SUNSTAR

CLINICAL STUDY PROTOCOL

POWER TOOTHBRUSHING FOR TREATING GINGIVITIS

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1. GENERAL INFORMATION

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Study Timeline:

Estimated date of first subject enrolled December 2017

Estimated date of last subject enrolled October 2018

Estimated date of last subject completes home use December 2018

2. BACKGROUND INFORMATION

2.1. Investigational product

ADA recommends brushing teeth twice daily with either a manual or power soft bristle toothbrush. Although the manual toothbrush is accepted and used widely, the efficient brushing movement that a power toothbrush generates helps remove plaque with little effort. This directly benefits adult users (including those with limited dexterity) and helps them to achieve and maintain good oral health.

The present investigational product is a rechargeable power toothbrush. The toothbrush has two speed settings. The brush head portion is removable for routine replacement. The circular brush head moves in a rotation-oscillation fashion. In the bristle configuration of the investigational device, the eight inner tufts include end-rounded nylon filaments, and the surrounding tufts include longer tapered filaments. This configuration was designed to fit tooth contours, in which the center bristles forming a flat rectangular area that covers the tooth surface, while the longer tapered bristles are designed to increase subgingival and interproximal access.

Two independent in-vitro efficacy studies have been conducted. The Subgingival Access Efficacy (SAE) and Interproximal Access Efficacy (IAE) are evaluated in-vitro using artificial plaque covered substrate placed around simulated anterior and posterior teeth.[1] The toothbrush is loaded with a 250 gram weight and controlled to brush in horizontal and vertical motions. The IAE was averaged over the results of horizontal and vertical brushing while the SAE over results of horizontal brushing. The IAE and SAE of the power toothbrush were found to be superior to an ADA reference flat trim manual toothbrush with statistical significance ($p<0.001$). Table 1 summarizes the in-vitro results conducted for the power and manual toothbrushes used in the study. The finding indicates that the tapered filament feature and unique bristle design enhance subgingival and interproximal access efficacies compared to a flat trimmed manual toothbrush.

Table 1. The Interproximal Access Efficacy (IAE) and Subgingival Access Efficacy (SAE) of the investigational power toothbrush product and an ADA reference manual toothbrush. The IAE and SAE are the result of the in-vitro efficacy study.[1]

Toothbrush	IAE (mm)	SAE (mm)
Power	11.3	1.40
Manual	9.8	0.02
% difference*	14%	194%

*% difference is the difference in percentage with respect to the average of the two numbers.

Moreover, the unique bristle design differentiates this device from other commercially available power toothbrushes with a similar rotation-oscillation movement. The in-vitro study results have shown the unique bristle design has superior access efficacy when compared to a commercially available rotation-oscillation power toothbrush. (Data on file)

The in-vitro access efficacy studies evaluate the effectiveness of the unique bristle design only in plaque removal in hard-to-reach areas. In-vitro studies are not able to test the effectiveness of the brushing movement the power brush generates, which helps the user to brush more easily. Moreover, in-vitro brushing on artificial plaque papers is not able to evaluate the effectiveness in treating and reducing gingivitis. Therefore, a clinical study is crucial to determine the clinical significance of the product in effectively treating and reducing gingivitis.

2.2. Known potential risks and benefits

The investigational device has no known potential risks. The literature published over the last 30 years has reported the rotation-oscillation power toothbrush to be safe compared to manual toothbrushes.[2] Moreover, a recent systematic review by Cochrane showed there was no apparent relationship between the use of a power toothbrush and soft tissue trauma.[2]

The benefits of the investigational device are as follows:

1. The unique bristle configuration is effective in removing plaque in the difficult-to-reach interproximal and subgingival areas, which should improve overall oral health if used regularly.
2. The Cochrane Collaboration, an independent healthcare research group, reported that clinical research shows that rotating-oscillating toothbrushes reduce plaque and gingivitis more than manual toothbrushes.[2]
3. The rotation-oscillation brushing movement helps facilitate more thorough brushing and makes brushing easier. This could benefits users with limited dexterity, such as elderly, people with disabilities.

This study will be conducted in compliance with the protocol, Standard Operating Procedures (SOPs), Good Clinical Practices (GCPs) Guidelines and applicable regulatory requirements. All study materials are to be reviewed by the Marquette University Institutional Review Board (IRB) prior to the study.

3. STUDY OBJECTIVES

The objective of this 12-week, parallel-arm, single-blinded, clinical study is to investigate efficacy and safety of a new power toothbrush in comparison with a standard ADA accepted manual brush.

3.1. Primary objective

Primary objective is to evaluate effectiveness of the product on gingivitis reduction compared to a flat trim manual toothbrush.

3.2. Secondary objectives

Secondary objectives are to evaluate the following:

- Effectiveness on plaque removal

- Hard and soft tissue damage

4. STUDY DESIGN

4.1. Clinical Parameters

4.1.1 Oral Cavity Exam/Oral Safety Exam

4.1.2 Modified Gingival Index[3]

4.1.3 Lobene Modified Turesky Plaque Index[4,5]

4.1.4 Full mouth periodontal charting of pocket depths and Bleeding Index

4.2. Description of Clinical Parameters

4.2.1. Oral cavity examination

Oral cavity examination for safety assessments will include evaluation of the lips, tongue, hard and soft palate, gingiva, all mucobuccal fold areas, inner surface of the cheeks and sublingual areas, tooth surfaces and restoration surfaces. All areas will be assessed and reported as normal or abnormal with an explanation of any abnormality. In particular, the cervical root area will be carefully examined.

4.2.2. Lobene modification of the Loe and Silness Gingival Index

The Modified Gingival Index[3] (MGI) will be measured on six sites – mesio-buccal, buccal, disto-buccal, mesio-lingual, lingual and disto-lingual - of all teeth using a 0-4 scale.

0 = Absence of inflammation. Normal gingiva.
1 = Mild inflammation: slight change in color, little change in texture of any portion of, but not the entire marginal or papillary gingival unit.
2 = Mild inflammation: criteria as above but involving the entire marginal or papillary unit.
3 = Moderate inflammation: glazing, redness, edema, and/or hypertrophy of the marginal or papillary gingival unit.
4 = Severe inflammation: marked redness, edema, and/or hypertrophy of the marginal or papillary gingival unit, spontaneous bleeding, congestion, or ulceration.
9 = Missing tooth or non-gradable tooth surface: a tooth surface will be considered non-gradable due to the presence of a crown, an extensive cervical restoration or a hypoplastic surface which could interfere with cleaning or cause plaque accumulation. Any surface graded as a 9 will not be included in the data analysis.

