Human Subjects Protocol (HSP)

Form Version: June 25, 2015

- **You are applying** for IRB review of the research described in this form.
- **To avoid delay**, respond to all items in order and include all required approvals and documents.
- **To complete the form**, click the underlined areas and type or paste in your text; double-click checkboxes to check/uncheck. For more tips, see www.uab.edu/irb/forms .
- **Mail or deliver all materials to AB 470**, 701 20th Street South, Birmingham, AL 35294-0104.

Indicate the type of review you are applying for:

☒ Convened (Full) IRB *or*

☐ Expedited—See the Expedited Category Review Sheet, and indicate the category(ies) here: ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7

1. IRB Protocol Title: Assessment of the Efficacy of Orthodontic Tooth Movement Using the Aerodentis System

2. Investigator, Contacts, Supervisors

a. Name of Principal Investigator: Dr. Chung How Kau
Degree(s)/Title: BDS, MScD, MBA, PhD, FAMS (Ortho), FFD (Ortho), Professor and Chair
BlazerID: ckau Dept/Div: Orthodontics Mailing Address: SDB 305 UAB ZIP: 35294-0007
Phone: 205-934-1289 Fax: ____ E-mail: ckau@uab.edu

b. Name of Contact Person: Brooke Brasher Title: Research Associate Phone: 205-975-3336
E-mail: bbrasher@uab.edu Fax: ____
Mailing Address (if different from that of PI, above): ____

INVESTIGATOR ASSURANCE STATEMENT & SIGNATURE

By my signature as Principal Investigator, I acknowledge my responsibilities for this Human Subjects Protocol, including:

- Certifying that I and any Co-Investigators or Other Investigators comply with reporting requirements of the UAB Conflict of Interest Review Board;
- Certifying that the information, data, and/or specimens collected for the research will be used, disclosed and maintained in accordance with this protocol and UAB policies;
- Following this protocol without modification unless (a) the IRB has approved changes prior to implementation or (b) it is necessary to eliminate an apparent, immediate hazard to a participant(s);
- Verifying that all key personnel listed in the protocol and persons obtaining informed consent have completed initial IRB training and will complete continuing IRB training as required;
- Verifying that all personnel are licensed/credentialed for the procedures they will be performing, if applicable;
- Certifying that I and all key personnel have read the *UAB Policy/Procedure to Ensure Prompt Reporting of Unanticipated Problems Involving Risks to Subjects or Others to the IRB, Institutional Officials, and Regulatory Agencies* and understand the procedures for reporting;
- Applying for continuing review of the protocol at least annually unless directed by the IRB to apply more frequently;
- Conducting the protocol as represented here and in compliance with IRB determinations and all applicable local, state, and federal law and regulations; providing the IRB with all information necessary to review the protocol; refraining from protocol activities until receipt of initial and continuing formal IRB approval.

Signature of Investigator: _____ **Date:** 7/14/16

3. Protocol Personnel

Including the PI, list all key personnel (each individual involved in the design and conduct of this protocol including recruitment, informed consent, analysis of the data, and reporting of the results). Complete either the UAB (3.a.) or non-UAB (3.b) table, as applicable. Use the checkboxes to show each person's role, whether the investigator has financial interests as defined by the UAB CIRB, and briefly describe the individual's responsibilities for the research and qualifications to perform those responsibilities. Insert additional rows as needed.

FDA: For studies involving investigational drugs, list all investigators who will be listed on FDA Form 1572 and include a copy of the 1572. Send the IRB a copy of Form 1572 any time you update the form with the FDA.

a. UAB Personnel

Name	Blazer ID	Role	Financial Interest?*	Protocol Responsibilities and Qualifications
Dr. Chung H Kau	ckau	Principal Investigator	☒ No ☐ Yes	IRB training; collection and analysis of data Oversight of all aspects of study.
Dr. Ejvis Lamani	ejvis	☒Sub-Investigator ☐Other	☒ No ☐ Yes	IRB training; collection and analysis of data
Dr. Terpsithea Christou	tetich	☒ Sub-Investigator ☐ Other	☒ No ☐ Yes	IRB training; collection and analysis of data
Brooke N Brasher	bbrasher	☐ Sub-Investigator ☒ Other	☒ No ☐ Yes	IRB training; patient consent and coordination of study
		☐ Sub-Investigator ☐ Other	☐ No ☐ Yes	
		☐ Sub-Investigator ☐ Other	☐ No ☐ Yes	

*** Financial Interest** – for each investigator listed above, answer **Yes** or **No** as to whether the investigator or an immediate family member has any of the following:

- An ownership interest, stock options, or other equity interest related to the investigator's institutional responsibilities of any value.
- Compensation greater than $5,000 in the previous two years when aggregated for the immediate family
- Proprietary interest including, but not limited to, a patent, trademark, copyright, or licensing agreement.
- Board of executive relationship, regardless of compensation.
- Any other Financial Interest as defined by the UAB CIRB.

