consent form must be used for enrolling subjects.

c. A HIPAA Authorization has been submitted and approved. The signature of each subject on the authorization document is required. Federal regulations also require each participant receive a copy of the signed authorization. The stamped, IRB-approved authorization form must be used for enrolling subjects.

3. Please note if external resources or Department of Defense (DoD) awards are being accepted/utilized for this project, it may not be initiated until any other reviews required as a condition of your funding have been completed.

4. You are required to promptly report all unanticipated problems involving risks to subjects or others (UPIRTSOs) to the IRB within 3 business days by phone at (210) 916-2598 or (210) 916-0606 or by email at usarmy.jbsa.medcom-bamc.mbx.bamc-irb@health.mil.

5. The protocol expiration date is noted above. If you plan to continue beyond this date, the required continuing review progress report is due to the SA IRB no later than six (6) weeks prior to expiration. The IRB will attempt to assist you by sending a reminder; however, submission of the continuing review report is your responsibility. Failure to submit the report on time will result in the expiration of your protocol and a requirement to cease all research activities until the entire protocol can be resubmitted.

6. Please be sure to maintain all records in accordance with the terms set forth in your protocol. You are required to have all records, including informed consent and HIPAA documents, available for review by the IRB or other federal agencies.

7. Any changes to your protocol, including any changes in personnel, may not be made without prior IRB approval. Please forward a request for any changes, along with their rationale to the SA-IRB for review and approval.

8. Please inform the IRB when the protocol is completed or changes status and forward any significant findings.

9. Abstract and/or manuscript submissions resulting from this research should be cleared IAW local publication clearance policies.

10. On behalf of the entire IRB, we wish you much success with your research protocol. If you have any questions, the POC is Col Karla Adams at 210-292-7497 or karla.e.adams2.mil@health.mil. Please include your project title and reference number in all correspondence.

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Date: 2024.03.07 13:16:28 -06'00'

Karla E. Adams
Col, USAF, MC
Chair, SA IRB

DEFENSE HEALTH AGENCY
BROOKE ARMY MEDICAL CENTER
3551 ROGER BROOKE DRIVE
JBSA FORT SAM HOUSTON, TEXAS 78234-4504

MCHE-ZQ

07 March 2024

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Date: 2024.03.07 13:16:28 -06'00'

Karla E. Adams
Col, USAF, MC
Chair, SA IRB

EIRB Protocol Template (Version 1.8)

1.0 General Information

***Please enter the full title of your protocol:**

Characterizing the effects of leukocyte-platelet-rich fibrin on sleep and perceived quality of life on mucogingival periodontal surgery healing

***Please enter the Protocol Number you would like to use to reference the protocol:**

1
* This field allows you to enter an abbreviated version of the Protocol Title to quickly identify this protocol.

Is this a multi-site protocol (i.e. Each site has their own Principal Investigator)?

No

Does this protocol involve the use of animals?

○ Yes ◉ No

2.0 Add departments

2.1 List sites associated with this study:

Is Primary?	Site Name
◉	**P and R** - 59th Medical Wing (59 MDW)

3.0 Assign project personnel access to the project

3.1 * Please add a Principal Investigator for the study:

Name	Role	Training Record
Seiler, David Luke	**Principal Investigator**	**View Training Record**

Responsibility

☐ Student
☐ Site Chair
☑ Resident
☐ Fellow

3.2 If applicable, please select the Research Staff personnel:

A) Additional Investigators

Name	Role	Training Record
Cayetano, Jess Jordan	Associate Investigator	View Training Record
Foerster, Henry A, DMD Lt Col	Associate Investigator	View Training Record
Synatzske, Angela M, DDS, MS	Associate Investigator	View Training Record

B) Research Support Staff

Name	Role	Training Record
No Research Support Staff have been added		

3.3 *Please add a Protocol Contact:

Name	Role	Training Record
Seiler, David Luke	Study Contact	View Training Record

The Protocol Contact(s) will receive all important system notifications along with the Principal Investigator. (i.e. The protocol contact(s) are typically either the Protocol Coordinator or the Principal Investigator themselves).

3.4 If applicable, please select the Designated Site Approval(s):

Name	Role	Training Record
No Designated Department Approval have been added		

Add the name of the individual authorized to approve and sign off on this protocol from your Site (e.g. the Site Chair).

4.0 Project Information

4.1 * What department(s) will be associated with this protocol?

☐ Dental Care

4.2 * Is the IRB of record for this study an IRB/HRPP that does NOT use EIRB? If Yes, complete the application according to the IRB/HRPP Determination.

If your Projects or Protocols are under the oversight of another IRB that does use EIRB, stop this submission and contact the core site and request an invitation as a performing site.

If your Project or Protocol is now being submitted for the first time to an IRB that does use EIRB, continue with this application and answer the questions to be reviewed by the IRB.

Answering yes means the board of record is an IRB that does NOT use EIRB.

○ Yes ◉ No

4.3 * Is this protocol research, expanded access, or humanitarian use device?

(•) Yes ( ) No

4.4 * What type of protocol is this?

- [ ] Behavioral Research
- [x] Biomedical Research
- [ ] Clinical trial (FDA regulated)
- [ ] Educational Research
- [ ] Expanded Access
- [ ] Humanitarian Use Device (HUD)
- [ ] Psychosocial Research
- [ ] Oral History
- [ ] Other

4.5 Are you conducting this project in pursuit of a personal degree?

(•) Yes ( ) No

4.7 * Is this human subjects research? (As defined by 32 CFR 219) Human subject means a living individual about whom an investigator (whether professional or student) conducting research:
(i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
(ii) Obtains, uses, studies, analyzes or generates identifiable private information or identifiable biospecimens.

(•) Yes ( ) No

4.8 * Do you believe this human subjects research is exempt from IRB review?

( ) Yes (•) No

5.0 Personnel Details

5.1 Does the Principal Investigator have a Permanent Change of Station (PCS) Date or Estimated Institutional Departure Date (EIDD)?

( ) Yes (•) No

5.2 List any Research Team members without EIRB access that are not previously entered in the protocol:

No results found

5.3 Are any Contractors or Subcontractors involved in this study? If yes, please list them and describe their role.

( ) Yes (•) No

No results found

5.4 Will you have a Research Monitor for this study?

- ○ Yes
- ◉ No
- ○ N/A

6.0 Data/Specimens

6.1 Does the study involve the use of existing data or specimens only (no interaction with human subjects)?

○ Yes ◉ No

7.0 Funding and Disclosures

7.1 Source of Funding:

Funding Source	Funding Type	Amount
: Other Graduate Medical Education Funding	: Other	29441

Total amount of funding:

29500

7.2 Do you or any other Investigator(s) have a disclosure of a personal interest or financial nature significant with sponsor(s), product(s), instrument(s) and/or company(ies) involved in this study?

○ Yes ◉ No

All personnel engaged in research must complete and attach a Conflict of Interest (COI) form.