4.2.3. Lobene Modification of the Turesky Plaque Index

Dental plaque will be evaluated using the Lobene modification[4] of the Turesky modification of the Quigley-Hein Plaque Index (PI)[5]. Disclosing solution will be used to identify the plaque (2 tone disclosing solution to be paineted on the teeth with a microbrush then 10 ml's tap water used to, swish, then rinse again with water). Plaque will be scored on six surfaces of all natural teeth (3 buccal, 3 lingual) or nearest uncrowned tooth using a 0 scale. Subjects will abstain from brushing for at least 7 hours but no more than 12 hours prior to their evaluation appointment.

0 = No plaque/debris

1 = Separate flecks of plaque at gingival margin

2 = A thin continuous band of plaque (up to 1 mm) at the gingival margin

3 = A band of continuous plaque up to 1/3 of the crown of the tooth

4 = Plaque covering at least 1/3 but less than 2/3 of crown of tooth

5 = Plaque covering 2/3 or more of the crown of the tooth

9 = Missing tooth or non-gradable tooth surface: a tooth surface is considered non-gradable due to the presence of a crown, an extensive cervical restoration or a hypoplastic surface which could interfere with cleaning or cause plaque accumulation. Any surface graded as a 9 will not be included in the data analysis.

4.2.4. Probing Pocket Depth

Full-mouth Probing Pocket Depth (PPD) will be measured on the six locations of each tooth (mesial-buccal, buccal, distal-buccal, mesial-lingual, lingual, distal-lingual) using a periodontal probe.

4.2.5. Bleeding On Probing Index

The Bleeding on Probing index (BOP) will be recorded from the gingival sulci of all teeth after periodontal probing at all six locations per tooth - mesial-buccal, buccal, distal-buccal, mesial-lingual, lingual, distal-lingual. The presence of any bleeding within 30 seconds of gentle probing will be considered a positive response and given a score of 1. Sites which do not bleed on probing will be scored as 0.

0 = No bleeding
1 = Bleeding

4.3. Primary endpoint

The primary endpoint of this study is reduction of gingivitis (change from baseline) as measured by BOP and MGI at baseline, and again at 12-week visits.

4.4. Secondary endpoints

The following indices and parameters are secondary endpoints.

- Reduction of BOP and MGI at two-week, four-week visits from the baseline
- Reduction of PPD at 2-week, 4-week and 12-week visits from the baseline
- Reduction in plaque by measuring PI at 2-week, 4-week and 12-week visits as well as after a single use
- Safety of the product: clinical examiners inspect for any hard or soft tissue damage
- Patient reported outcomes from an exit survey and user diary