If the investigator has a Financial Interest, a disclosure has to be made to the UAB CIRB. A completed CIRB evaluation has to be available before the IRB will complete its review.

b. Non-UAB Personnel - Include individuals who will interact or intervene with participants, obtain consent, or have access to private, identifiable information for research purposes.

Name	Title	Do the Non-UAB personnel have their own IRB approval?	Financial Interest?*	Protocol Responsibilities and Qualifications
Name: Institution:	☐ Sub-Investigator ☐ Other	☐ No - UAB IRB will determine if they are engaged in research. ☐ Yes - attach IRB approval	☐ No ☐ Yes	

c. Do the investigators listed above include any students using this research for their thesis or dissertation?

☒ No, continue with Item 3.d.
☐ Yes, complete the following

Student Name	Thesis/Dissertation Title

d. Is the principal investigator a student, fellow, or resident? ☐Yes ☒No

If Yes, complete items below and obtain signature of faculty advisor or supervisor:

Supervisor's Name: ____
Degree(s) / Job Title: ____
Additional Qualifications pertinent to the study: ____
Telephone: ____
E-Mail: ____
Signature: ____

e. Describe the principal investigator's activities related to this protocol and provisions made by the PI to devote sufficient time to conduct the protocol: **Dr. Kau will show whether or not the Aerodentis device reduces orthodontic treatment time by comparing the time for standard orthodontic treatment to the actual time observed with Aerodentis use.**

f. Is medical supervision required for this research? ☐Yes ☒No

If Yes, who will provide the supervision?

☐ PI will provide -*OR*- Name:____ Telephone:____

If other than PI, obtain signature of person providing medical supervision:

Signature _____

g. Describe the process that ensures that all persons assisting with the research are adequately informed about the protocol and their research-related duties and functions: **Dr. Kau has had extensive training and experience in orthodontic research. Dr. Kau has been in frequent contact with members of the Aerodentis team and has helped in writing the proposal for this study. He has kept in touch through weekly email correspondence and multiple conference calls. Dr. Kau has also visited Aerodentis headquarters in Israel to learn about their orthodontic system. Dr. Kau will train all UAB team members included in research. Dr. Kau and co-investigators will assess the efficacy and safety of the Aerodentis system for orthodontic tooth movement and alignment.**

4. Funding

Is this study funded? ☒Yes ☐No

If No, specify that costs of the study will be covered by funds from the UAB department or other source named:____

If Yes, attach one copy of completed application or request for funding sent to sponsor, and complete a-d.

a. Title of Grant or Contract: **Assessment of the Efficacy of Orthodontic Tooth Movement Using the Aerodentis System**

b. PI of Grant or Contract: **Dr. Chung How Kau**

c. Office of Sponsored Programs Proposal Number: **000513374**
(*or enter "Pending" and provide upon receipt from OSP*)

d. Sponsor, Funding Route (*check and describe all that apply*):

☐ Gov't Agency or Agencies—Agency name(s):____
- ☐ Department of Defense (DoD): Identify DoD component:____
- ☐ Department of Energy (DOE)
- ☐ Department of Justice (DOJ)
- ☐ Department of Education

☐ NIH Coop. Group Trial—Group name:____

☐ Private Nonprofit (e.g., Foundation)—Name:____

☒ Industry, investigator-initiated—Name: **Dror Ortho-Design Ltd.** Describe the funding arrangement: **We are utilizing a UAB Clinical Trials Agreement between the Board of Trustees and Dror Ortho-Design Ltd.**
Note. Western IRB reviews industry-sponsored protocols unless the investigator initiated the research, or the study qualifies for expedited review or involves gene therapy.

☐ UAB Departmental/Division Funds—Specify:____

5. Locations Involved

a. Describe the facilities available for the conduct of the research. For research on UAB campus, include building names and room numbers: **UAB School of Dentistry, Department of Orthodontics Clinic, SDB 305**

b. Indicate all "performance sites" that will provide space, services, facilities, potential or actual participants, or other support for this protocol.

- ☐ The Kirklin Clinic (TKC)
- ☐ University of Alabama Hospital (UAHosp)
- ☐ The Children's Hospital of Alabama (TCHA)
- ☐ Callahan Eye Foundation Hospital (CEFH)
- ☐ UAB Highlands
- ☐ Jefferson County Dept. of Health (JCDH)
- ☐ Birmingham Veterans Affairs Medical Center (BVAMC)
- ☐ General Clinical Research Center (GCRC)—inpatient
- ☐ General Clinical Research Center (GCRC)—outpatient
- ☐ General Clinical Research Center (GCRC) at The Kirklin Clinic (TKC)
- ☐ Other (i.e., Any performance site not listed above, including those covered by subcontracts related to this protocol)—Describe:____

c. Is this study a clinical trial requiring clinical services at one of the performance sites listed in Item b above? ☐Yes ☒No
If Yes, Fiscal Approval Process (FAP)-designated units complete a FAP submission and send to fap@uab.edu. For more on the UAB FAP, see www.uab.edu/osp/clinical-billing-review.