8.0 Study Locations

8.1 Is this a collaborative or multi-site study? (e.g., are there any other institutions involved?)

○ Yes ◉ No

8.2 Study Facilities and Locations:

			FWA or DoD	Assurance	Is there an	IRB Reviewing for

Institution	Site Name	Site Role	Assurance Number	Expiration Date	agreement?	Site
Air Force	AFPDS	Performance site				: WHASC IRB Protocol Office

Other:

Other Institution Site	Site Role	FWA or DoD Assurance Number	FWA or DoD Expiration Date	Is there an agreement?	IRB Reviewing for Site
No results found					

8.3 Are there international sites?

Attach international approval documents, if applicable, when prompted. Note: Ensure local research context has been considered

○ Yes ◉ No

8.4 Is this an OCONUS (Outside Continental United States) study?

○ Yes ◉ No

Select the area of responsibility:

Have you obtained permission from that area of responsibility? (This is a requirement prior to study approval)

○ Yes ○ No

9.0 Study Details

9.1 Key Words:

Provide up to 5 key words that identify the broad topic(s) of your study

L-PRF, Healing, Sleep, Quality Life

9.2 Background and Significance:

Include a literature review that describes in detail the rationale for conducting the study. Include descriptions of any preliminary studies and findings that led to the development of the protocol. The background section should clearly support the choice of study variables and explain the basis for the research questions and/or study hypotheses. This section establishes the relevance of the study and explains the applicability of its findings

Inflammatory cells flood the body when a person is under stress physically or mentally. [1] Studies have shown that periodontal mucogingival surgeries cause more stress to patients than other dental surgeries because they tend to be the most painful and disruptive for patients. [2] Coincident with the inflammatory response due to the procedure itself, there is the potential for an exaggerated systemic inflammatory reaction to the post-procedure stress patients have after periodontal surgery.[3] Of the many conditions that induce stress in patients, changes to sleep patterns are of particular concern because the stress caused by sleep disruption can

diminish the body's natural repair processes that occur during sleep.[4] These disruptions can last for extended periods of time depending on the extent of the surgery, which compounds the stress experienced by these patients, further reducing healing post-surgical performance outcomes.[5, 6]

The effects that sleep disruptions have on bone metabolism are important because most periodontal surgical procedures involve alveolar bone. Studies have shown that bone metabolism-regulating hormones have diurnal patterns. Furthermore, disruptions to circadian rhythms in gene knockout studies have been shown to cause detrimental alterations bone metabolism, demonstrating the importance of sleep in bone metabolism homeostasis.[4] It was recently demonstrated that altered sleep patterns in shift workers who experience chronic sleep disruption increase the odds ratio for periodontal disease.[7] If disrupted sleep increases the risk for periodontal disease due to dysregulations of bone homeostasis, it may also negatively affect healing in surgical interventions.[6] Sleep Quality Index (SQI) is a summary index of the cardiopulmonary coupling (CPC) biomarkers of sleep quality, sleep stability, fragmentation, and periodicity, and provides a valuable measure of sleep health.[8] Analyzing the changes in SQI index throughout the healing period will allow for the assessment of post-surgical sleep quality.

Surgical intervention resulting in poor sleep quality may also reduce a patient's perceived quality of life (QoL) thus increasing stress and systemic inflammation.[9] The impact of non-surgical and surgical interventions for periodontal disease have been evaluated using patient-centered outcomes, such as QoL questionnaires.[10] The questionnaires include a subjective evaluation of the individual's oral health, functional well-being, emotional well-being, expectations and satisfaction with care, and sense of self.[11-13] In multiple studies, patients perceived an improvement in their QoL after initial periodontal therapy whereas surgical therapy has led to decreases in perceived QoL.[10] However, there are few studies or methods about how to improve QoL by reducing post-operative inflammation.[14-16]

One of the potential ways that has shown promise is leukocyte-platelet-rich fibrin (L-PRF), an autologous fibrin clot that has been shown to positively influence postoperative healing cascades.[17] Rich in growth factors, L-PRF improves healing times through accelerated tissue migration at the site of surgery which ultimately reduces inflammation.[18] There have been reports of improved soft tissue healing, increased QoL, and patient reported reduction in pain following the use of L-PRF.[19-21] However, due to conflicting studies regarding the efficacy of L-PRF in comparison to control groups, further investigation is required.[22] Therefore, this prospective cohort study aims to evaluate the relationship between L-PRF, sleep, and perceived QoL on healing in patients undergoing periodontal mucogingival surgery compared to standard surgical intervention.

9.3 Objectives/Specific Aims/Research Questions:

Describe the purpose and objective(s) of the study, specific aims, and/or research questions /hypotheses

Specific Aim 1: Determine if subjects' self-perceived QoL after periodontal mucogingival surgery is influenced by differences in tissues healing with and without L-PRF at the tissue donor site.

Objective 1. Document subjects' perceived QoL pre/post-surgery with QoL questionnaire (pre-surgical, 24 hr, 72hr, one week post operative appointment, two week post-operative appointment).

Objective 2: Measure clinical indicators to determine presence of infection and healing status at one-week post-operative appointment.

Objective 3: Measure clinical indicators to determine presence of infection and healing status at the two-week post-operative appointment.

Specific Aim 2: Determine if tissue healing with and without L-PRF at the tissue donor site after periodontal mucogingival surgery influences quality and/or quantity of sleep before and during the healing phase.

Objective 1: Characterize pre-surgical sleep quality via SQI over a 3-7-day period using a sleep monitoring device for sleep and vital signs.

Objective 2: Characterize post-surgical sleep quality via SQI over a two-week period using a sleep monitoring device.

Objective 3: Measure clinical indicators to determine presence of infection and healing status at the one-week post-operative appointment.

Objective 4: Measure clinical indicators to determine presence of infection and healing status at the two-week post-operative appointment.

9.4 Study Design:

Describe study design in one to two sentences (e.g., prospective, use of existing records/data /specimens, observational, cross-sectional, interventional, randomized, placebo-controlled, cohort, etc.). Specify the phase – Phase I, II, III, or IV – for FDA-regulated investigational drug research

Prospective cohort study on subjects undergoing mucogingival surgery with and without L-PRF placed at palatal harvest site. Evaluating sleep, perceived quality of life and post-operative healing.

9.5 Target Population:

Describe the population to whom the study findings will be generalized

Subjects undergoing periodontal mucogingival surgery.

9.6 Benefit to the DoD:

State how this study will impact or be of benefit to the Department of Defense

Knowledge of the patient's QoL after surgery may help providers provide patients with post-operative instructions that optimize healing. Knowledge of decreasing postoperative pain may return our ready airmen to duty in a more expedient manner. Knowledge of sleep quality can suggest optimal healing and sleep patterns for all airmen undergoing treatment.

10.0 Study Procedures, Data Management, and Privacy

10.1 Study Procedures:

Describe step-by-step how the study will be conducted from beginning to end

Pre-Op Appointment: After informed consent is obtained at the pre-op appointment, subjects undergoing mucogingival surgery will be given a sleep monitoring device (SleepImage® Ring 2019, SleepImage, Denver, CO) and will complete a baseline QoL survey (Qualtrics Survey, 2002, Qualtrics, Seattle WA).[11, 23-26] The sleep monitoring app will be downloaded on the subjects' phone and each subject will be trained on the function of the application by the principal investigators. Principle investigators (PI) will assist subjects to download the app and establish an account during the pre-op appointment. Subjects will create an account using their personal email, date of birth, and first/last name which will generate an unidentifiable subject number, which will be tracked in a secured file (Master Key of identifiable PII) accessible only by the PIs. The subject will accrue no fees upon creation of the account. Subjects will be instructed to contact the PIs with any malfunction or questions regarding the use of the application. The application will record sleep quality index (SQI), sleep efficiency, fragmentation, latency, duration, sleep opportunity and periodicity. This specific study will only utilize the SQI as the primary outcome variable. Subjects will be instructed to wear the device nightly throughout the study. The subject will be instructed to complete the same QoL questionnaire at 24 hours, 72 hours, as well as at the one week and two week post-operative appointments (study will last a total of three weeks).