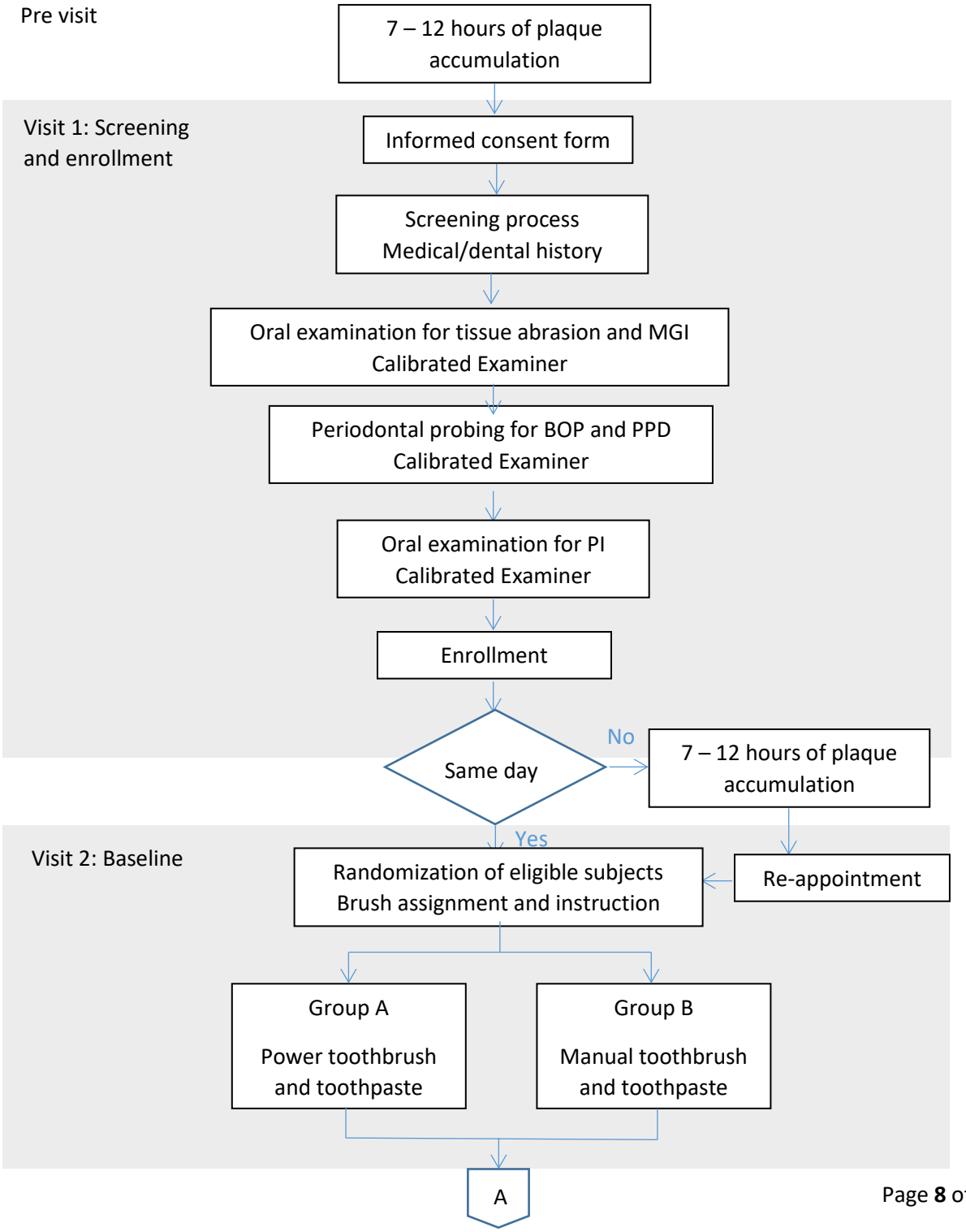
4.5. Study procedure

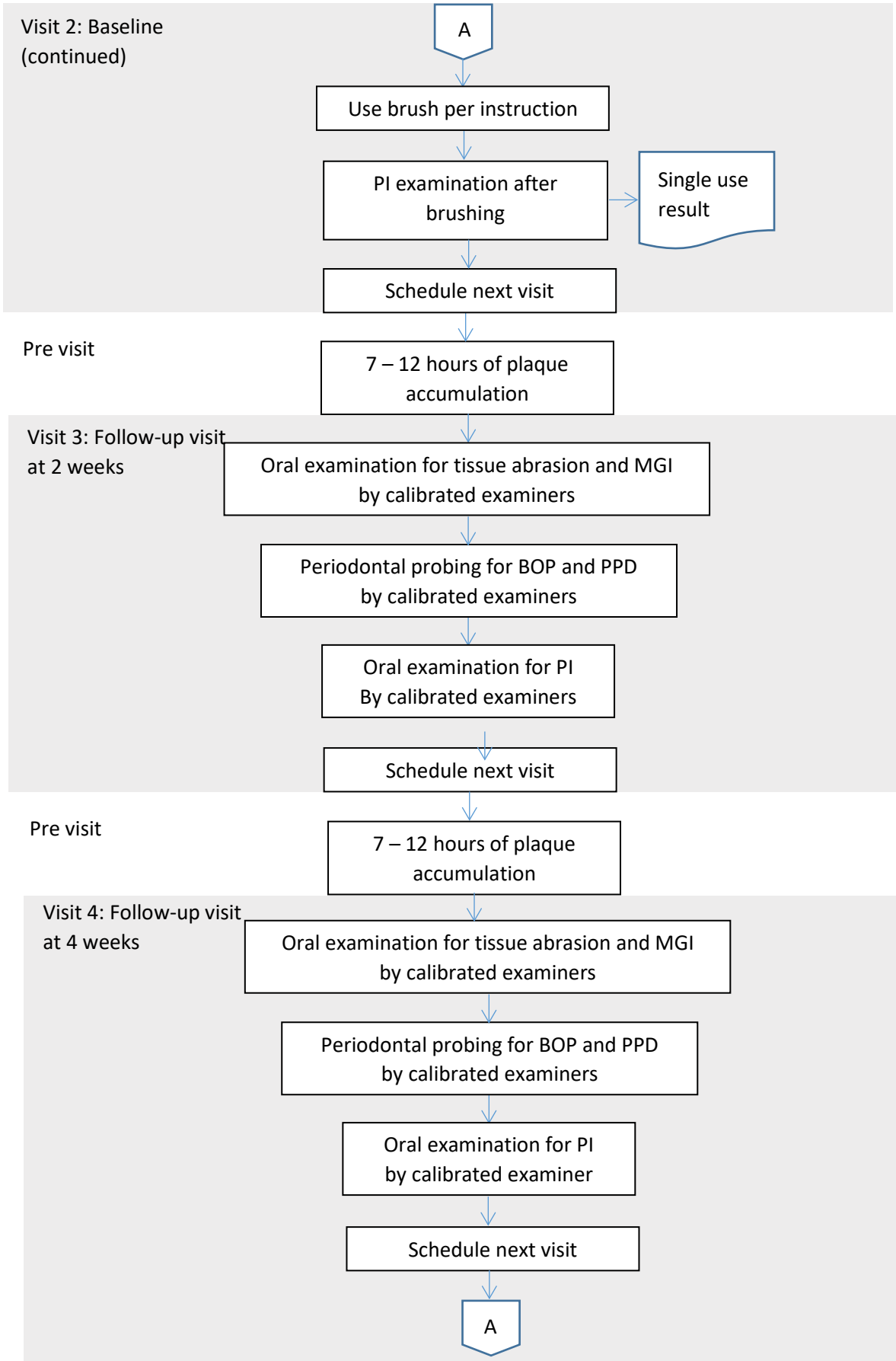
The study to be conducted will be single-blinded, randomized controlled, parallel design. The study population will consist of Seventy-two (72) male and female subjects conforming to the following admission criteria. The subjects meeting the admission criteria with an anticipation of 40% dropout rate will be stratified into two groups balanced for MGI, BOP, PI, and gender using screening data. In this single-blind design, product assignment will be randomized after screening, and only the PI and the Study coordinator will have access to the randomization key.

One group will be assigned to a new power toothbrush while the control group will be assigned an ADA approved manual toothbrush. The study involves a 12-week home use of the respective toothbrushes. Both groups will refrain from the regular use of mouthwash and any interdental device, such as floss, floss picks, toothpicks, water flossing device or interdental brush, during the length of the study. Written instructions on brushing and professional brushing demonstration will be provided at the outset of the study and each participant from both test and control groups will also receive a 2-minute timer to help them monitor their brushing time. Before each visit, subjects are expected to have at least 7 hours, but no more than 12 hours of accumulated, non-brushed, undisturbed plaque/debris.

The study includes four or five visits – screening, baseline, 2-week follow-up, 4-week follow-up and 12-week follow-up. Schematic 1 summarizes the study procedure and visits and Table 2 details procedures in this study. The Screening and the baseline visit may happen on the same day.

Schematic 1. Study and visit procedures




Visit 2: Baseline (continued)
A
Use brush per instruction
PI examination after brushing
Single use result
Schedule next visit
Pre visit
7 – 12 hours of plaque accumulation
Visit 3: Follow-up visit at 2 weeks
Oral examination for tissue abrasion and MGI by calibrated examiners
Periodontal probing for BOP and PPD by calibrated examiners
Oral examination for PI By calibrated examiners
Schedule next visit
Pre visit
7 – 12 hours of plaque accumulation
Visit 4: Follow-up visit at 4 weeks
Oral examination for tissue abrasion and MGI by calibrated examiners
Periodontal probing for BOP and PPD by calibrated examiners
Oral examination for PI by calibrated examiner
Schedule next visit
A