d. Is this a field study? ☐Yes ☒No
If Yes, describe the community and include information about how the community will be involved in the design, implementation and analysis of the research. This would include focus groups, training local facilitators/community health advisors:____

e. Is the study to be undertaken within a school, business, or other institution that does not have an institutional review board? ☐Yes ☒No
If Yes, attach a statement of any contacts with and approvals from the appropriate institution officials.
Note. Documentation of all such approvals must be received by the UAB OIRB before IRB approval will be issued.

f. Has this protocol or project been reviewed by another IRB, similar review board, or departmental review committee(s) that authorizes the use of its patient populations? ☐Yes ☒No
If Yes, provide name of the review board(s):____ and for each board listed, enter either the date of latest approval(s) or "PENDING":____ or reasons not approved:____. *If this protocol is subsequently rejected or disapproved by another review board, the UAB IRB must be notified promptly.*
Attach copies of approvals/disapprovals.

g. Will any of the participants be from the Birmingham Veterans Affairs Medical Center? ☐Yes ☒No

If Yes, attach VA IRB approval or notification from the VA Research and Development Department that the study has been submitted to the VA IRB for review.

h. Will the study be conducted at or recruit participants from the Jefferson County Department of Public Health (JCDH)? ☐Yes ☒No
If Yes, attach notification that the protocol has been approved by JCDH or the Alabama Department of Public Health IRB.

6. Multi-Site Studies

a. Is the investigator the lead investigator of a multi-site study? ☐Yes ☒No
b. Is UAB a coordinating site in a multi-site study? ☐Yes ☒No
c. If you answered **Yes** to *a* or *b*, describe the management of information obtained in multi-site research that might be relevant to the protection of participants. Include, at a minimum, the following items:

- IRB approvals from other sites
- Unanticipated problems involving risks to participants or others. (For example, if there is an unanticipated problem involving risks to participants or others, which site is responsible for reporting it?)
- Interim results.
- Protocol modifications.

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7. Drugs: Will any drugs or supplements be used/studied in this protocol? ☐Yes ☒No
If Yes, attach the Drug Review Sheet.

8. Devices: Will any devices be studied in this protocol or used for a purpose other than for which they were approved by the FDA? ☒Yes ☐No
If Yes, attach the Device Review Sheet.

9. Special Approvals

a. Does this project involve the use of radioisotopes? ☐Yes ☒No
If Yes, attach documentation of approval from the Radiation Safety Division.

b. Does this project include patients with contagious infections (e.g., mumps, measles, chickenpox, TB, meningitis)? ☐Yes ☒No
If Yes, attach documentation of approval from Chairman of the Infection Control Committee of the appropriate facilities.

c. Does this project involve obtaining remnant biopsy or surgical material from the Department of Pathology or any other source? ☐Yes ☒No
If Yes, attach documentation of approval from the entity or individual providing the materials (e.g., the UAB Division of Anatomic Pathology Release of Pathologic Materials).

d. Does this project require obtaining any remnant clinical laboratory specimens, body fluids, or microbiological isolates from the Department of Pathology or any other source? ☐Yes ☒No
If Yes, attach documentation of approval from the entity or individual providing the materials (e.g., the UAB Division of Laboratory Medicine Release of Pathologic Materials).

e. Does this project use stored (existing) specimens from a repository? ☐Yes ☒No

If Yes, attach documentation of approval for use of specimens, and describe how existing specimens are labeled:____

10. Use of Specimens

Does this project involve collecting specimens from participants and storing them for future research? ☐Yes ☒No

If Yes, complete a-h. If no, skip to Item 11

a. How will specimens be obtained, processed, distributed, and stored?

b. How will specimens be labeled (e.g., unique identifier, medical record number, Social Security number, name, date of birth)?

c. How will clinical data associated with the specimens be collected and stored?

d. What participant-identifying information will be collected and linked to the specimens?

e. What steps will be taken to maximize the confidentiality of linked identifiers? For example, procedures could include using a password-protected computer database to link identifiers, with limited personnel knowledgeable of the password, or coded identifiers released without the ability to link to clinical data (also called "stripped" or "anonymized" specimens).

f. Will specimens be shared with other investigators in the future? ☐Yes ☐No
If Yes, what identifiers, clinical information and demographic information will be shared; or will the specimens be stripped of identifiers (i.e., anonymized)? Also **if yes**, outline your procedure for assuring IRB approval for release and use prior to release of specimens.

Note. Investigators who receive and/or use these specimens must document approval from the appropriate IRB(s) before the specimens may be released.

g. Will biological samples be stored for future use? ☐Yes ☐No
If Yes, indicate whether they will be used for the disease under study in this protocol or research on other diseases.

h. Is genetic testing planned? ☐Yes ☐No
If Yes, describe the planned testing here and see "DNA/Genetic Testing" in the Guidebook for consent requirements.

11. Gene Therapy

Does this project involve gene therapy or administering recombinant materials to humans? ☐Yes ☒No

If Yes, submit the Gene Therapy Project Review Panel Report –OR- If this is a vaccine trial that is exempt from the NIH Guidelines For Research Involving

Recombinant DNA Molecules, submit the Protocol Oversight Review Form For Clinical Vaccine Trials.

