Study title: Efficacy of a Novel Brushing Device

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Please find the attached protocol used for this study

Study Protocol

Efficacy of a Novel Brushing Device

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Table of Contents

Study Overview

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Subjects	Recruit 60 subjects. Each subject will make 1-2 visits. The entire study is estimated to take approximately 6 months.
Inclusion/Exclusion Criteria	Potential subjects will be given a checklist of the inclusion and exclusion criteria to determine if they are eligible to participate. A study staff will confirm the eligibility by the "yes" and "no" responses accordingly. **Inclusion Criteria (All answers should be yes):** • Between the ages of 5-17 • In good general health • Fluent in English • Parent or guardian willing and able to provide written informed consent • Have 16 scorable teeth (non crown/bridge/or full amalgams) • Have had a dental cleaning and exam in the past 24 months **Exclusion Criteria (To qualify, all answers must be no):** • Have advanced periodontal disease or severe gum disease • Have mouth or teeth pain that prevents brushing in any areas • Have intraoral piercings (tongue or lip) that cannot be removed • Have non-controlled diabetes • Have any autoimmune or infectious disease or any medical condition that would delay wound healing • Have untreated visible cavities or untreated dental work • Had oral or gum surgery in the previous 2 months • Take antibiotic premedication for dental procedures • Undergoing or require extensive dental or orthodontic treatment • Current smoker • Generalized recession over 1mm
Study Objectives	To compare plaque removal efficacy of an automated mouthpiece-based toothbrush to a manual toothbrush, and to assess effect on oral soft tissues.
Study Design	• Single Site • Parallel Design • 60 Subjects stratified by dentition (primary, mixed, and permanent) are randomized evenly to 2 treatment groups • Randomized, blinded, 2 treatment groups
Study Duration	• 2 visits • Each study visit will take approximately 90 minutes
Study Devices	List of Devices: **Primary Investigation**: (All 60 subjects) 1. Automated brush: 30 subjects 2. Manual toothbrush: 30 subjects

Study Summary	**Visit 1: Screening (may be by telephone)** • Inclusion / Exclusion reviewed • Consent if in person visit • Subject will be asked to abstain from brushing, flossing, gum or mouthwash for 24 hours prior to visit 2 • Schedule next visit **Visit 2:** • Consent • Review Inclusion / Exclusion Questionnaire • Randomization to experimental or control group • Intraoral Evaluation by dental examiner • Plaque disclosing and plaque score • Intraoral photographs: (1 anterior, one posterior right and one posterior left) • Brushing instructions • Supervised and Timed Brushing with assigned product and measured toothpaste • Restain with plaque disclosing solution and 2nd plaque index as well as gingival abrasion • Intraoral photographs (1 anterior, one posterior right and one posterior left) • Subject questionnaire

Background Information

A healthy mouth is a crucial condition for a healthy body.

Maintaining good oral health requires good oral hygiene meaning good plaque control. Plaque is one of the main etiological factors in dental decay[1] and the principal etiologic factor for periodontal diseases [2] which, beyond the discomfort they can inherently cause, are linked to more systemic conditions such as cardiovascular disease, pre-term low birthweight babies, Alzheimer's disease, [3] and stroke. [4]

It is now well recognized that tooth brushing is the most efficient plaque control method,[5] at least when used in an optimal way.

Although toothbrushes have greatly evolved, from pig bristles to connected sonic devices, dexterity is still the key component to an efficient cleaning routine. Regardless of the type of toothbrush, if it cannot be used properly, plaque cannot be removed properly. And it has been shown in recent research that on a population with a general good health, the plaque score reduction is only an average 42% (range 30-53%) for manual toothbrushes [6] and 46% (range 36-65%) for powered ones. [7]

Based on these observations, the sponsor has developed a powered teeth cleaning device to bypass the variability of each individual dexterity according to which cleaning is performed by a contraction and a relaxation, according to successive cycles in the presence of a liquid dentifrice, of a mouthpiece made of a resilient material receiving and enclosing all the teeth of an arch.