Surgical appointment:

Blood (40 mL) will be collected at the beginning of the surgical appointment and spun using a horizontal centrifuge for the group receiving L-PRF (Horizon 6, horizontal PRF centrifuge machine, 2022, Drucker Diagnostics, Port Matilda, PA). L-PRF (test group selected via computerized randomization scheme with allocation 1:1 ratio) will be made from the blood collected as per manufacturer's protocol (4 vials of blood, centrifuged at 700g for 16 minutes at room temperature). Though some providers choose to use PRF routinely in mucogingival periodontal surgeries, for this study it will be for research purposes. Subjects not receiving L-PRF will have mucogingival surgery initiated without a prior blood draw.
The periodontal surgery will be completed by preparing the recipient site as per standard of care. The tissue harvested from the roof of the mouth will be harvested by removing the upper layer of epithelium and connective tissue technique. This technique requires secondary healing to occur and is usually the area of most pain for subjects. [20, 21] The L-PRF will be placed on donor site (for research purposes) in the experimental group and secured with palatal stent for hemostasis (for research purposes) which will remain in place for 48 hours immediately after surgery. The control group will receive an available clotting material such as Helitape®, Helicote®, or Surgicel®, which is the standard of care, placed on the donor site and secured with a palatal stent for hemostasis with identical post-operative wearing instructions as the experimental group. All subjects will receive post-operative ibuprofen and acetaminophen for pain management. Time and amount of medication will be annotated and recorded at post-operative appointments.

Post-Op Appointments:
At the follow-up appointments, subjects will complete the one- and two-week questionnaires to evaluate their perceived QoL since the time of the surgical intervention (see questionnaire). The healing of the palatal harvest site will be evaluated by two calibrated clinicians using the Landry et al. healing index on a scale of 1-5 (see data collection sheet).[18] The provider will complete a routine post-operative examination which includes visualizing and palpation of surgical area for swelling, removal of sutures, evaluation of pain, noting any purulence upon palpation, noting any tenderness upon palpation of lymph nodes, and temperature obtained to indicate yes/no for infection. This data collection is considered standard of care. At the final follow-up appointment subjects will return the SleepImage ring to the primary investigators. If the sleep monitoring device is lost or damaged prior to the end of the trial, the study will cover the cost of replacement.

10.2 Data Collection:

Describe all the data variables, information to be collected, the source of the data, and how the data will be operationally measured.

After informed consent is obtained at the pre-op appointment, subjects undergoing mucogingival surgery will be given a sleep monitoring device (SleepImage® Ring 2019, SleepImage, Denver, CO) and will complete a baseline QoL (Qualtrics XM®, 2002, Qualtrics, Seattle WA) [11, 23-26] The sleep monitoring app will be downloaded on subjects' phones and each subject will be briefed on the function of the application. Subjects will be instructed to wear the device nightly throughout the study. The subject will be instructed to complete the same QoL questionnaire at 24 hours, and 72 hours, as well as at the one-week and two-week post-operative appointments. The subjects' medical history will be coded and the following conditions will be noted: L-PRF, no-PRF, type of surgery, type of sedation, experience level of clinician, length of surgery, size of harvest, smoking, diabetes. Subjects' age and sex will also be documented. All of these parameters are reflected in the total data collection sheet. The mucogingival surgery will have been recommended and accepted by subjects as the standard of care.

At the follow-up appointments, subjects will complete the one- and two-week questionnaires to evaluate their perceived QoL since the time of the surgical intervention (see questionnaire). The healing of the palatal harvest site will be evaluated by two calibrated clinicians using the Landry et al. healing index on a scale of 1-5 (see data collection sheet).[18] The provider will complete a routine post-operative examination which includes visualizing and palpation of the surgical area for swelling, removal of sutures, evaluation of pain, noting any purulence upon palpation, noting any tenderness upon palpation of lymph nodes, and temperature obtained to indicate yes/no for infection. This data collection is considered standard of care. Data from the QoL surveys will be analyzed using Qualtrics® data system. Sleep data will be extracted and analyzed in the SleepImage® portal.

10.3 At any point in the study, will you request, use, or access health information in any form, including verbal, hard copy and electronic?

◉ Yes ○ No

10.4 Review the definitions below and respond to the following two questions. If you are not sure of the answers, email DHA.PrivacyBoard@mail.mil for assistance. The *Military Health System (MHS)* is defined as all DoD health plans and DoD health care providers that are organized under the management authority of, or in the case of covered individual providers, assigned to or employed by, the Defense Health Agency (DHA), the Army, the Navy, or the Air Force *MHS workforce members* are employees, volunteers, trainees, and other persons whose conduct, in the performance of work for the MHS, is under the direct control of the MHS, whether or not they are paid by the MHS. *MHS business associates* are persons or entities that provide a service to the MHS and require protected health information (PHI) to provide the service.

Are you an MHS workforce member?

◉ Yes, I am an MHS workforce member
○ No, I am not an MHS workforce member

10.5 Have you consulted with an MHS data expert to determine the data elements required for your study?

Consulting with a data expert often saves time later in the compliance process because the data expert can advise on the data available in the numerous MHS information systems, the quality of that data and the methods for encrypting and collapsing data. To schedule a consult with an MHS data expert, send an email to: (**DHA.PrivacyBoard@mail.mil**)

○ Yes, then complete the questions below according to the data consult
◉ No, then complete the questions below according to the best of your knowledge

10.6 Indicate how you will request data from the MHS. Select all that apply.

☐ Talking with MHS health care providers or MHS health plans about specific research participants
☐ Obtaining MHS hard copy records specific to research participants
☑ Obtaining data from an MHS information system(s)

10.7 If you are obtaining data from an MHS information system(s), indicate whether you plan to receive a data extract or whether you plan to access an MHS information system directly to create a data set.

A data extract is when the MHS or a contractor provides the data set directly to the researcher. When receiving a data set through data extract, the researcher may indicate whether the data elements should be provided as is, encrypted or collapsed. In contrast to a data extract, access to an information system means that the researcher may directly access an MHS information system and create a data set for the research study

☐ Data Extract
☑ Access

10.8 Do you intend to request de-identified data from the MHS in your research study?

There are different two methods for de-identifying data pursuant to HIPAA:
1) Safe Harbor Method: Removing all of the identifiers listed in Table 1 below, provided that the researcher does not have actual knowledge that the remaining data can be used alone or in combination with other information to identify the individual who is the subject of the information
2) Statistical Method: An expert, with appropriate knowledge of and experience with generally accepted statistical and scientific principles and methods for rendering information not individually identifiable, determines that the data is not individually identifiable

○ Yes ◉ No

10.9 Indicate the MHS information system(s) from which you will seek to obtain data

If you do not know which system(s) contains the data elements you need, refer to the Guide for DoD Researchers on Using MHS Data or request guidance from an MHS data expert at: **DHA.PrivacyBoard@mail.mil**.

Below is a list of commonly used MHS systems. If the system from which you seek to obtain data is not listed below, list the name of the system in the "Other MHS Systems" category below
PHI Systems:

MHS Information System	Requesting Data
: MHS Genesis	: Yes

PII-Only Systems:

MHS Information System	Requesting Data
No results found	

De-Identified Data & Other Systems:

Information System	Requesting Data
No results found	

10.10 Do you intend to merge or otherwise associate the requested data with data from any sources outside of the MHS, including other DoD systems that are not part of the MHS?