12. HIPAA Privacy and Security

Will the PI or others obtain, review, or make other use of participants' "personal health information" (i.e., information, whether oral or recorded in any form or medium that (a) is created or received by a health care provider and (b) relates to past, present, or future physical or mental health or condition of an individual; or provision of health care; or payment for provision of heath care)? ☒Yes ☐No

If Yes, complete a-e as described.

a. Will the data/information be stored or managed electronically (on a computer)? ☒Yes ☐No

b. Is the principal investigator requesting that the UAB IRB waive patient HIPAA authorization from another institution or entity (e.g., insurance company, collaborating institution). ☐Yes ☒No
If Yes, attach copy of privacy notices from institution/entity, and provide the name of institution/entity:____

c. Indicate which, if any, of the listed entities below would provide information or maintain health information collected for this protocol and/or where health information that been collected will be stored/maintained.

- ☐ The Kirklin Clinic
- ☐ University of Alabama Hospital
- ☐ The Children's Hospital of Alabama
- ☐ Callahan Eye Foundation Hospital
- ☐ UAB Highlands
- ☐ Jefferson County Department of Health
- ☒ School of Dentistry
- ☐ School of Health Professions
- ☐ School of Medicine
- ☐ School of Nursing
- ☐ School of Optometry
- ☐ University of Alabama Health Services Foundation
- ☐ UAB Health Centers
- ☐ Viva Health
- ☐ Ophthalmology Services Foundation
- ☐ Valley Foundation
- ☐ Medical West - UAB Health System Affiliate

Health System Information Systems:

- ☐ HealthQuest
- ☐ Cerner Millennium (Lab, Radiology, UED, Surgery)
- ☐ EMMI - Master Member Index
- ☐ Horizon - IPV (IVR/CDA/CRIS)
- ☐ CareFlow Net
- ☐ Eclipsys (PIN)
- ☐ IMPACT
- ☐ None—**If None, skip to Item 13.**

d. Indicate which of the listed identifiers would be associated/linked with the protected health information (PHI) used for this protocol.

- ☒ Names
- ☐ Geographic subdivisions smaller than a State
- ☐ Elements of dates (except year) related to an individual
- ☒ Telephone numbers
- ☐ Fax numbers
- ☐ Email addresses
- ☐ Social security numbers
- ☒ Medical record numbers
- ☐ Health plan beneficiary numbers
- ☐ Account numbers
- ☐ Certificate/license numbers
- ☐ Vehicle identifiers and serial numbers
- ☒ Device identifiers and serial numbers
- ☐ Biometric identifiers
- ☐ Web universal resource locators (URLs)
- ☐ Internet protocol address numbers
- ☒ Full-face photographic images
- ☐ Any other unique identifying number—Describe:____

  Note. Codes are not identifying as long as the researcher cannot link the data to an individual
- ☐ None—**If None, skip to Item 13.**

e. Choose one plan to describe your use of the personal health information:

- ☐ The data collected meet the specifications for a "limited data set"
  —Attach Data Use Agreement or Business Associate Agreement
- ☒ Research staff will obtain authorization from each patient to use the information
  —Attach Patient Authorization form, complete except for patient name and IRB protocol number
- ☐ PI requests Waiver of Patient Authorization to use the information
  —Attach Waiver of Authorization and Informed Consent form

PROPOSED RESEARCH

- The IRB will not accept grant applications and/or sponsor's protocols in lieu of the items as outlined below.
- Do not separate responses from items. Instead, insert your response to each item below the item, keeping the information in the order of this form.
- Number each page of the Human Subjects Protocol (i.e., Page *X* of *Y*).

13. Purpose—in nontechnical, lay language

Summarize the purpose and objectives of this protocol, including any related projects, in one short paragraph.

The purpose of this study is to evaluate the efficacy of the Aerodentis system for orthodontic tooth movement in an open label, two-arms, non-inferiority clinical study. This open label, two-arm study will follow 45 patients for up to fifteen (15) months. Thirty participants will wear the Aerodentis device, and fifteen participants will wear Invisalign. Patients will be assigned to participate in the treatment group using the Aerodentis device at home for 10 hours daily or in the control group using

clear correctors for the duration of up to 15 months. Outcome assessments will be performed every 4 weeks. Assessments will include tooth movement and quality of life assessments.

14. Background—in nontechnical, lay language

Summarize in 2-3 paragraphs past experimental and/or clinical findings leading to the formulation of this study. Include any relevant past or current research by the Principal Investigator. For drug and device studies summarize the previous results (i.e., Phase I/II or III studies).

Dror Orthodesign is a medical device company that designs, develops, and manufactures pioneering orthodontic solutions to improve dental care and orthodontic treatment. The company's flagship Aerodentis system is an aesthetic alternative to conventional braces and clear aligners that is faster, more effective, safer and more comfortable.