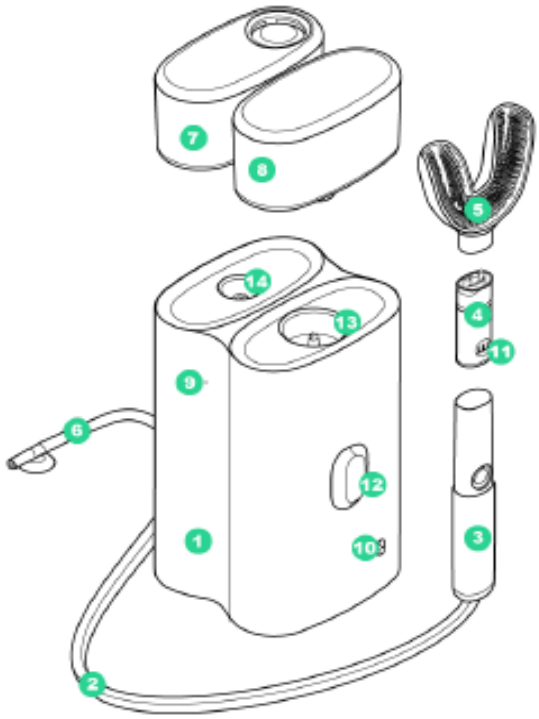
Description of the Device Studied

Device Classification

Device is in class 1, 501K exempt according to the 21 CRF 872 section 6865.

Mechanism of Action

The automated brush is a device aiming at improving and automating tooth brushing by bypassing the user's dex**t**erity variability. To this end, it is composed of a combination of an injection pump and a vacuum pump that allows for the injection and the evacuation of a cleaning liquid into a supple TPE bristled mouthpiece enclosing one arch at a time. The border of the mouthpiece, the oral vestibule and the cheek create an airtight environment inside the mouthpiece, the suction of the liquid generates successive depressions allowing plaque disruption by the motion of the mouthpiece bristles onto the teeth surfaces.



Item	Designation	Material (if applicable)
#1	Body	ABS
#2	Hose	Food grade silicon
#3	Handpiece	TPU
#4	Mouthpiece connector	ABS
#5	Mouthpiece	TPE
#6	Anchor Waste	Food grade silicon
#7	Water tank	PC
#8	Liquid dentifrice cartridge	PET
#9	LED status indicator	ABS
#10	On/Off power button	ABS
#11	On/Off cycle button	TPU
#12	Cartridge connection	TPU
#13	Water connection	TPU

ABS: Acrylonitrile butadiene styrene
TPU: Thermoplastic elastomer
PET: Polyethylene terephthalate

Study Objectives and Purpose:

Primary Objective: To compare the effects of the test brushing device versus a manual brush on plaque removal

Secondary Objective: To determine if soft tissue abrasion differs between test and control group

Study Design:

This is 2 visit, single-blinded, randomized controlled clinical trial.

All subjects will sign an Institutional Review Board (IRB)-approved informed consent form before any study procedures may be performed. This study will be completed according to applicable Good Clinical Practices and the Declaration of Helsinki.

This study includes

Number of Subjects:

The target number of subjects to be randomized to this study are 60 subjects.

Duration of subject participation and duration of study:

All subjects will have two visits and should complete the study in approximately two weeks. The visits may be combined following a telephone screening. Each appointment will be approximately 90 minutes.

Schedule of Events:

Procedures	Performed by:	Visit 1	Visit 2
Informed Consent	Research Staff	X	
Inclusion/Exclusion Criteria/Review	Research Staff	X	X
Enrollment	Research Staff	X	
Intra oral Examination	Examiner	X	
Randomization	Research Staff		X
Intra oral Examination (Pre & Post)	Examiner		X
Intra-oral photographs (Pre & Post)	Research Staff		X
Plaque disclosing index (Pre & Post)	Examiner		X
Brushing Dispense & Instruction	Research Staff		X

Study Product Usage	Subject		**X**
Schedule Next Study Visit	Research Staff	**X**	
Subject Compensation	Research Staff	**X**	**X**

Selection and Withdrawal of Subjects:

Potential subjects will be recruited via flyers or direct contact at the Center for Pediatric Dentistry, with a phone number to call. A study staff will go over a checklist of the inclusion and exclusion criteria to determine if they are eligible to participate. At the initial visit a dental examiner will confirm the eligibility by the "yes" and "no" responses accordingly and ask additional questions as appropriate. Subjects who sign the informed consent form are screened for eligibility at the baseline visit. Subjects meeting all eligibility criteria shall begin the study procedures.