- ○ Yes, will merge data
- ◉ No, will not merge data

10.11 Indicate the data elements about research participants or relatives, employers, or household members of the research participants that you will request from MHS hard copies or from MHS information systems.
If you will merge data, also indicate non-MHS data elements about research participants or relatives, employers, or household members of the research participants that you will have access to in any form or medium.

Direct and Indirect Identifiable Data Elements	DHA Hard Copies	DHA Data Elements to be Accessed	DHA Data Elements Verbal	Extracted DHA Digital Data	Downloaded DHA Digital Data	Non-DHA Hard Copies or Digital
1. Names	☐	☑	☐	☐	☐	☐
2. Postal address with only town, city, state, and zip code	☐	☐	☐	☐	☐	☐
3. Postal address with all geographic subdivisions smaller than state, including street						

address, city, county, precinct, zip code and their equivalent geocodes, except for the initial three digits of a zip code if, according to the current publicly available data from the Bureau of Census: 1) the geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and 2) the initial three digits of a zip code from all such geographic units containing 20,000 or fewer people is changed to 000	☐	☐	☐	☐	☐	☐
4. Dates including all elements (except year) directly related to an individual, including birthdate, admission date, discharge date, and date of death	☐	☐	☐	☐	☐	☐
5. Ages over 89 and all elements of dates (including year) indicative of such age, unless you will only request a single	☐	☐	☐	☐	☐	☐

category of "age 90 or older"						
6. Telephone Numbers	☐	☑	☐	☐	☐	☐
7. Fax Numbers	☐	☐	☐	☐	☐	☐
8. Email Addresses	☐	☑	☐	☐	☐	☐
9. Social Security Numbers	☐	☐	☐	☐	☐	☐
10. Medical Record Numbers (MRN) (including record ID)	☐	☑	☐	☐	☐	☐
11. Health Plan Beneficiary Numbers (including DEERS ID, Electronic Data Interchange Personal Identifier (EDIPI) or Number (EDIPN))	☐	☐	☐	☐	☐	☐
12. Account Numbers	☐	☐	☐	☐	☐	☐
13. Certificate /License Numbers	☐	☐	☐	☐	☐	☐
14. Vehicle identifiers and serial numbers, including license plate numbers	☐	☐	☐	☐	☐	☐

15. Device identifiers and serial numbers	☐	☐	☐	☐	☐	☑
16. Web Universal Resource Locators (URLs)	☐	☐	☐	☐	☐	☐
17. Internet Protocol (IP) address numbers	☐	☐	☐	☐	☐	☐
18. Biometric identifiers, including finger and voice prints	☐	☐	☐	☐	☐	☐
19. Full-face photographic images and any comparable images	☐	☐	☐	☐	☐	☐
20. Any other unique identifying number, characteristic, or code (including non-military provider IDs)	☐	☐	☐	☐	☐	☑
21. Free Text Fields	☐	☐	☐	☐	☐	☐

If you are obtaining SSNs, provide a justification as to why and explain why a substitute cannot be used.

Due to guidelines stated within DoDI 1000.30, Reduction of SSN Use within DoD, the reduction or elimination of SSN usage must occur wherever possible. If SSNs are required to complete the project, the PI must provide a justification and explanation as to why a substitution cannot be used.
For example:

- If alternatives to SSN (e.g., EDIPNs or pseudo person IDs) are sufficient in other instances, will those alternatives to SSN usage be sufficient to respond to Congressional inquiries and /or Senior DoD stakeholders inquiries?
- Are alternatives to SSN used first?
- Are those alternatives to SSN insufficient to combine data from multiple data sources? Is

the issue that some individuals do not possess alternatives ID numbers and SSN is the only way to identify them?

a. Will you receive or obtain health information?

Note: *If you indicate you are not receiving health information, the answer must be consistent with the DHA data source. For a non-health information data request, if you are a non-MHS employee or non-MHS business associate, you may not access an information system that has PHI or LDS. For both MHS and Non-MHS employees and MHS business associates, you may* ***NOT*** *include data elements in the above table on: 1) lines 10 or 11, 2) line 21 if the free text field comes from a PHI or LDS system, and 3) lines 12, 13, or 18 if the account numbers, certificate and license numbers, biometric data, or any other data elements are health information created or received by an MHS health care provider, health plan, or business associate in relation to the physical or mental health or condition of an individual or payment for health care.*

- (●) Yes, I will receive or obtain health information
- ( ) No, I will not receive or obtain health information

b. If no data elements were checked in the above table, is it possible that the requested DHA data is or will be identifiable because of any unique data elements, triangulation, or small cell size?

- [x] Data elements were checked in the above table, STOP HERE.

NOTE: *A unique data element includes any unique features that alone are not identifiable but that could be used to identify an individual within the context of other information, such as any type of code (such as diagnosis or procedural), rank of general or admiral, gender, or race. Triangulation means using different data elements that when combined can be used to identify an individual, such as including the above lists of unique data elements in a data set. Determining whether an individual is identifiable through triangulation requires consideration of all data elements in combination. Within the military, the use of rank and/or diagnosis code, procedural codes, or any other code that changes on a predictable basis, increases the possibility of identification. Small cell size means that there is only a small number of eligible individuals that satisfy the category description. Department of Defense Manual 6025.13, Medical Quality Assurance and Clinical Quality Management in the Military Health System MHS, provides that the threshold for de-identifying data within the MHS requires a cell size of three, but also states that the de-identification standards must meet the DoD implementation of the HIPAA Privacy Rule. Centers for Medicare and Medicaid also gives guidance on small cell size stating that no data cell less than 11 may be published or displayed. However, the Office for Civil Rights' OCR, which is the official regulatory office for the HIPAA Privacy Rule, provides that OCR does not designate a universal value for small cell size in accordance with the de-identification standard; instead, the cell size should be set at a level that is appropriate to mitigate risk of identification by the anticipated recipient of the data set. This means that a cell size of 3 or 11 may not meet the HIPAA Privacy Rule requirements if the cell size level does not appropriately mitigate risk of identification by the anticipated recipient of the data set.*

Note: If dates are altered as a means of de-identifying the data, diagnosis and procedural codes need to be rolled-up or collapsed. If dates are provided "as time between events," the roll-up is not necessary.

- [ ] Yes, the DHA data will become identifiable
- [ ] No, the DHA data will not become identifiable

10.12 Do you believe it is possible for the MHS data to become identifiable because of triangulation, a small cell size, or any unique data element(s)?

Triangulation means using different data elements that are not themselves identifiable but that when combined can be used to identify an individual. For example, triangulation would use rank and race together to determine the identity of an individual with a particular health condition.

Small cell size means that there is only a small number of eligible individuals that satisfy the category description. Guidance for acceptable cell size is available from the Centers for Medicare and Medicaid Services. For example, the rank category of four star generals with a particular diagnosis may be less than 30, so the rank category may need to be expanded to include lower ranks.

A unique data element includes any unique features that are not explicitly enumerated in the categories of data in rows 1 – 20 of the table above (in Section 10.10), but that could be used to identify an individual. Unique data elements include characteristics that are not themselves identifying, such as the rank of general or admiral, or a race or gender, but within the context of other information could be identifiable.