The Aerodentis system is intended for the treatment of tooth malocclusion and is treated by applying force, over time, to teeth requiring alignment. Traditionally, the force has been created by attaching brackets to the teeth and creating tension through the stretching of flexible wire connected between the brackets. Alternatively, aligners are used for the treatment of tooth malocclusion. In these devices, a series of mouthpieces are used, where the force created by each mouthpiece on the treated teeth is designed to push the teeth in small, one step increments, toward the desired result. The Aerodentis system is an individually-fitted, plastic dental mouthpiece that is inserted and worn by the patient according to the dental practitioner's treatment plan. The Aerodentis system is comprised of a plastic mouthpiece containing an inflatable balloon that provides pressure (force) on the selected teeth designated to be moved to a final treated state. This allows patients complete freedom from orthodontic devices during the day. The inflatable balloon is inflated to the desired pressure using an electrical air pump unit that is programmed by the dental practitioner using Dror Orthodesign proprietary software; thus creating a course treatment specially designed for each patient.

The Aerodentis system was invented by Dr. Nadav, DMD, MSc, a specialist in orthodontics and dentofacial orthopedics and developed over seven years by a highly skilled team of engineers, orthodontics, industrial designers and dental technicians. The company is backed by a seasoned multidisciplinary team of executive professionals and researchers. Uniquely positioned to lead the market toward adopting this safe and effective platform, Dror Orthodesign is expanding the options for patients who can benefit from orthodontic treatment.

The Aerodentis system is CE-approved and is being used by doctors in Israel and Europe. CE marking on a product is a manufacturer's declaration that the product complies with the essential requirements of the relevant European health, safety and environmental protection legislation.

Dror Orthodesign is a privately held company with headquarters in Jerusalem, Israel. Dror Orthodesign has provided payment to Medistat for statistical services on this study.

15. Participants (Screening and Selection)

a. How many participants are to be enrolled at UAB? 45, 30 active and 15 control
If multi-center study, total number at all centers: ____

b. Describe the characteristics of anticipated or planned participants.
Sex: male and female
Race/Ethnicity: all races
Age: 12-60 with adult dentition (permanent teeth)
Health status: medically fit and well

Note. If data from prior studies indicate differences between the genders or among racial/ethnic groups in the proposed research or if there are no data to support or to negate such differences, Phase 3 clinical trials will be required to include sufficient and appropriate entry of gender and racial/ethnic subgroups so that trends detected in the affected subgroups can be analyzed. If ethnic, racial, and gender estimates are not included in the protocol, a clear rationale must be provided for exclusion of this information. If prior evidence indicates that the results will not show gender or racial differences, researchers are not required to use gender or race/ethnicity as selection criteria for study participants. They are, however, encouraged to include these groups. See Section II. Policy of the NIH POLICY AND GUIDELINES ON THE INCLUSION OF WOMEN AND MINORITIES AS SUBJECTS IN CLINICAL RESEARCH – Amended, October, 2001) for further details.

c. From what population(s) will the participants be derived?

Incoming patients seeking orthodontic treatment

Describe your ability to obtain access to the proposed population that will allow recruitment of the necessary number of participants:

Patients will be screened by the orthodontic faculty members, Drs. Kau, Lamani, and Christou, at the orthodontic clinic

Describe the inclusion/exclusion criteria:

Inclusion:

1. **Permanent dentition**
2. **Patients that in the opinion of the investigator will be compliant with device use. Compliance is determined by patient questionnaire.**
3. **Class I malocclusion with crowding of ≤6 mm between the anterior teeth from the right first premolar to the left first premolar, on the upper and lower. Mild class II, class II subdivision.**
4. **Good oral hygiene, as determined by investigator orthodontist.**

Exclusion:

1. **Any medical or dental condition that, in the opinion of the investigator, could negatively affect study results during the expected length of the study. Conditions can include poor oral hygiene, extensive dental treatments, or periodontal disease.**
2. **Patient is currently using any investigational drug or any other investigational device.**
3. **Patient plans to relocate or move during the treatment period.**
4. **Allergic to acetaminophen (use of aspirin or non-steroidal anti-inflammatory drugs is excluded for patients while on the study).**
5. **Use of bisphosphonates (osteoporosis drugs) during the study.**
6. **Pregnant females. Orthodontic treatment is not advised in pregnant females. Hormonal changes may affect tooth movement, the unborn fetus can be affected during mandatory x-rays, and unexpected complication in pregnancy may arise that could negatively affect orthodontic treatment.**
7. **Patients that, in the opinion of the investigator orthodontist, are unable to comply with safe and effective device use.**
8. **Patients that are likely unwilling to be compliant with device use, as determined by the questionnaire for compliance.**

d. If participants will comprise more than one group or stratification, describe each group (e.g., treatment/intervention, placebo, controls, sham treatment) **and** provide the number of participants anticipated in each group.

This is an open label, two-arm, non-inferiority study. Patients will be systematically assigned to a treatment group (wearing the Aerodentis device) or control group (wearing clear aligners).

Participants from the control group come from both current patients treated on site and new patients coming into the orthodontics clinics, requesting treatment with clear aligners.

e. Indicate which, if any, of the special populations listed below will be involved in the protocol. Include the Special Populations Review Form (SPRF) if indicated.

