

**Clinical Study to Evaluate the Safety and Efficacy
of the BriteSmile 2000 In-Office Tooth whitening
system.**

Protocol # ALGD-BWT-0799

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SUMMARY

A six month blind clinical study was conducted to evaluate the safety tooth whitening efficacy of the BriteSmile 2000 Tooth Whitening System. Seventy five subjects were selected to participate in this parallel, blind, three compartment, and randomized clinical study. The subjects were balanced into three groups based upon a minimal shade of D4 on the Vita Shade Guide and assigned a treatment regimen as follows:

Group 1. BriteSmile Gel alone

Group 2. Placebo Gel + BriteSmile Light

Group 3. BriteSmile Gel + Light (BriteSmile 2000 Tooth Whitening System)

Tooth whitening was performed according to the standard BriteSmile method. Basically, the soft tissues were isolated using commercial barrier materials and whitening gel was placed upon the teeth. The BriteSmile metal halide light was then placed in front of the teeth and the treatment carried out for three periods of twenty minutes each. After each 20 minute the gel was removed and a fresh layer of gel was applied.

Change in tooth color was measured by both objective and subjective methods. The objective tooth color measurement involved the use of Minolta™ CR221 chroma-meter. The subjective color measurements involved the use of Vita shade guide and self-reported whitening effectiveness. The objective measurements or the chroma-meter readings were obtained for teeth #'s 7, 8, 9 and 10 in the L*, a*, b* color space at

baseline, post-treatment, 3 month recall and 6 month recall. Calculation of color change (ΔE) was performed using the Commission Internationale de L'Eclairage (CIE L*a*b*) color difference equation. The subjective changes in the color of teeth #7, 8, 9, and 10 were measured by using the Vita shade guide at baseline, post treatment, three month recall and six month recall. The color change was measured by arranging the tab in the order of brightness as recommended by the manufacturer. The improvement in tooth color was then calculated using the standard tab counting technique. Panelist perceptions of the improvement in tooth color were examined using questionnaires.

Product safety was evaluated by clinical examinations of the oral hard and soft tissues after treatment at three month recall and at six month recall. Data concerning dental hypersensitivity was collected by the use of panelist questionnaires.

Results from this clinical study showed a mean post-treatment ΔE of 7.70 ± 1.94 for BriteSmile, a mean ΔE of 4.04 ± 1.44 for the gel 15% hydrogen peroxide gel alone and a mean ΔE of 2.19 ± 0.64 for the placebo gel plus the light. Statistical analysis using the F test showed significant differences ($p < 0.01$) between the groups, indicating that the BriteSmile procedure is significantly better when compared against the controls. The shade guide measurements confirmed these results and showed a mean improvement of 8.24 ± 1.30 tabs for BriteSmile, a mean improvement of 5.4 ± 2.29 tabs for the gel alone and a mean improvement of 1.0 ± 1.98 tabs for the placebo gel plus the metal halide light. Statistical analysis by the F-test again significant differences ($p < 0.01$) between the three groups, thus indicating that the BriteSmile system has a significantly greater tooth whitening efficacy when compared to the gel alone or the light plus the gel. The

panelists also confirmed the above results; 84% of the panelists indicated that the BriteSmile group greatly whitened their teeth as compared to 16% for the gel alone and 8% for the placebo plus the light.

Color reversion was measured at the three and six month recall. The chroma meter reversion at three and six months for the BriteSmile group was ΔE of 0.76 and ΔE of 1.71 respectively. Statistical analysis by the F-Test did not show significant differences ($p > 0.1$). The shade guide results confirmed the above findings and showed a mean reversion of 0.54 tabs at the three month recall and 1.06 tabs at the six month recall. Statistical analysis by the F-Test did not show significant differences ($p > 0.1$). The results were also confirmed by the panelist self assessment of color. At the three month and the six month recall approximately 95% of the panelists reported a non to slight reversion of color. All the subjects in this group had whiter teeth six months following the whitening procedure when compared to baseline.