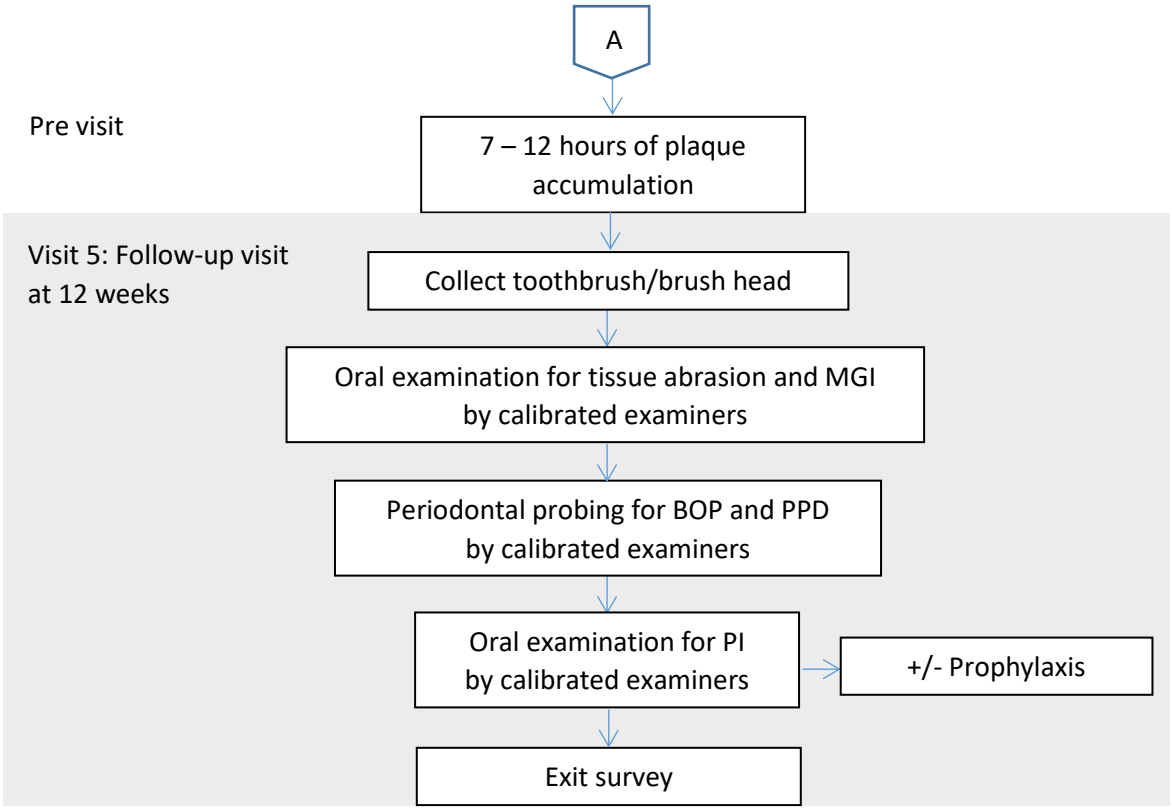

A
Pre visit
7 – 12 hours of plaque accumulation
Visit 5: Follow-up visit at 12 weeks
Collect toothbrush/brush head
Oral examination for tissue abrasion and MGI by calibrated examiners
Periodontal probing for BOP and PPD by calibrated examiners
Oral examination for PI by calibrated examiners
+/- Prophylaxis
Exit survey

Table 2. Procedure overview during visits

Procedure	Performed by	Visit				
		Screening	Baseline	2-week	4-week	12-week
Plaque accumulation	Subject	X	X	X	X	X
Patient information						
Informed consent form	Study coordinator/staff	X				
Patient demographics	Study coordinator/staff	X				
Medical/dental history	Study coordinator/staff	X				
Oral examination	Blinded examiners					
Oral cavity abrasion exam	Examiners 1 and 2	X	X	X	X	X
Gingival Index (MGI)	Examiners 1 and 2	X	X	X	X	X
Probing Pocket Depth	Examiners 1 and 2	X	X	X	X	X
Bleeding Index	Examiners 1 and 2	X	X	X	X	X
Plaque Index	Examiners 3 and 4	X	X*	X	X	X
Examiner calibration	All examiners	X				X
Others						
Inclusion/exclusion criteria	Study coordinator/staff	X	X			
Prophylaxis	Dental hygienist					X
Randomization	Unblinded staff/study coordinator		X			
Product introduction and instruction	Unblinded staff/study coordinator		X			
Brushing at clinic	Subject		X			
Scheduling future visit	Study coordinator/staff	X	X	X	X	
Collect used brushes	Unblinded staff/study coordinator					X
Exit survey	Subject					X

*Twice

Visit 1: Screening and enrollment

Subjects will be asked to report to the clinic with at least 7 but no more than 12 hours of accumulated, non-brushed, undisturbed plaque/debris. Prior to screening, subjects will sign a consent form after having gone over the consent with a member of the study staff and having all questions answered. In this visit, subjects will be asked about dental and medical history related to the admission and exclusion criteria.

At the screening exam, subjects will receive an oral soft tissue exam with periodontal probing, modified Gingival Index on the Ramjford teeth, and the amount of stain and calculus will be noted. Following these examinations, the subject's plaque will be disclosed with Trace 28 solution (4 drops under tongue) and they will swish for 10 seconds. Next, subjects will rinse with 10 ml. of tap water twice for 10 seconds each. Disclosed plaque will then be recorded on buccal and lingual surfaces of the Ramjford teeth using the Lobene modification of the Turesky Plaque Index. If baseline happens on the same day then full mouth GI and BOP will be carried out prior to disclosing for full mouth plaque measurements. Subjects who meet the admission criteria will be allowed to enroll. If a subject fails the screening exam due to oral disease such as, but not limited to dental caries and periodontitis, the subject will be appropriately referred to the main Marquette University School of Dentistry (MUSoD) screening clinic to insure that they will be given an opportunity for full diagnosis and treatment at the school of dentistry or some other appropriate clinic.

Each clinical index will be scored by one of two or three calibrated examiners. The oral cavity/oral safety exam and all measures of inflammation, the MGI, PPD and BOP will be carried out by examiners #1 and 2 while disclosing and scoring of the PI will be scored by examiners #3 and 4. A fifth examiner who is dual calibrated will be used if needed. Each examiner will be calibrated to the indices used, and will demonstrate repeatability of measures initially at the screening/calibration phase as well as during the study.

Visit 2: Baseline

Subjects who have signed consent form and met all the inclusion criteria and none of the exclusion criteria will be entered into the baseline procedure (day 0). This visit may occur the same day as screening.

In this visit, subjects will first be evaluated for signs of soft or hard tissue trauma, and then full mouth Modified Gingival Index followed by full mouth probing of pocket depth and assessment of BOP. Teeth with calculus will be recorded. After these data are recorded each subject will be disclosed and full mouth Plaque scores assessed and recorded by a calibrated examiner. Any scorable teeth that have plaque buildup on any six tooth sites will be recorded. The subjects will then leave the examining area to the randomization and toothbrush distribution area where they will be provided their assigned brush out of site of the examiners. Group A will be given a power toothbrush, while Group B will be given a manual toothbrush. Both groups will also be given a two minute timer and the same fluoride toothpaste (Colgate Cavity Protection toothpaste) as well as the appropriate set of written instructions on tooth brushing. The subjects in the test group will follow the instructions provided by the manufacturer, while subjects in the control group will be given a standard written and both groups provided visual instructions on proper brushing. A study staff member will be available to answer any questions pertaining to the instructions and coach patients toward optimal brushing technique. Then the subjects will be required to use the brush assigned for two minutes before being sent back to the examiner to

have a post-brushing plaque index recorded. These pre- and post 2-minute brushing data will be collected to assess single use effect differences between the toothbrush types. Subjects will be reappointed and instructed to bring their assigned brush to the subsequent exam sessions in a brown bag to avoid unmasking any of the examiners.