- ☐ Pregnant Women: Attach SPRF—Pregnant Women, Fetuses, Neonates/Nonviable Neonates
- ☐ Fetuses: Attach SPRF—Pregnant Women, Fetuses, Neonates/Nonviable Neonates
- ☐ Neonates/Nonviable Neonates: SPRF—Pregnant Women, Fetuses, Neonates/Nonviable Neonates
- ☐ Prisoners: Attach SPRF—Prisoners
- ☒ Minors (<18 years old): Attach SPRF—Minors
- ☒ Employees or students at institution where research conducted
- ☐ Persons who are temporarily decisionally impaired
- ☐ Persons who are permanently decisionally impaired (e.g., mentally retarded)
- ☐ Non-English Speakers

For each box checked, describe why the group is included **and** the additional protections provided to protect the rights and welfare of these participants who are vulnerable to coercion: **During the consent process, participants will neither be encouraged nor discouraged to be involved with the trial. Participants will be fully informed of the risks, benefits, and alternatives to participating in the trial. Also, they will be allowed to withdraw from the trial at any time. Students will be notified that their class standing and grades at UAB will not be affected. Students will not be offered or receive any special consideration when taking part in the research study. Employees will be notified that taking part in the study is not a part of UAB duties and refusing participation will not affect their job or relationship with UAB. Employees will not be offered or receive any special consideration when taking part in the study.**

f. List any persons other than those directly involved in the study who will be at risk. If none, enter "None": **None**

g. Describe the process (e.g., recruitment, chart review) that will be used to seek potential participants (e.g., individuals, records, specimens). Research recruitment by non-treating physicians/staff may require completion of Partial Waiver of Authorization for Recruitment/Screening. (See http://main.uab.edu/show.asp?durki=61981.)

Patients coming into the UAB orthodontic clinic, seeking treatment, will be screened by either Dr. Kau, Lamani, or Christou. If the patients meet initial inclusion criteria during the screening process, the patient will be told about the study, and ask to fill out a questionnaire to determine if the patient is a good fit, and will be compliant throughout the study. Patients who are approved, will be consented on the Aerodentis study. Those who are not approved to wear the Aerodentis device, will be offered standard orthodontic care.

h. If you will use recruitment materials (e.g., advertisements, flyers, letters) to reach potential participants, attach a copy of each item. If not, identify the source (e.g., databases) from which you will recruit participants.

Flyers will be used as well as clinic patients.

i. Describe the procedures for screening potential participants.

All orthodontic patients who meet the inclusion criteria will be invited to participate.

16. Protocol Procedures, Methods, and Duration of the Study—in nontechnical language

a. Describe the procedures for all aspects of your study. Tell us what you are doing.

A participant is required to wear the Aerodentis device or conventional clear correctors. Initial photos of participants will be reviewed by Dr. Chung How Kau and Dr. Orit Nadav to establish a pool of eligible potential participants. After a pool of potential patients has been established, participants will be randomly selected for one of the two groups. Those wearing the Aerodentis device will be asked to answer a quality of life questionnaire about the individual's experience with it. Follow-up assessments will be conducted every 4 weeks for both Aerodentis participants and clear corrector participants. During these assessment's, we will look at movement of teeth, any side effects or discomfort the individual may be facing, patient assessment of whether the Aerodentis device is being used regularly, the individual's quality of life, and how well the device is working out for the individual. Both intraoral (entire face) and extraoral (teeth only) photos will be taken of patients, during certain time points of the study, as requested by PI or sponsor. If a participant enters and completes the entire study, then that individual will be in the study for up to 15 months.

The force value is set by the dental practitioner, based on the same common orthodontic criteria considered in force application in treatment with brackets. Whereas in brackets the force is changed by replacement of, for example, the wires and band attachments, in the Aerodentis system the force is changed by increasing the air pressure within the inflatable element. The value of the applied forces in Aerodentis falls within the optimal force range for conventional orthodontic treatment. In treatment with braces the applied force is usually between 50 to 200 grams and the doctor knows which force to apply according to the specific case. The Aerodentis system is pre-calibrated to apply an average force of 80 grams on all teeth that are in treatment. If needed, the force can be programmed to a lower (50 grams) or higher (100-140 grams) force according to the doctor's decision. For example, in cases of compromised dentition or a particularly sensitive patient, the force can be lowered to 50 grams. In cases of insufficient treatment progress, the doctor can apply a higher force of 120-140 grams, as is often done with conventional treatments. Thus, progressive treatment can be performed without the need to change hardware components or aligner trays.

b. What is the probable length of time required for the entire study (i.e., recruitment through data analysis to study closure)?

24 months

c. What is the total amount of time each participant will be involved?

15 months

d. If different phases are involved, what is the duration of each phase in which the participants will be involved? If no phases are involved, enter "not applicable."