- (●) Yes, I believe there is a reasonable possibility the MHS data will become identifiable
- ( ) No, I believe there is no reasonable possibility the MHS data will become identifiable

10.13 Have you completed and uploaded an appropriate HIPAA document (i.e. HIPAA Authorization will be obtained or Waiver/alteration of HIPAA Authorization is being requested)?

- (●) Yes
- ( ) No
- ( ) N/A

If yes, please check which one.

- [x] HIPAA Authorization
- [ ] HIPAA Waiver (Full or Partial)
- [ ] Other (please provide copies when uploading Other Study Documents)

10.14 Managing Data (Data Management and/or Sharing Plan) and/or Human Biological Specimens for this Study:

Include in this section the plan for acquiring data (both electronic and hard copy), access during the study, data/specimen storage and length of time stored, shipment/transmission, and the plan for storage and final disposition at the conclusion of the study. Describe any data agreements in place for accessing data within and/or outside of your institution (e.g., Data Sharing Agreement, Data Use Agreement, Business Agreements, etc.)

The SleepImage Ring application will track sleep metrics (sleep quality, sleep opportunity, sleep apnea, sleep pathology) and data will be stored in an online database accessible to the PIs and the subject. Data from the SleepImage Ring application will be tracked using an unidentifiable number generated by the app. Subject's personal email will be used as the account username and their password will be shared with the PIs and recorded in the Master Key in the case of lost passwords. SleepImage maintains the intellectual properties of subjects' sleep data, however all data will be managed according to SleepImage's privacy policy. PIs will download data directly from the subject portal to extract data. The Master Key of identifiable PII will be kept separately from a confidential password-protected research spreadsheet located and stored on a government computer that will only be accessible by the PI or AIs utilizing their Common Access Card (CAC). The spreadsheet will contain the subject's unique randomized study ID number. Additional information contained within this spreadsheet may include the type of periodontal surgery, the diagnosis and level of difficulty of the periodontal surgery, and the length of the procedure to be used in a statistical analysis. Subsequently, the subjects will be coded, using only their study number throughout the procedure and analysis. The government computer is CAC and PIN protected and contains system firewall protection. There is no intention of linking with external databases or systems nor will transmission of subject information and data for collaborative use be anticipated. Subject materials that do not contain subject identification will be maintained in a locked cabinet in a locked room. A copy of the study procedures specific to the subject will be placed in the subject's dental record. Once the study is complete, the subject information and data will not be utilized for further research or analysis beyond the protocol stipulations unless additional IRB approval is received. This document will be the only location identifying the subject with their study number. Upon study completion, the Master Key will be destroyed by deleting the spreadsheet from the hard drive of the government computer. All blood samples collected for L-PRF use will be discarded in a biohazard bin after the procedure. No blood samples will be stored for further investigative purposes.

Is this a data repository?

○ Yes ◉ No

10.15 Managing Data (Data Management and/or Sharing Plan) and/or Human Biological Specimens for Future Research:

If the study involves collecting, storing, or banking human specimens, data, or documents (either by the Investigator or through an established repository) for FUTURE research, address. How the specimens/data will be used, where and how data/specimens will be stored (including shipping procedures, storage plan, etc.), whether and how consent will be obtained, procedures that will fulfill subjects' request as stated in the consent, whether subjects may withdraw their data/specimens from storage, whether and how subjects may be recontacted for future research and given the option to decline, whether there will be genetic testing on the specimens, who will have access to the data/specimens, and the linkage, the length of time that data/specimens will be stored and conditions under which data/specimens will be destroyed.

N/A

Is this a data repository?

○ Yes ◉ No

11.0 Statistical/Data Analysis Plan

11.1 Statistical Considerations:

List the statistical methods to be used to address the primary and secondary objectives, specific aims, and/or research hypotheses. Explain how missing data and outliers will be handled in the analysis. The analysis plan should be consistent with the study objectives. Include any sub-group analyses (e.g., gender or age group). Specify statistical methods and variables for each analysis. Describe how confounding variables will be controlled in the data analysis

Statistical Analysis: All dichotomous or categorical variables will be presented initially as counts with percentages. Any analysis looking at two dichotomous or categorical variables will be compared using Chi-Square test. Continuous outcome variables will be initially assessed for normality by the Shapiro-Wilks test and then presented as means with standard deviations if normally distributed; independent t-test will be used determine any group differences between such variables (i.e. post-surgery – pre-surgery) or an ANOVA for three or more normally distributed variables. Otherwise, non-normally distributed outcomes will be presented as median and interquartile range (IQR) and analyzed using Wilcoxon Sign-Ranked Test or Mann-Whitney U Test for three or more variables. To test the relationship between QoL, sleep quality, healing outcomes, and intervention use, adjusted linear regression will be performed with guidance from a biostatistician. Significance will be set to $p < 0.05$. Any additional data collection or analyses will be determined in coordination and consultation with other investigators and the biostatistician through Qualtrics® and SleepImage® software. Subgroup analyses will be conducted in subjects with the following conditions: anxiety or depressive medications, smoking, sleep apnea, pulmonary disease, diabetes, autoimmune disorders, and chronic pain management as well as subject age and sex.

11.2 Sample Size:

Sample Size Estimation/Power Analysis:

The required sample size is 80, 40 subjects will receive the standard treatment and 40 the experimental intervention. It was calculated by using a priori analysis to provide a power of 80%, false positive rate of 5%, a 10% margin of error, and a 10% calculated dropout rate.

11.3 Total number of subjects requested (including records and specimens):

80

11.4 If you are recruiting by study arm, please identify the arms of the study and how many subjects will be enrolled in each arm

11.5 Please provide a justification for your sample size

Sample Size Estimation/Power Analysis:

The required sample size is 80, 40 subjects will receive the standard treatment and 40 the experimental intervention. It was calculated by using a priori analysis to provide a power of 80%, false positive rate of 5%, 10% margin of error, and 10% calculated drop-out rate.

11.6 Data Analysis Plan: Complete description: Background, Objectives, Design, Step by Step how the project is going to be done, Data analysis plan:

Statistical Analysis: All dichotomous or categorical variables will be presented initially as counts with percentages. Any analysis looking at two dichotomous or categorical variables will be compared using Chi-Square test. Continuous outcome variables will be initially assessed for normality by the Shapiro-Wilks test and then presented as means with standard deviations if normally distributed; independent t-test will be used determine any group differences between such variables (i.e. post-surgery – pre-surgery) or an ANOVA for three or more normally distributed variables. Otherwise, non-normally distributed outcomes will be presented as median and interquartile range (IQR) and analyzed using Wilcoxon Sign-Ranked Test or Mann-Whitney U Test for three or more variables. To test the relationship between QoL, sleep quality, healing outcomes, and intervention use, adjusted linear regression will be performed with guidance from a biostatistician. Significance will be set to $p < 0.05$. Any additional data collection or analyses will be determined in coordination and consultation with other investigators and biostatistician.

12.0 Participant Information

12.1 Subject Population:

Sample population: 80 non-emergency subjects (active-duty, retired, dependents, retired-dependents) at the USAF Graduate Periodontics Program, Lackland AFB, Texas. Subjects who meet the eligibility requirements listed below will be offered the opportunity to participate in the study. If the subject agrees to participate, they will complete an informed consent.

12.2 Age Range:

Check all the boxes that apply. if the age range of potential subjects (specimens, records) does not match the range(s) selected, please specify in the text box.