Visit 3: Two-week follow-up

The first follow-up will take place two weeks after the baseline visit. Subjects can schedule the visit for any time between two days before and after the two-week use period (12-16 day range). Clinical examinations will be given to the subjects in the same order as the baseline visit with the exception that no second plaque index will be recorded. All subjects must present with 7 to 12 hours of undisturbed plaque. The oral safety exam will include a thorough examination of the gingiva to look for any signs of gingival trauma, irritation or abrasion. Any subjects who show signs of gingival trauma that appears to be toothbrush related will be exited from the study. The recorded findings will be reported as Adverse Events. In addition, any site in the mouth that shows an increase in probing pocket depth of 2 mm or greater from the baseline measurement will have that particular site treated with subgingival scaling and root planing or whatever the PI deems appropriate therapy. If subjects meet any of the discontinuation criteria, they will be withdrawn from the study.

Visit 4: Four-week follow-up

This visit should take place four weeks after the baseline visit within three days before and after the four week mark (25-31 day range). Subjects will receive full mouth examinations in the same order as the previous visit. Additionally, inspection for signs of gingival trauma and increase in PPD greater than 2 mm from the baseline will be conducted and evaluated. The PI will determine if any subject meets the discontinuation criteria as well as appropriate therapy to treat.

Visit 5: 12-week follow-up

In this visit, subjects will return the products, including manual toothbrush, or brush head, brush handle, and charger. The procedure is similar to the four-week follow-up visit, in which full mouth clinical examination will be carried out as before on each of the subjects. The subjects' disclosed plaque will be evaluated as usual. The examined results will be recorded. Prophylaxis will be carried out as needed.

The used brushes/brush heads will be returned to sponsor at the end of the trial and examined for wear as an additional measure of compliance.

1. SELECTION AND WITHDRAWAL OF SUBJECTS

5.1. Admission Criteria

A subject who meets all the following criteria will be eligible to enroll in this study.

1. Age range 18 – 65 years
2. Routine manual toothbrush user
3. A Subject who agrees to use the assigned toothbrush as the only cleaning device for the study duration, refraining from daily interdental cleaning and/ or antiseptic mouthrinsing.
4. Mild to moderate gingivitis as measured by
    A. Modified Gingival Index (MGI) average score of at least 1.2, and / or
    B. Bleeding on Probing (BOP) of at least 20% of all sites but not more than 50% of sites.

5. Probing Pocket Depth (PPD) of 4 mm or lower
6. At least 20 natural teeth – scoreable (crowns or bridgework are non-scoreable).

5.2. Exclusion Criteria

Any subject meeting one of the following criteria will not be included in the study.

1. Daily user of interdental cleaning devices, such as floss, floss picks, toothpicks, interdental brush, water flossing device
2. Regular user of antimicrobial mouthrinses within one week of entry into study
3. Professional prophylaxis within one month of entry into the study
4. Use of antibiotics within one month prior to the baseline exam
5. Signs of moderate to severe periodontitis or caries, categorized as PPD of 5 mm of higher and attachment loss of 3 mm or higher
6. Subjects with orthodontic bands and/or dental appliances.
7. Participated in an oral care related study in the last 90 days prior to this study
8. Pregnant or lactating women
9. Patients with a history of significant cardiovascular disease, diabetes, cancer, AIDS, or other organ impairment that would preclude their participation in the study
10. Acute/concurrent illness such as hepatitis, herpes simplex infections, influenza, etc.
11. History of rheumatic fever, cardiovascular valvular disease, artificial joint replacement or kidney or liver disorders
12. Chronic use of NSAID's (≥ 325 mg/day)
13. Current Smoker (within the last 3 months)
14. Other medical or dental conditions that would affect the study
15. Inability to commit to all necessary study visits from baseline to 12 weeks

5.3. Discontinuation criteria

The oral safety exam at the follow-up visits will include a thorough examination of the gingiva to look for any signs of gingival trauma, irritation or abrasion, as well as a periodontal probing. Any subjects who show signs of gingival trauma that appears to be toothbrush related will be exited from the study and the findings reported as Adverse Events. In addition, subjects may be discontinued due to the following reasons.

1. Voluntary discontinuation: subjects are free to discontinue their participation in the study at any time.
2. Safety concerns: the principal investigator may terminate a subject's participation if gingival trauma occurs and appears to be toothbrush related
3. Significant non-compliance to protocol: the principal investigator may terminate a subject's participation if subjects are shown to be non-compliant to the protocol
4. Incorrect enrollment: subjects who did not meet admission/exclusion criteria
5. Subject received any type of dental treatment/care other than those required in the study, for example use of interdental devices, mouthrinses, chewing gum or prophylaxis treatment, without consent of the investigator

Subjects who discontinue should be asked to a follow-up visit to observe any Adverse Events.

5.4 Rescue treatment

Subjects may receive prophylaxis if needed. Other rescue treatments may be performed on subjects based upon the PI's decision.

If a subject fails the screening exam due to oral disease such as, but not limited to dental caries and periodontitis, the subject will be appropriately referred to the main MUSoD screening clinic to insure that they will be given an opportunity for full diagnosis and treatment at the school of dentistry or some other appropriate clinic.

6. SAFETY ASSESSMENT

All staff involved in this study will have reviewed the following description of Adverse Events and Adverse Device Effect

6.1. Adverse Event (AE)

An AE is any untoward and unintended medical occurrence in a subject. This definition does not imply that there is a relationship between the AE and the medical device under investigation. An AE which is possibly related, is one that may have been caused by the medical device, or treatment, however there is insufficient information to determine the likelihood of this possibility.

- Possibly related: temporal relationship of the onset of the event, relative to the use/administration of the medical device, is reasonable but the event could have been due to another, equally likely cause.
- Non-related (unlikely): temporal relationship of the onset of the event, relative to the use/administration of the medical device, is not reasonable or another cause can itself explain the occurrence of the event.

Ambiguous cases should be considered as possibly related.

6.2. Adverse Device Effect (ADE)

An ADE is any untoward and unintended response to a medical device. This definition includes any event resulting from insufficiencies or inadequacies in the instructions for use of the medical device or any event that is a result of a user error. This definition also includes treatment- or procedure-related events. ADEs can only occur from the time of medical device use/administration. Here the event is related to the use of the medical device where there is a probable/definite relationship that the event may have been caused by the medical device, or treatment.

- Probably related: temporal relationship of the onset of the event, relative to the use/administration of the medical device, is reasonable and the event is more likely explained by the medical device/treatment than by any other cause.
- Definitely related: temporal relationship of the onset of the event, relative to the use/administration of the medical device, is reasonable and there is no other cause to explain the event.