—

e. List the procedures, the length of time each will take, and the frequency of repetition, and indicate whether each is done solely for research or would already be performed for treatment or diagnostic purposes (routine care) for the population. *Insert additional table rows as needed.*

Procedure	Length of Time Required of Participants	Frequency of Repetition	Research (Res) – OR- Routine Care
Screening	**10 minutes**	**once**	☐Res ☒Routine
Compliance questionnaire	**10 minutes**	**once**	☒Res ☐Routine
Take pictures of teeth for final approval	**10 minutes**	**once**	☒Res ☐Routine

Review of photos for establishing pool of participants	**24 hours**	**once**	☒Res ☐Routine
Consent	**20 minutes**	**once**	☒Res ☐Routine
Fitting of appliance (Aerodentis or Invisalign)	**1 hour**	**once**	☐Res ☒Routine
Quality of life questionnaire – Aerodentis	**5 minutes**	**once every 4 weeks**	☒Res ☐Routine
Aerodentis device wear	**10 hours**	**daily**	☒Res ☐Routine
Clear Correctors wear	**24 hours everyday**	**daily**	☐Res ☒Routine

f. Will an interview script or questionnaire be used? ☒Yes ☐No
If Yes, attach a copy.

g. Will participants incur any costs as a result of their participation? ☒Yes ☐No
If Yes, describe the reason for and amount of each foreseeable cost.
Participantswill be required to pay $5000 for Aerodentis, or $5000 for conventional clear aligners. Participants wearing the Aerodentis device will be ask to pay for treatment to assure compliance use with device. This is the same cost as all other UAB orthodontic patients incur for conventional clear aligner treatment, although, the participants wearing the Aerodentis device will be given compensation because the device is not familiar in the US and as a result the participants have uncertainty regarding its success and efficacy. Participants in the control group will be asked to pay regular price, without compensation, because Invisalign is a familiar treatment in the US and as a result the patient is certain regarding its process and results.

h. Will participants be compensated? ☒Yes ☐No
If Yes, complete i-v:
i. Type: (e.g., cash, check, gift card, merchandise): Check – Aerodentis group only**ii.** Amount or Value: **One check for $1000, three checks for $550, one check for $850**
iii. Method (e.g., mail, at visit): At visit
iv. Timing of Payments: (e.g., every visit, each month): one check for $1000 at participant recruitment, three refunds of $550 each – depending on compliance of a minimum of 10 treatment hours a day, after every two months of treatment, and final refund of $850 at treatment completion.
v. Maximum Amount of Payments per Participant: $3500 - Aerodentis group only

17. Describe the potential benefits of the research.

Aerodentis applies pulsating physiological force to move teeth gradually into the desired position and occlusion. It is well established in the literature that pulsating orthodontic force, which mimics the normal, natural physiology of the body, is an effective modality for orthodontic treatment. Subsequent clinical and research data has shown that the application of pulsating force accelerates orthodontic correction, as well as facilitating additional benefits when compared to continuous force. The controlled Individual Force Prescription enables the PIs' to prescribe an accurate force level and pulsating cycle, depending on how orthodontic treatment progresses for each individual. Also with Aerodentis, patients can properly brush and floss and do not have to worry about bothersome food traps, like with wearing braces, which can lead to plaque and tooth decay.

18. Risks

a. List the known risks—physical, psychological, social, economic, and/or legal—that participants may encounter as a result of procedures required in this protocol. Do not list risks resulting from standard-of-care procedures. *Note. Risks included in this protocol document should be included in the written consent document.*

- **Gums, cheeks, or lips may be irritated by mouthpiece.**
- **Failure to wear the appliance for the required treatment time and/or not using the product as directed by your doctor can lengthen the treatment time and affect the ability to achieve the desired results.**

b. Estimate the frequency, severity, and reversibility of each risk listed.
Mild, when wearing device. Patient may stop wearing device if risks occur.

c. Is this a therapeutic study or intervention? ☒Yes ☐No
If Yes, complete the following items:

i. Describe the standard of care in the setting where the research will be conducted: **The most common standard of care for orthodontic movement of teeth in correcting malocclusion is by providing mechanical forces, involving a system of metal archwires and brackets, typically referred to as orthodontics, and known to many as "braces". The basic system is augmented with elastics, metal bands, headgear, retainers, and other ancillary devices as dictated by the specific treatment. These forces are static in that they are only adjusted at specific visits but then stay constant and do not change between visits.**

ii. Describe any other alternative treatments or interventions: **Participants may choose not to participate in the Aerodentis clinical trial and continue receiving routine orthodontic treatment at UAB's Department of Orthodontics.**

iii. Describe any withholding of, delay in, or washout period for standard of care or alternative treatment that participants may be currently using: **N/A**

d. Do you foresee that participants might need additional medical or psychological resources as a result of the research procedures/interventions? ☐Yes ☒No
If Yes, describe the provisions that have been made to make these resources available.

____

e. Do the benefits or knowledge to be gained outweigh the risks to participants? ☒Yes ☐No
If No, provide justification for performing the research:____

19. Precautions/Minimization of Risks

a. Describe precautions that will be taken to avoid risks and the means for monitoring to detect risks.
All aspects of this study will be monitored by the PI, Dr. Chung How Kau, and Co-PIs'. All data will be encrypted and only accessible by the PI. Safety analysis will be performed at every visit, and patients may be ask to stop treatment if adverse events occur.