- ☐ 0-17
- ☑ 18-24
- ☑ 25-34
- ☑ 35-44
- ☑ 45-54
- ☑ 55-64
- ☑ 65-74
- ☑ 75+

18-99

12.3 Gender:

- [x] Male
- [x] Female
- [ ] Other

12.4 Special categories, check all that apply

- [ ] Minors /Children
- [ ] Students
- [ ] Employees - Civilian
- [ ] Employees - Contractor
- [ ] Resident/trainee
- [ ] Cadets /Midshipmen
- [x] Active Duty Military Personnel
- [ ] Wounded Warriors
- [ ] Economically Disadvantaged Persons
- [ ] Educationally Disadvantaged Persons
- [ ] Physically Challenged (Physical challenges include visual and/or auditory impairment)
- [ ] Persons with Impaired Decisional Capacity
- [ ] Prisoners
- [ ] Pregnant Women, Fetuses, and Neonates
- [ ] Non-English Speakers
- [ ] International Research involving Foreign Nationals - Headquarters Review is necessary

You must also consider the requirements of DoDI 3216.02, Enclosure 3, paragraph 7.e.

12.5 Inclusion Criteria:

Order Number	Criteria
1	1. Age 18-99 2. Require a mucogingival periodontal surgery procedure 3. Have not taken antibiotics for one month 4. Are planned for non-emergent periodontal surgery 5. Are American Society of Anesthesiologists (ASA) Class I, II, III

12.6 Exclusion Criteria:

Order Number	Criteria
1	1. <18 years old, > 100 years of age 2. Currently pregnant or within 6 months postpartum 3. Female subjects who are nursing 4. Subjects who are decisionally challenged 5. ASA Class IV 6. Have undergone antibiotic therapy within one month prior to enrollment 7. Have undergone chronic therapy within one month prior to enrollment with medications that could affect periodontal status or healing. 8. Incompatible mobile device

13.0 Recruitment and Consent

13.1 Please describe the recruitment process, including how subjects will be identified and selected for the study.

Subjects will be screened based upon the inclusion and exclusion criteria as they present for evaluation for periodontal surgery. The daily appointment schedule will be reviewed to determine possible research candidates. Potential candidates will be either approached by the research team or will be verbally referred to the research team by the treating doctor. The study will then be explained to the potential subject in a safe and private location by a member of the research team. Subjects who meet the inclusion criteria will be approached by the PI or AIs and asked if they wish to participate in the study. Following explanation of the study and providing the subject a reasonable amount of time to make an informed decision, the informed consent for the study will be completed and the subject scheduled for surgery. A subject's verbal or written authorization must precede any physician referrals to the research team for possible recruitment and study participation.

13.2 Compensation for Participation:

Subjects will not be paid for participation in this study

13.3 Please describe the pre-screening process. If no pre-screening, enter Not Applicable in the text editor

Subjects referred to the Air Force Post-Graduate Dental School Clinic for periodontal surgery that meet the inclusion criteria and do not meet any exclusion criteria for this protocol will be approached by the PI or AIs for potential enrollment during their pre-surgical evaluation. The daily appointment schedule will be reviewed to determine possible research candidates. Potential candidates will be either approached by the research team or will be verbally referred to the research team by the treating doctor. The study will then be explained to the potential subject in a safe and private location by a member of the research team. A subject's verbal or written authorization must precede any physician referrals to the research team for possible recruitment and study participation. The study will then be explained to the potential subject in a safe and private location and smartphone compatibility will be determined for each subject.

13.4 Consent Process: Revised Common Rule, Section 219.116: General requirements for informed consent, whether written or oral, are set forth in this paragraph and apply to consent obtained in accordance with the requirements set forth in paragraphs (b) through (d) of this section. Broad consent may be obtained in lieu of informed consent obtained in accordance with paragraphs (b) and (c) of this section only with respect to the storage, maintenance, and secondary research uses of identifiable private information and identifiable biospecimens.

Are you requesting a waiver or alteration of informed consent?

○ Yes ◉ No

Please explain the consent process:

A copy of the informed consent document will be given to the patient. During the pre-op appointment, the PI will review the terms of service for the application. Benefits, risks, and complications of participation in the study will be explained to the patient so that they best understand their proposed role in the research and what to expect. After the patient has read and understood the informed consent document, he/she will be given the opportunity to discuss the opportunity to participate in the study with friends and/or family. The PI or AIs will be available to answer any questions regarding the study. The patient will then accept or decline participation in the study. If they accept, the patient will sign the informed consent form and research-related HIPAA Authorization Document. The consenting investigator will sign the informed consent form and will attest that the informed consent process was followed, the patient understood the information contained in the informed consent, and that the patient voluntarily gave their consent for participation in the study. The subject will receive a copy of the signed informed consent document and the HIPAA Authorization Document and a second copy of

each will be placed in the research record of the subject. The consenting investigator will document the informed consent process in the research record as well as the dental record of the patient.

13.5 DoDI 3216.02 requires an ombudsman to be present during recruitment briefings when research involves greater than minimal risk and recruitment of Service members occurs in a group setting. If applicable, you may nominate an individual to serve as the ombudsman.

- (•) N/A
- ( ) Propose ombudsman

13.6 Withdrawal from Study Participation:

Explain the process for withdrawal and specify whether or not the subjects will be given the opportunity to withdraw their data their data/specimens in the event they wish to withdraw from the study

At any time during the study, the subject can request to be withdrawn and have their data withdrawn. If they chose to withdraw, their surgical procedure will be continued as planned without participating in the study and subjects can remove their data from the device application.

14.0 Risks and Benefits

14.1 Risks of Harm:

Identify all research-related risks of harm to which the subject will be exposed for each research procedure or intervention as a result of participation in this study. Consider the risks of breach of confidentiality, psychological, legal, social, and economic risks as well as physical risks. Do not describe risks from standard care procedures; only describe risks from procedures done for research purposes

Potential risks associated with mucogingival surgery are that some subjects could experience bleeding, bruising, and possible infection. There is a risk of graft failure and palatal tissue necrosis. Additionally, there is a risk that the L-PRF will not reduce the subject's pain. There is a risk for potential pain, discomfort, bruising, and swelling at the site of the blood draw. Additionally, there is a risk for breach in confidentiality, since identifiable PII will be obtained for each subject. The SleepImage ring may disrupt sleep due to the vexation caused by the new wearable device.

14.2 Measures to Minimize Risks of Harm (Precautions, safeguards):

For each research procedure or intervention, describe all measures to minimize and/or eliminate risk of harms to subjects and study personnel

The patient will be monitored for approximately 15-30 minutes following surgery. The operating resident and periodontics faculty are
readily available and well-trained in the treatment of medical emergencies related to periodontal surgery. The mucogingival surgery and L-PRF blood draw will be completed by a credentialed provider and/or periodontal resident. Any injury or adverse effects, appropriate clinical care will be given or the subject will be referred to the appropriate provider.