6.3. Serious Adverse Event (SAE)

An SAE is an AE/ADE occurring during any study phase of the medical device that fulfills one or more of the following criteria that the device:

- Results in death
- Is immediately life-threatening
- Requires in-subject hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability or incapacity
- Is a congenital abnormality or birth defect
- Is an important medical event that may jeopardize the subject or may require medical intervention to prevent one of the outcomes listed above

If a non-related AE becomes an SAE, i.e. fulfilling one or more of the above criteria, action should be taken.

6.4. Recording of Adverse Events and Adverse Device Effects

At all follow-up visits, adverse changes will be assessed by asking subjects and carrying out the oral safety exam. Subjects may report adverse events at any time of the study. All adverse changes the investigator believes “possibly”, “probably” or “definitely” were caused by the device must be recorded on the case report form as AEs. Time of onset, action taken, outcome and the investigator’s opinion on the relationship of the device to each adverse reaction/change in the oral cavity will also be recorded.

6.5. Reporting of Serious Adverse Events

If any SAE occurs, the PI or other personnel is responsible to inform the sponsor within 24 hours after they become aware of the event. The PI also will also inform the IRB committee of SAEs. The PI and sponsor will investigate the event and determined if it is related to the device. If it is a device-related, a report will be issued to the regulatory authority.

7. STATISTICAL ANALYSIS

Each of the two research groups' patients will be assessed clinically at four time points (Baseline, 2 weeks, 4 weeks and 12 weeks). These measures will be compared against one another and over time using a between-within factors repeated measures ANOVA.

Further evaluation of interproximal and marginal scores will also be evaluated with a post hoc analysis.

7.1. Sample size

Assuming an alpha/p-value of 0.05, and a power of 0.95, the minimum number of subjects needed (after all drop-outs have been removed) is 44. Due to the length of the study and multiple visits required within the length of the study, the potential for moderately high drop-out rates is set at 40%. 72 subjects will be initially enrolled; 36 will be assigned to the power toothbrush group, and 36 will be assigned to the manual toothbrush group.

7.2. Demographics and other baseline characteristics

Subject demographics (e.g. age and sex), oral care habits (e.g. flossing and smoking) and baseline characteristics (e.g. MGI, BOP and PI) will be presented by treatment group and in total. Measurements of recorded teeth with calculus will not be included in statistical analysis.

7.3. Significance level

Unless stated otherwise, significance level is 0.05. A p-value may be complemented by confidence interval.

7.4. Method

Reductions in gingivitis – BOP, MGI and PPD – and plaque – PI from baseline scores after 2 weeks, 4 weeks and 12 weeks of use will be evaluated. For each subject, mean score of each index will be calculated as well as reductions from baseline at three time points. Additionally, numbers of abrasion sites found will be compared.

Assuming evaluated scores for the test and control groups are denoted U_{Test} and $U_{Control}$, respectively, the null hypothesis will be tested.

H_0: $U_{Test} - U_{Control} = 0$

H_1: $U_{Test} - U_{Control} \neq 0$

8. ACCESS TO SOURCE DOCUMENTS

Access to source documents should be limited during the study. Blinded examiners will have access until the end of the study. All source documents will be made available to Sponsor, any third party with written permission from Sponsor and regulatory agencies.

9. ETHICAL CONSIDERATION

All subjects in this study will receive a standard of oral care. No placebo is involved. This study protocol must be reviewed and approved by the Marquette University IRB prior the study.

10. DATA HANDLING AND RECORD KEEPING

All patient data will be kept in individual booklets with all clinical research forms included. After each visit the patient data booklets will be reviewed by the study coordinator to ensure complete data collection and then kept in a locked file cabinet in the office of the Principle Investigator.

For any subjects screened but found ineligible their screening documents (health history/ charting) will be kept in a screen fail notebook with an explanation as to what the reason was for the screen fail.

11. FINANCING

Each subject will receive reimbursement for expense from the trip to the clinic at the end of baseline and follow-up visits. Reimbursement of $25 will be given at the baseline and 2-, 4- and 12-week visits in the form of Gift/Gas cards.

12. PROTOCOL AMENDMENT

If it is necessary for the study protocol to be amended, the amendment and/or a new version of the study protocol (Amended Protocol) must be notified to or approved by the MU IRB, and if applicable, also the local regulatory authority, before implementation. Local requirements must be followed.

Sponsor will distribute administrative changes, amendments and new versions of the protocol to the principal investigator.

13. MONITORING

Sponsor will meet with staff members who are involved to review the protocol and ensure that the study will be conducted in accordance with the following:

- Good Clinical Practices (GCPs) Guideline
- The study contract
- Conditions imposed by the IRB
- Any applicable local or federal regulatory requirements

14. STAFF TRAINING

The principal investigator will maintain a record of all individuals involved in the study – dental assistant, oral examiners, and other staff – and ensure appropriate training is given and any new information relevant to the performance of the study is forwarded to involved staff members.

15. REFERENCES

[1] Yankell SL, Shi X, Spirgel CM. data on file with Sunstar

[2] Yaacob M, Worthington HV, Deacon SA, Deery C, Walmsley AD, Robinson PG, Glenny AM. Powered versus manual toothbrushing for oral health. Cochrane Database of Systematic Reviews 2014, Issue 6

[3] Lobene RR, Weatherford T, Toss NM, Lamm RA, and Meanaker L. A Modified Gingival Index for Use in Clinical Trials. Clin, Prev. Dent., Vol. 8, No. 1, Jan-Feb, pp:3-6, 1986

[4] Lobene RR, Soparkar PM, Newman MB. Use of dental floss. Effect on plaque and gingivitis. Clin Prev Dent. 4: 5-8, 1982

[5] Turesky S, Gilmore ND, Glickman I. Reduced Plaque Formation by the Chloromethyl Analog of Vitamin C, J. Periodont. 41:41-43, 1970

PATIENT SCHEDULE

SCREENING WILL BE CARRIED OUT IN ALL CLINICS AT MUSOD USING PERIO FACULTY

BASELINE – APPROXIMATELY 1.25 HOURS

RESEARCH ASSISTANT / STUDY COORDINATOR
- CHECKS PATIENT IN AND CONFIRMS 7-12 HOURS PLAQUE ACCUMULATION
- GIVES COPY OF CONSENT FORM
- PATIENT GIVEN RECORD TO CARRY THROUGH THE APPOINTMENT TO EACH STATION
- DIRECTS TO 1ST EXAMINERS

1ST EXAMINERS – ORAL CAVITY EXAM, GINGIVAL INDEX, PROBING POCKET DEPTH, BLEEDING INDEX

2ND EXAMINERS – PLAQUE INDEX PRE-BRUSHING

PI / STUDY COORDINATOR
- ASSIGNS TOOTHBRUSH
- OHI DEMO & WRITTEN INSTRUCTIONS (TOOTHBRUSH USAGE AND STUDY PARTICIPATION)
- GIVES TUBE OF TOOTHPASTE & TIMER
- PT BRUSHES TO DEMONSTRATE COMPREHENSION OF INSTRUCTIONS THEN GIVES BRUSH BACK TO PI/STUDY COORDINATOR