Inclusion Criteria:

5-17 years of age
In good general health
Fluent in English
Willing and able to sign assent or informed consent as age appropriate
Parent or guardian willing and able to provide written informed consent
Be willing and able to carry out all study procedures (written and verbal) and be available at all times required for participation.
16 scoreable teeth (non-crown/bridge/ or full amalgams)
Has had a dental exam and cleaning within 24 months

Exclusion Criteria:

Advanced periodontal disease or severe gum disease
Mouth or tooth pain that prevents brushing in any areas

Have intraoral piercings (tongue or lip) that cannot be removed
Have non-controlled diabetes
Have any autoimmune or infectious disease or any medical condition that would delay wound healing
Have untreated visible cavities or untreated dental work
Had oral or gum surgery in the previous 2 months
Take antibiotic premedication for dental procedures
Undergoing or require extensive dental or orthodontic treatment, (space maintainers or removable appliances ok)
Current smoker
Generalized gingival recession over 1 mm

Withdrawal Criteria

Study participation is voluntary. The subject may refuse to consent or may withdraw from this study at any time without penalty or loss of benefits to which he/she is otherwise entitled. The Principal Investigator may terminate a study subject's participation in this study without his/her consent (e.g., for safety or significant non-compliance) or other reasons that may warrant withdrawal.

The study team will document whether or not each subject completed the study. If, for any subject, study treatment or assessments were discontinued, the reason will be recorded.

Subjects that withdraw from the study may be replaced but their study ID will not be re used and no further subject's data will be collected after date of withdrawal.

Subjects Study Visits

Welcome Subject and Consent

A research staff member who is currently trained in human subjects will greet the subject, and complete an eligibility inclusion/ exclusion form, and perform the consent process. Potential subjects are given the IRB-approved consent form to read and are provided the opportunity to ask questions about the study.

If any subject does not meet the requirement, they will not be screened further and will be thanked for their time.

If the potential subject does meet the requirement, study procedures may begin.

Enrollment

As part of study participation, each subject will be assigned a Subject ID number. This Subject ID number will be maintained throughout the study. The subject ID number which was assigned to them will not be re-used.

Study Visits

A dental examiner will review their eligibility questionnaires, ask any additional questions to clarify eligibility, and perform an intraoral evaluation which will determine eligibility and provide an initial baseline of the intraoral cavity prior to in-mouth use of the test product.

Visit 1: May be combined with visit 2 if subject has abstained from brushing, flossing and mouthwash for 24 hours

- Demographic information
- Medical history taken
- A dental examiner will perform an intraoral evaluation. The oral cavity will be evaluated and assessed for any abnormalities that may interfere with the brushing procedure, such as oral piercings.
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- Instructions given to abstain from brushing, flossing, gum or mouthwash for 24 hours prior to visit 2
- Gift card dispensed
- Schedule next visit

Visit 2:

- Review Inclusion / Exclusion Questionnaire
- Randomization
- Pre-brushing Intraoral Evaluation and plaque index
- Intraoral photographs pre-brushing
- Verbal review of brushing instructions
- Supervised and Timed Brushing with assigned products
- Dental examiner performs post- brushing intraoral evaluation and plaque index
- Intraoral photographs post-brushing
- Subject questionnaire
- Gift card dispensed

Randomization

Subjects will be randomized with a subject identification number throughout their study visits. A randomization table will be used by study staff to determine if the subject is a test or control brush.

Product Use

Subjects will be given verbal brushing instructions for the test or control brush.

For the control group, the toothbrush bristles will be dampened with water and toothpaste, will be pre-dispensed (on a clean surface) by the study staff to assure that all subjects are given the same quantity of toothpaste and to assure that the proper amount of toothpaste will be given. The same toothpaste will be provided to all the subjects. The subject will use the device directly over the sink.

Subjects will be reminded of the brushing instructions and will be timed during their brushing.

For the test group, the mouthpiece will be inserted by patient under the supervision of the study staff. The subject will use the device directly over the sink. If the subject is having any difficulty or uncomfortable, the in-mouth testing will be stopped immediately and reported to the Principal Investigator.

Assessment of Safety and Adverse Event Reporting

Definitions

Adverse Events (AEs) and Serious Adverse Events (SAEs) are defined by the ICH Guideline for Good Clinical Practice (ICH GCP) as follows:

Adverse Event: Any untoward medical occurrence in a patient or clinical investigations subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An adverse event

(AE) can therefore be any unfavorable and unintended sign (including abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

AEs include any clinically significant deterioration of a subject's medical status, after enrolled and signing an Informed Consent Form. The AE may involve any organs or systems and can be represented by the new onset or the deterioration of a disease, a syndrome, a symptom, a physical sign, as well as by findings and results of instrumental examinations and laboratory tests. Any medically relevant and untoward change from baseline, including frequency or pattern changes for a fluctuating condition (e.g., migraine), occurring after enrollment. All such occurrences must be recorded and reported accordingly, whether they appear causally related to the study product, or not.