14.3 Confidentiality Protections (for research records, data and/or specimens):

Describe in detail the plan to maintain confidentiality of the research data, specimens, and records throughout the study and at its conclusion (e.g., destruction, long term storage, or banking). Explain the plan for securing the data (e.g., use of passwords, encryption, secure servers, firewalls, and other appropriate methods). If data will be shared electronically with other team members/collaborators outside the institution, describe the method of transmission and safeguards to maintain confidentiality. Explain whether this study may collect information that State or Federal law requires to be reported to other officials or ethically requires action, e. g., child or spouse abuse

The randomized subject log (Master Key of identifiable PII) will be kept separately from a confidential password-protected research spreadsheet located and stored on a government computer that will only be accessible by the PI or AIs utilizing their Common Access Card (CAC). The research spreadsheet will contain the subject's unique randomized study ID number. Additional information contained within this research spreadsheet may include the type of periodontal surgery, the diagnosis and level of difficulty of the periodontal surgery, and the length of the procedure to be used in a statistical analysis. Subsequently, the subject will be coded, using only their study number throughout the procedure and analysis. The government computer is CAC and PIN protected and contains system firewall protection. There is no intention of linking with external databases or systems nor will transmission of subject information and data for collaborative use anticipated. Subject materials that do not contain subject identification will be maintained in a locked cabinet in a locked room. A copy of the study procedure (periodontal surgery performed) specific to the subject will be placed in the subject's dental record. During the sleep data collection period, the application will store the subject's sleep parameters as previously discussed. Once the study is complete, the subject information and data will not be utilized for further research or analysis beyond the protocol stipulations unless additional IRB approval is received. This document will be the only location identifying the subject with their study number.Data from the SleepImage Ring application will be tracked using an unidentifiable number generated by the app. Subject's personal email will be used as the account username and their password will be shared with the PIs and recorded in the Master Key in the case of lost passwords. SleepImage maintains the intellectual properties of subjects' sleep data, however all data will be managed according to SleepImage's privacy policy (**http://sleepimage.com/privacy-policy/**). In their privacy policy, SleepImage sates that all subjects have the right to object and erasure, the policy states that subjects have the right to "stop processing and delete personally identifiable data."

14.4 Potential Benefits:

Describe any real and potential benefits of the research to the subject and any potential benefits to a specific community or society

If the individuals in the research are considered experimental subjects (per 10 USC 980), and they cannot provide their own consent, the protocol must describe the intent to directly benefit all subjects

There are no direct benefits to the patients for participating in this study. However, patients may benefit from reduction of post-operative pain and reduction of post-operative consumption of pain medications. The use of L-PRF may also potentially enhance the healing process and improve surgical outcomes for future subjects.

14.5 Privacy for Subjects:

Describe the measures to protect subject's privacy during recruitment, the consent process, and all research activities, etc.

The study will be explained to the potential subject in a safe and private location. The subject will be given a copy of the informed consent document and HIPAA authorization document to review

on their own time at home. Throughout all clinic visits and research procedures, the subject will be in a private dental treatment room. All study related materials will be kept in a private office, on a private computer that is Common Access Card (CAC) accessible only. Additionally, the Master Key of identifiable PII and the research spreadsheet containing data will be password protected and kept totally separate from each other, both physically and electronically. As stated above, PII is stored by SleepImage, for as long as they deem necessary. However, subjects have individual rights to object and erasure of all personally identifiable data.

14.6 Incidental or Unexpected Findings:

Describe the plan to address incidental findings and unexpected findings about individuals from screening to the end of the subject's participation in the research. In cases where the subject could possibly benefit medically or otherwise from the information, state whether or not the results of screening, research participation, research tests, etc., will be shared with subjects or their primary care provider. State whether the researcher is obligated or mandated to report results to appropriate military or civilian authorities and explain the potential impact on the subject

Throughout the duration of the study, any incidental findings will be discussed with the patient just as they would during any routine dental visit. Depending on if the incidental finding is within the same surgical area of study involvement, then the discussion would be made whether or not to have the patient proceed in the study or withdrawal the patient from the study. If it is a finding that is warranted to consult with the patient's primary care provider, that would be addressed at that time.

15.0 Study Monitoring

15.1 Your study requires either Data and Safety Monitoring Plan (DSMP) or a Data and Safety Monitoring Board (DSMB).

- ○ DSMP
- ○ DSMB
- ○ Both
- ◉ Not Applicable

16.0 Reportable Events

16.1 Reportable Events: Consult with the research office at your institution to ensure requirements are met. Describe plans for reporting unexpected adverse events and unanticipated problems. Address how unexpected adverse events will be identified, who will report, how often adverse events and unanticipated problems will be reviewed to determine if any changes to the protocol or consent form are needed and the scale that will be used to grade the severity of the adverse event.

Consult with the research office at your institution to ensure requirements are met

• Describe plans for reporting expected adverse events. Identify what the expected adverse events will be for this study, describe the likelihood (frequency, severity, reversibility, short-term management and any long-term implications of each expected event)

• Describe plans for reporting unexpected adverse events and unanticipated problems. Address how unexpected adverse events will be identified, who will report, how often adverse events and unanticipated problems will be reviewed to determine if any changes to the research protocol or consent form are needed and the scale that will be used to grade the severity of the adverse event

Subjects will be monitored preoperatively, perioperatively and postoperatively in the Air Force Post-Graduate Dental School. The subject will be monitored for approximately 15-30 minutes following mucogingival surgery. The subject will be monitored and appropriate emergency medical treatment will be delivered by the resident, or faculty in the event of any adverse reactions.
The operating resident and periodontics faculty are readily available and well-trained in the treatment of medical emergencies related to periodontal surgery. The mucogingival surgery and L-PRF blood draw will be completed by any current Air Force periodontal resident or staff member. Post-operative healing assessment will be completed by principle investigators only. If at any time a subject experiences any injury or adverse effects, appropriate clinical care will be given or the subject will be referred to the appropriate provider.
All events requiring prompt reporting will be sent within three (3) business days of the research team's knowledge of the event by phone (210-916-2598) or by e-mail (usarmy.jbsa.medcom-bamc.mbx.bamc-irb@health.mil) to the office of the San Antonio Institutional Review Board. A complete written report will follow the initial notification within ten (10) business days.

17.0 Equipment/non-FDA Regulated Devices

17.1 Does the study involve the use of any unique non-medical devices/equipment?

○ Yes ◉ No

18.0 FDA-Regulated Products

18.1 Will any drugs, dietary supplements, biologics, or devices be utilized in this study?

- ☐ Drugs
- ☐ Dietary Supplements
- ☐ Biologics
- ☑ Devices
- ☐ N/A

18.3 Device Details:

- ☑ Are device(s) in this research being used in accordance to the approved labeling?
- ☐ Are device(s) in this research being used in a manner other than its approved labeling?

When adding a device indicate in the details section of the device if the use is either used in accordance to the approved labeling or in a manner other than it's approved labeling

View Details	Device Name
⊟	SleepImage Ring

Manufacturer/Supplier of Device	SleepImage
Where will the Devices Be Stored	AFPDS with the PI
Will Devices be supplied at no Cost	Yes
Is this a HUD (HDE)	No
HDE Number	
Who holds the IDE	PI holds the IDE

IDE details	Device measures sleeping patterns in subjects one week prior to surgery and two weeks post-operatively. This will be used in accordance to its FDA approved label.

18.4 Reporting Requirements for FDA-regulated research under IND and IDE:

Describe the process for complying with FDA regulatory requirements for adverse event reporting and adverse device effects reporting to the sponsor

SleepImage ring is strictly used as a monitoring device in this study and sleep efficiency results will be reported to the primary care provider in the case of adverse reporting.