RESEARCH ASSISTANT
- TAKES PATIENT TO 2ND EXAMINERS FOR POST-BRUSHING PLAQUE INDEX

2ND EXAMINERS – PLAQUE INDEX POST-BRUSHING

RESEARCH ASSISTANT
- BRINGS THEM BACK TO GET THEIR BRUSH / PASTE
- CONFIRMS NEXT VISIT (DATE & TIME)
- BASELINE INFORMATION SHEET
- RECOVERS PATIENT RECORD FROM PATIENT / GIVES PATIENT THEIR HONORARIUM

2 WEEKS VISIT – APPROXIMATELY 60 MINUTES

RESEARCH ASSISTANT / STUDY COORDINATOR
- CHECKS PATIENT IN
- 2 WEEK VISIT INFORMATION SHEET
- CONFIRMS 7-12 HOUR PLAQUE ACCUMULATION
- PATIENT GIVEN RECORD TO CARRY THROUGH THE APPOINTMENT TO EACH STATION
- DIRECTS TO 1ST EXAMINERS

1ST EXAMINERS – ORAL CAVITY EXAM, GINGIVAL INDEX, PROBING POCKET DEPTH AND BLEEDING INDEX

2ND EXAMINERS – PLAQUE INDEX

RESEARCH ASSISTANT
- CONFIRMS NEXT VISIT (DATE & TIME)
- COMPLETES 2 WEEK VISIT EXIT INFORMATION SHEET
- RECOVERS PATIENT RECORD FROM PATIENT/ GIVES PATIENT THEIR HONORARIUM

4 WEEKS VISIT – APPROXIMATELY 60 MINUTES

RESEARCH ASSISTANT / STUDY COORDINATOR

- CHECKS PATIENT IN
- 4 WEEK VISIT INFORMATION SHEET
- CONFIRMS 7-12 HOUR PLAQUE ACCUMULATION
- PATIENT GIVEN RECORD TO CARRY THROUGH THE APPOINTMENT TO EACH STATION
- DIRECTS TO 1ST EXAMINERS

1ST EXAMINERS – ORAL CAVITY EXAM, GINGIVAL INDEX, PROBING POCKET DEPTH AND BLEEDING INDEX

2ND EXAMINERS – PLAQUE INDEX

RESEARCH ASSISTANT

- CONFIRMS NEXT VISIT (DATE & TIME)
- COMPLETES 4 WEEK VISIT EXIT INFORMATION SHEET
- GIVES NEW TOOTHBRUSH/TOOTHBRUSH HEAD AND/OR TUBE OF TOOTHPASTE **PRN**
- RECOVERS PATIENT RECORD FROM PATIENT/ GIVES PATIENT THEIR HONORARIUM

12 WEEKS VISIT – APPROXIMATELY 60 MINUTES

RESEARCH ASSISTANT / STUDY COORDINATOR

- CHECKS PATIENT IN
- 12 WEEK VISIT INFORMATION SHEET
- COLLECTS TOOTHBRUSHES/ CONFIRMS 7-12 HOUR PLAQUE ACCUMULATION
- PATIENT GIVEN RECORD TO CARRY THROUGH THE APPOINTMENT TO EACH STATION
- DIRECTS TO 1ST EXAMINERS

1ST EXAMINERS – ORAL CAVITY EXAM, GINGIVAL INDEX, PROBING POCKET DEPTH AND BLEEDING INDEX

2ND EXAMINERS – PLAQUE INDEX

RESEARCH ASSISTANT

- COMPLETES 12 WEEK VISIT EXIT INFORMATION SHEET
- PATIENT EXIT QUESTIONAIRE
- TAKES SUBJECT TO RDH FOR PROPHYLAXIS PRN
- RECOVERS PATIENT RECORD FROM PATIENT/ GIVES PATIENT THEIR HONORARIUM

PATIENT RECORD

ITEMS INCLUDED IN THE RECORD ARE AS FOLLOWS:

PATIENT APPOINTMENT SCHEDULE

BASELINE VISIT INFORMATION SHEET
BASELINE VISIT – ORAL CAVITY EXAM, GINGIVAL & BLEEDING INDEX/ PD CHARTING
BASELINE VISIT – PLAQUE INDEX PRE- AND POST-BRUSHING

2 WEEK VISIT INFORMATION SHEET
2 WEEK VISIT – ORAL CAVITY EXAM, GINGIVAL & BLEEDING INDEX/ PD CHARTING
2 WEEK VISIT – PLAQUE INDEX

4 WEEK VISIT INFORMATION SHEET
4 WEEK VISIT – ORAL CAVITY EXAM, GINGIVAL & BLEEDING INDEX/ PD CHARTING
4 WEEK VISIT – PLAQUE INDEX

12 WEEK VISIT INFORMATION SHEET
12 WEEK VISIT – ORAL CAVITY EXAM, GINGIVAL & BLEEDING INDEX/ PD CHARTING
12 WEEK VISIT – PLAQUE INDEX

SCREENING RECORD
INCLUSION/EXCLUSION CRITERIA
MUSOD MEDICAL/DENTAL HEALTH HISTORY
CONSENT FORM
PATIENT EXIT QUESTIONAIRE FORM
THE FOLDER WILL ALSO CONTAIN:
LABELS (2 EACH VISIT) FOR THE 12 WEEK TOOTHBRUSH/TOOTHBRUSH HEAD COLLECTION

EXAMPLE:

#101 D.O.E
12 WEEK

SUNSTAR POWERED TOOTHBRUSH STUDY

MARQUETTE UNIVERSITY SCHOOL OF DENTISTRY

IMPORTANT NOTES

Throughout the study you must refrain from daily flossing or interdental cleaning and daily use of mouthwash, or any other toothbrush or paste other than that which has been provided.

Chewing gum is discouraged.

For each clinic visit you must have at least 7 but no more than 12 hrs. of accumulated, non-brushed, undisturbed plaque/debris before each appointment.

Do not have your teeth cleaned professionally during the study.

If you should have any dental problems during the study, do not refrain from seeking proper treatment. Please inform us of any dental treatment as this might preclude you from further participation in the study.

If you should have any other questions or concerns, please call Dr. Cathy Winters (920) 517-5263.

APPOINTMENTS:

BASELINE **DATE** _____ **TIME** _____

2 WEEKS **DATE** _____ **TIME** _____

4 WEEKS **DATE** _____ **TIME** _____

12 WEEKS **DATE** _____ **TIME** _____

PLEASE NOTE: If you are unable to keep your appointment, please contact Dr.Winters. This action may exit you from further participation in the study. We will try to reschedule, but there are limitations to the availability of the examiners and clinic hours.