Serious Adverse Event: Any adverse event occurring at any dose that results in any of the following outcomes:

- Death
- Life threatening adverse event
- Inpatient hospitalization, or prolongation of existing hospitalization
- Persistent or significant disability/incapacity
- Congenital anomaly/birth defect

Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

Documenting and Reporting Adverse Events

General Procedures for All Adverse Events

All clinical complaints, symptoms, or signs that meet the adverse event definition will be recorded on the Adverse Reaction Form using a recognized medical term or diagnosis that accurately reflects the event. Source documentation should be maintained that allows for clear identification of each adverse event and the following parameters required for the form:

- AE description
- Date of onset
- Date of resolution
- Outcome
- Severity
- Seriousness
- Relationship to study product (causality)
- Actions taken

Adverse events will be assessed by the investigator or designee for severity, relationship to the study intervention, possible etiologies, and whether the event meets the criteria as a serious adverse event and therefore requires immediate notification of the sponsor.

For data collection purposes, the outcome of all adverse events recorded on the Adverse Reaction Form will be designated as of the completion of the final evaluation or examination. However, the investigator is responsible for following all adverse events until resolution or until no longer of clinical concern and providing these data to the sponsor.

Baseline and Post-use Safety Evaluation

Participant safety shall be monitored from the time each participant signs the Informed Consent Form until conclusion of the study. Participant safety shall be monitored to detect any deviations in the medical health or dental status present at baseline.

Device Deficiencies

All device deficiencies use or user errors, and equipment failures will be documented. Use or user errors will be captured as part of the source documentation

Statistical Analysis Plan

Multiple sites within each subject will be evaluated using a Turesky Modification of the Quigley-Hein Plaque Index [8] at the treatment visit both before and after brushing.
To assess the device effect after brushing, a paired t-test will be applied on the change outcome. An unpaired t-test will be used to compare the efficacy of both devices. A visual analog assessment will be done will be done on all subjects. The number and percentage of reactions related to each brushing method will be collected and the final tolerance score estimated.

The selection of 60 participants is expected to identify statistically significant differences in clinical parameters before and after brushing among the subjects of the study. The power analysis was based upon a recent study by Klonowicz et al [9] in which a significant reduction of plaque was achieved after brushing of $p<0.05$.

Access to Source Data

This study will collect data on the performance of the study device. The data will be used without any personally identifiable information will be stored in the case report forms and entered into a spreadsheet for statistical analysis.

Case Report Forms

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site investigator. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. Only staff that have been delegated by the Principal Investigator will be able to enter or make changes to data in the study documentation.

Study Confidentiality

Study records, including each subject's signed consent form and eligibility, and other study-related documents pertaining to the conduct of the study shall be kept in a secure area. Confidentiality shall be maintained. The results of this research project may be presented at meetings or in publications; however, subject identity will not be disclosed in such publications.

Subject Confidentiality

Subjects enrolled in the study shall be assigned a Subject ID number. All recorded data are then entered per the unique Subject ID. Subject information shall remain confidential. However, consent forms that identify subjects may be inspected by the sponsor, its authorized designees and regulatory agencies including but not limited to, the Department of Health and Human Services (DHHS), the United States Food and Drug Administration (FDA) and other foreign regulatory bodies. Because of the need to release information to these parties, absolute confidentiality cannot be guaranteed. Only authorized personnel associated with the conduct and/or review of the study and the resultant data shall have access to information that links subject identifiers to the corresponding assigned study code. Disclosure of subject information to personnel other than those permitted by study staff, its designees or representatives, or appropriate regulatory agencies is prohibited.

Risk and Benefit Analysis

The subject may be uncomfortable with another person watching them brush or experience some bleeding or sensitivity during this brushing procedure. All procedures conducted in the brushing procedure are like what is experienced during a routine tooth brushing. The examiner will perform a thorough pre intraoral evaluation to check for any type of abnormal abrasion or wound in the mouth. If there is any predisposing condition in the subject's mouth, the dental examiner will inform the subject and may recommend the subject not participate in the study. The risk of permanent harm or injury, or disability as a result of participation in this research study is minimal. Participation is not expected to cause any oral conditions different from those normally experienced in routine brushing with a manual toothbrush. There is a chance that use of the research study products may involve risks that are currently unknown. The subject will be asked to report any discomfort or irritation that may be experienced while using research study products.

Anticipated Clinical Benefits

Participation in this trial may not result in direct benefit to the subject. The information collected from subjects will be used to improve future product design and function.

Compensation

Participants in this study will receive up to $50 in gift cards for their participation. A $25 gift card will be given at the end of each visit. No therapeutic or other benefit will be received by participating in the study.

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