If study involves drugs or devices skip Items 19.b. and 19.c., go to Item 20, and complete the Drug or Device Review Sheet, as applicable.

b. If hazards to an individual participant occur, describe (i) the criteria that will be used to decide whether that participant should be removed from the study; (ii) the procedure for removing such participants when necessary to protect their rights and welfare; and (iii) any special procedures, precautions, or follow-up that will be used to ensure the safety of other currently enrolled participants.
Participants will be removed from the study if any risks are incurred as judged by the PI, Dr. Chung How Kau or Co-PIs', Dr. Ejvis Lamani or Dr. Christou. All information received on the participant will be stored on a UAB Department of Orthodontics owned encrypted computer locked in the PI's office. At the end of the study, the data will be stored on the UAB School of

Dentistry's server. All participants will be notified if any data is lost or stolen or any risks develop after they have consented to participate in the study.

c. If hazards occur that might make the risks of participation outweigh the benefits for all participants, describe (i) the criteria that will be used to stop or end the entire study and (ii) any special procedures, precautions, or follow-up that will be used to ensure the safety of currently enrolled participants.
If the foreseeable hazards to the participants outweigh the benefits of continuing the study, the study will be stopped. All participants will be notified if any risks develop after the have consented to participate in the study. All currently enrolled participants will be able to discontinue participation at any time without penalty.

20. Informed Consent

a. Do you plan to obtain informed consent for this protocol? ☒Yes ☐No
If Yes, complete the items below.
If No, complete and include the Waiver of Informed Consent or Waiver of Authorization and Informed Consent, as applicable.

b. Do you plan to document informed consent for this protocol? ☒Yes ☐No
If Yes, complete the items below.
If No, complete the items below **and** include the Waiver of Informed Consent Documentation.

c. How will consent be obtained? **The informed consent documents will clearly state the purpose of the study, description of the procedure, associated risks, benefits, and alternatives, the ability to refuse to participate in the study or discontinue participation at any time without penalty. Each participant will be given time to read the informed consent and ask questions if necessary.**

d. Who will conduct the consent interview? **PI, Co-PI, or Research Coordinator**

e. Who are the persons who will provide consent or permission? **Patients and parents of minor participants.**

f. What steps will be taken to minimize the possibility of coercion or undue influence?
During the consent process, participants will neither be encouraged nor discouraged to be involved with the trial. Participants will be fully informed of the risks, benefits, and alternatives to participating in the trial. Also, they will be allowed to withdraw from the trial at any time.

g. What language will the prospective participant or the legally authorized representative understand? **English**

h. What language will be used to obtain consent? **English**

i. If any potential participants will be, or will have been, in a stressful, painful, or drugged condition before or during the consent process, describe the precautions proposed to overcome the effect of the condition on the consent process. If not, enter "no such effect."
No such effect.

j. If any project-specific instruments will be used in the consenting process, such as flip charts or videos, describe the instrument(s) here, and provide a copy of each. If not, enter "not used."
Not used

k. How long will participants have between the time they are told about the study and the time they must decide whether to enroll? If not 24 hours or more, describe the proposed time interval and why the 24-hour minimum is neither feasible nor practical. **24 hour**

21. Procedures to Protect Privacy

Describe the provisions included in the research to protect the privacy interests of participants (e.g., others will not overhear your conversation with potential participants, individuals will not be publicly identified or embarrassed).

Participants will be taken to a private area in UAB's orthodontic clinic and will be fully informed about the risks, benefits, and alternatives of participating in the clinical trial. The participants will be allowed to ask questions prior to signing the consent form.

22. Procedures to Maintain Confidentiality

a. Describe the manner and method for storing research data and maintaining confidentiality. If data will be stored electronically anywhere other than a server maintained centrally by UAB, identify the departmental and all computer systems used to store protocol-related data, and describe how access to that data will be limited to those with a need to know.

Participants will be given a unique code that is linked to the name. The code will be assigned at the time the consent form is signed and only known by the listed staff involved in research. Images, intraoral photographs, codes, and names will be stored on a UAB Orthodontic Department owned encrypted computer. This computer will be locked in the PI's office and will only be accessible to those directly involved in the study. At the end of the study, all data will be stored on the UAB School of Dentistry's server.

b. Will any information derived from this study be given to any person, including the subject, or any group, including coordinating centers and sponsors? ☒Yes ☐No

If Yes, complete i-iii.

i. To whom will the information be given? **Michael Nadav, CEO of Aerodentis**

ii. What is the nature of the information? **Intraoral and extraoral photos, tooth movement measurements, compliance data, quality of life questionnaire.**

iii. How will the information be identified, coded, etc.? **Each patient will be assigned a unique patient ID, solely for research purposes.**

23. Additional Information

In the space below, provide any additional information that you believe may help the IRB review the proposed research, or enter "None."

Attached forms:

-Protocol oversight Review Form
-Informed consent
-Appendix A, picture of Aerodentis console
- Compliance questionnaire
- Quality of life questionnaire
- Device review sheet
- Aerodentis user guide
- Aerodentis system risk analysis
- Aerodentis Proposal