NOTE: This appointment schedule will be sent to the patient prior to the start of the study. A 2nd copy will be given at the baseline visit. The 3rd copy will remain in the patient record.

CONFIDENTIAL

DENTAL HISTORY

How did you hear about the study? _____

What are your feelings about the condition of your teeth? _____

_____

What are your feelings about your past dental experiences? _____

_____

Dental Experience: Do you now or have you had

_____ Toothaches _____ clenching/grinding day or night _____ orthodontics
_____ Bad breath _____ pain in or near ear _____ root canal work
_____ Pain in chewing _____other sore or painful _____bridgework, or partial
_____Canker sores areas in the mouth dentures
_____Bleeding gums _____missing teeth
_____Gum surgery – if Yes, where? _____
_____Wisdom tooth removal – if Yes, when & where? _____

List surgical procedures in sequence by date: _____

_____

_____

Have you had regular dental check-ups? Yes No Date of last check-up: _____

Dietary Profile: Do you eat or drink between meals? Yes No

Does your diet include any of the following:

Chewing gum	Yes	No	cookies/cakes/pastries	Yes	No
Candy bars	Yes	No	sugar in coffee or tea	Yes	No
Candy	Yes	No	breath mints/cough drops	Yes	No

Oral Hygiene Status – How often do you brush? _____ Type of toothpaste?_____
Type of brush? Power/manual Hard /soft bristle? How often do you change the brush:_____
Do you use dental floss? Yes No If Yes, how often? Frequent (daily)
Sporadic (weekly)
Infrequent (monthly or less)

What is your major dental concern? _____

_____

To the best of my knowledge, I have answered every question completely and accurately, I will inform study group of any change in my health and/or of medication.

Patient's signature: _____

Reviewed by: _____

Date: _____

INFORMED CONSENT: POWERED TOOTHBRUSH STUDY

INTRODUCTION. I, , hereby agree to participate in the research study entitled, powered tooth brushing on tooth / dental plaque and gingivitis. I understand that while the program will be under the supervision of Dr.'s Andrew Dentino and Dr. Cathy Winters other professional persons may be designated to assist or act for them.

PURPOSE. The purpose of the study is to examine over a three month period of time how the use of a new powered toothbrush compares to an ADA accepted manual brush in removing dental plaque and reducing gingivitis.

PROCEDURES. I will have a dentist examine my teeth and gums for the presence of dental plaque, tartar, and gingivitis four to five times over an approximately three month period. I will also be given an oral cancer screening examination at my first (screening) visit.

The experimental aspect of this study is the short-term (3 month/12 week) comparison of the use of a new powered toothbrush compared to an ADA accepted manual brush with regard to their ability to remove plaque and reduce gingivitis. I agree to avoid daily use of mouthrinse and/or floss for the duration of the study.

My participation in the project will be to come to the dental clinic four/five times over a three month time period. I will be asked to brush my teeth only with the assigned toothbrush and toothpaste for two minutes twice a day. My first visit will be a screening appointment which will take approximately 45 minutes at which time I will be asked to fill out a medical and dental history, and then be given an oral examination by a dentist to see if I meet the entrance requirements of the study. If I meet the entrance criteria, I will be invited to participate in the study. For those subjects who qualify for the study there will be three to four additional appointments. The second visit is called the "baseline" appointment and will take approximately an hour and 15 minutes. At this visit I will have a dental professional re-examine my teeth and gums for plaque and gingivitis. After this I will be randomly assigned to either a manual or power brush and given toothpaste to use at home as directed. I understand that I must use only my assigned brush during the study. I understand that any questions I have regarding the use of the brush or the need for replacement must be directed to the study coordinator, Dr. Cathy Winters. At the following visits, 2, 4 and 12 weeks after the baseline visit, my teeth and gums will be examined again as before and I will return the assigned brush to the study coordinator at the last visit.

I understand that approximately 72 subjects will be involved in this study.

RISKS. I have been informed of the discomforts and risks which I may reasonably expect as part of the study. These include minor discomfort involved with an examination of the gums which will involve periodontal probing as a part of the screening visit, and possibly a dental cleaning (prophylaxis) at the

end. In addition, I may experience more gingivitis by not using interdental cleaners and mouthrinses during the length of the study. The toothbrush I will be assigned is likely to be different from the one I currently use, and it may have a different feel to it.

BENEFITS. I understand that the information obtained may be useful scientifically and helpful to others.

MONETARY BENEFITS. I understand that I will receive $100.00 which will be paid to me in $25 dollar gift cards, one at each appointment, starting from the baseline visit. I further understand that I will not be paid for any visits that I do not complete.

ALTERNATIVE PROCEDURES. I understand that the appropriate alternative procedure which might be advantageous for me is to not participate in the study and seek standard dental care and use commercially available toothbrushes and toothpaste.

CONFIDENTIALITY. I have been promised that any information obtained from this investigation that can be identified with me will remain confidential or will be disclosed only with my permission. However, I am in agreement that scientific data or medical information not identifiable with me resulting from the study may be presented at meetings and published so that the information can be useful to others. This includes the possibility that your medical and dental records gathered in this study may be reviewed by the sponsor (Sunstar) as part of reviewing information pertinent to the study, and could include the FDA, the ADA and the IRB at Marquette University inspecting records from this study.

RESEARCH SUBJECTS' RIGHTS. I have read or have had read to me all of the above. Dr. Dentino/Dr. Winters has explained the study to me and answered all of my questions. I have been told of the risks or discomforts and possible benefits of the study.

If at any time I have any medical problems or questions, I may contact the Principle investigator, Dr. Dentino at (414) 288 5944 during the day, or Dr. Winters at (920) 517-5263 or Dr. Keerthi Kamreddy at (254) 979-2544, after hours. I also understand that if I have questions or concerns about my rights as a research participant I may contact the Office of Research Compliance at Marquette University at 414-288-7570 for further information related to the research and my rights as a subject.

I realize I have not released Marquette University from liability for negligence. In the event of physical injury resulting from biomedical and behavioral research procedures, medical treatment in the amount not to exceed $500 is available for such physical injury, but no monetary compensation is available for wages lost because of such physical injury.

A description of this clinical trial will be available on http://www.ClinicalTrails.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this web site at any time.

WITHDRAWAL. I understand that I do not have to take part in this study, and my refusal to participate will not prejudice my present of future relationship with Marquette University School of Dentistry. The results of this study may be published, but my records will not be revealed unless required by law.

I understand my rights as a research subject, and I voluntarily consent to participate in this study. I understand what the study is about and how and why it is being done. I will receive a signed copy of this consent form.

Subject Signature	Date
Signature of Subjects' Representative*	Date

* Only required if subject not competent

Signature Witness	Date
Signature of Investigator	Date