18.5 Sponsor (organization/institution/company):

☑ N/A

If applicable, provide sponsor contact information:

Kathy Hiser
kathy.hiser@SleepImage.com
720-708-4207 (office)
719-221-2788 (mobile)

19.0 Research Registration Requirements

19.1 ClinicalTrials.gov Registration:

- ◉ Registration is not required
- ○ Registration pending
- ○ Registration complete

19.2 Defense Technical Information Center Registration (Optional):

- ◉ Registration is not required
- ○ Registration pending
- ○ Registration complete

20.0 References and Glossary

20.1 References:

[1] P.M. Bartold, L.J. Walsh, A.S. Narayanan, Molecular and cell biology of the gingiva, Periodontology 2000 24(1) (2000) 28-55.

[2] O. Al-Bayati, K. Font, N. Soldatos, E. Carlson, J. Parsons, C.A. Powell, Evaluation of the need to prescribe opioid medication to control post-surgical pain of different periodontal/oral surgeries, J Periodontol 92(7) (2021) 1030-1035.

[3] M.R. Daian, A. Petroianu, L.R. Alberti, E.E. Jeunon, [Stress in surgeries], Arq Bras Cir Dig 25 (2) (2012) 118-24.

[4] C. Song, J. Wang, B. Kim, C. Lu, Z. Zhang, H. Liu, H. Kang, Y. Sun, H. Guan, Z. Fang, F. Li, Insights into the Role of Circadian Rhythms in Bone Metabolism: A Promising Intervention Target?, Biomed Res Int 2018 (2018) 9156478.

[5] W.S. Livingston, H.L. Rusch, P.V. Nersesian, T. Baxter, V. Mysliwiec, J.M. Gill, Improved Sleep in Military Personnel is Associated with Changes in the Expression of Inflammatory Genes and Improvement in Depression Symptoms, Front Psychiatry 6 (2015) 59.

[6] K.N. Kunze, K. Movasagghi, D.M. Rossi, E.M. Polce, M.R. Cohn, A.V. Karhade, J. Chahla, Systematic Review of Sleep Quality Before and After Arthroscopic Rotator Cuff Repair: Are Improvements Experienced and Maintained?, Orthop J Sports Med 8(12) (2020) 2325967120969224.

[7] J.S. Park, Y. Jeong, J. Jung, J.J. Ryu, H.K. Lim, S.K. Jung, I.S. Song, Shift work sleep disorder is closely associated with an increased risk for periodontal disease, J Clin Periodontol 48 (8) (2021) 1066-1075.

[8] S. Magnusdottir, H. Hilmisson, R.J. Thomas, Cardiopulmonary coupling-derived sleep quality is associated with improvements in blood pressure in patients with obstructive sleep apnea at high-cardiovascular risk, J Hypertens 38(11) (2020) 2287-2294.

[9] M.H. Bonnet, D.L. Arand, We are chronically sleep deprived, Sleep 18(10) (1995) 908-11.

[10] C. Theodoridis, A. Violesti, M. Nikiforidou, G.C. Menexes, I.D. Vouros, Short-Term Impact of Non-Surgical and Surgical Periodontal Therapy on Oral Health-Related Quality of Life in a Greek Population-A Prospective Cohort Study, Dent J (Basel) 8(2) (2020).

[11] D.A. Shugars, M.A. Gentile, N. Ahmad, M.F. Stavropoulos, G.D. Slade, C. Phillips, S.M. Conrad, P.T. Fleuchaus, R.P. White, Jr., Assessment of oral health-related quality of life before and after third molar surgery, J Oral Maxillofac Surg 64(12) (2006) 1721-30.

[12] S.K. Ng, W.K. Leung, Oral health-related quality of life and periodontal status, Community Dent Oral Epidemiol 34(2) (2006) 114-22.

[13] L. Sischo, H.L. Broder, Oral health-related quality of life: what, why, how, and future implications, J Dent Res 90(11) (2011) 1264-70.

[14] A. Makino-Oi, Y. Ishii, T. Hoshino, N. Okubo, H. Sugito, Y. Hosaka, C. Fukaya, T. Nakagawa, A. Saito, Effect of periodontal surgery on oral health-related quality of life in patients who have completed initial periodontal therapy, J Periodontal Res 51(2) (2016) 212-20.

[15] A. Bäumer, D. Kappesz, A.K. Ozga, C. Mertens, P. Eickholz, B. Pretzl, Oral health-related quality of life and standard of treatment in aggressive periodontitis patients more than 5 years after therapy, J Clin Periodontol 45(11) (2018) 1347-1355.

[16] A. Saito, K. Ota, Y. Hosaka, M. Akamatsu, H. Hayakawa, C. Fukaya, A. Ida, K. Fujinami, H. Sugito, T. Nakagawa, Potential impact of surgical periodontal therapy on oral health-related quality of life in patients with periodontitis: a pilot study, J Clin Periodontol 38(12) (2011) 1115-21.

[17] J. Meza-Mauricio, C.P. Furquim, A. Geldres, G. Mendoza-Azpur, B. Retamal-Valdes, V. Moraschini, M. Faveri, Is the use of platelet-rich fibrin effective in the healing, control of pain, and postoperative bleeding in the palatal area after free gingival graft harvesting? A systematic review of randomized clinical studies, Clin Oral Investig 25(7) (2021) 4239-4249.

[18] R. Pippi, Post-Surgical Clinical Monitoring of Soft Tissue Wound Healing in Periodontal and Implant Surgery, Int J Med Sci 14(8) (2017) 721-728.

[19] M.A. Bahammam, Effect of platelet-rich fibrin palatal bandage on pain scores and wound healing after free gingival graft: a randomized controlled clinical trial, Clin Oral Investig 22(9) (2018) 3179-3188.

[20] O. Osagie, B.D. Saheeb, E.P. Egbor, Do the bioactive effects of platelet-rich plasma and platelet-rich fibrin influence the oral health related quality of life following impacted third molar surgery? A randomized comparative study, Niger J Clin Pract 24(5) (2021) 712-717.

[21] A. Lektemur Alpan, G. Torumtay Cin, PRF improves wound healing and postoperative discomfort after harvesting subepithelial connective tissue graft from palate: a randomized controlled trial, Clin Oral Investig 24(1) (2020) 425-436.

[22] C.E. Abad, I. Sanz-Sanchez, V. Serrano, J. Sanz Esporrin, I. Sanz-Martin, M. Sanz, Efficacy of the application of leukocyte and platelet-rich fibrin (L-PRF) on alveolar ridge preservation. A randomized controlled clinical trial, Clin Implant Dent Relat Res 25(3) (2023) 592-604.

[23] R.P. Bartsch, A.Y. Schumann, J.W. Kantelhardt, T. Penzel, P. Ivanov, Phase transitions in physiologic coupling, Proc Natl Acad Sci U S A 109(26) (2012) 10181-6.

[24] F. US, SleepImage System (K182618) Indications for Use, 2021.

[25] G. Barbato, REM Sleep: An Unknown Indicator of Sleep Quality, Int J Environ Res Public Health 18(24) (2021).

[26] F. US, FDA US. Software as a Medical Device (SaMD), 2021.

20.2 Abbreviations and Acronyms:

L-PRF: Leukocyte-platelet-rich fibrin
QoL: Quality of Life
SQI: Sleep Quality Index
CPC: Cardiopulmonary Coupling
ANOVA: Analysis of Variance
IQR: Interquartile Range
PI: Primary Investigator
PII: Personal Identifiable Information
AI: Additional Investigator