Examination of the plaque and gingivitis indexes showed significant reductions in plaque immediately following the whitening procedure in all three groups. However, statistically significant (two tailed, type two t-test, $p < 0.05$) reduction in plaque at the three month and the six month recall was observed in the BriteSmile group and in the placebo gel plus the light group and not in the gel alone group. For the gingivitis scores, significant differences ($p < 0.05$) were only found in the BriteSmile group when the baseline GI data was compared with the 6 month recall data.

Post treatment clinical evaluations did not show significant adverse effects

attributable to product usage. Subjective questionnaire concerning post-treatment hypersensitivity showed no sensitivity in 76% of the BriteSmile population, 68% in the gel alone population and 84% in the placebo gel plus the light. Slight hypersensitivity was reported in the majority of the remaining panelists.

In summary, the results of this study show that the BriteSmile procedure is significantly more effective at whitening teeth when compared to the 15% hydrogen peroxide gel alone and the placebo gel plus the light. The major adverse reaction attributable to the product is slight post-treatment hypersensitivity, the levels of which are less or comparable to the levels reported for other ADA approved tooth whitening products. The results also show a significant reduction in plaque accumulation and a significant reduction in gingivitis (six months following the whitening treatment) in the BriteSmile group. The reason for this is unclear but warrants further investigation.

INTRODUCTION

Tooth whitening was first reported as a treatment option to enhance esthetics of the teeth over a hundred years ago (1). Since then, significant effort has been directed towards understanding the nature of tooth discoloration and devising methods to improve dental esthetics. In a society such as ours, discolored teeth are considered unattractive. Hence, a potential to produce psychological problems such as lack of self-esteem and confidence is present (2). This is easy to understand because the mouth is located at the anatomic foci of the face and the teeth are clearly visible during everyday activities such as talking and laughing.

Currently, several methods are available to restore discolored dentition. These include laminates or porcelain veneers, full coverage, bonding, and mechanical or chemical stain removal (3 - 5). The clinical procedure to restore stained dentition depends upon variables such as, the nature and intensity of stain, the age of the patient, desired esthetic effect, etc. Of these methods, laminates and full coverage crowns are considered most invasive because sound tooth structure is removed to achieve an acceptable level of esthetics (3). The least invasive procedures to remove discoloration from acceptably shaped discolored dentition involve the use of oxygenating chemicals such as hydrogen peroxide. This method has been suggested to be the safest means to restore discolored dentition because it does not entail removal of sound tooth structure, it is the least invasive and the agents used in this procedure have a record of safety (3, 6-10).

Vital teeth can be whitened either chairside or via the fabrication of a mouth guard. The chairside method is an in office procedure (3,4), and is commonly referred to as 'power bleaching'. This method uses a 30-35% hydrogen peroxide solution in conjunction with heat and light to increase the kinetics of stain removal. The second method involves fabrication of a mouth guard in which a peroxide preparation is placed and the mouth guard is worn over the teeth to obtain the desired esthetic effect. This is usually referred to as "Doctor Prescribed at Home Use Method" or "night guard vital bleaching". The predominant type of peroxide used in this method is 10% urea or carbamide peroxide (6-9).

Currently both the chairside methods and tray whitening methods suffer from disadvantages. The disadvantages of the power bleaching or the chairside method are as follows:

- a) 30% hydrogen peroxide is difficult to work with,
- b) Rubber dam placement is necessary,
- c) Several visits are necessary, and;
- d) Equipment is costly

The disadvantages of the tray method are as follows:

- a) Requires impressions and trays,
- b) May take 2-4 weeks,
- c) Compliance is a problem, and;
- d) Not user friendly

To overcome the above disadvantages, BriteSmile Inc. has developed an In-Office tooth whitening system called BriteSmile 2000. This system is considered to be unique when compared to other ADA accepted professionally applied bleaching products because it utilizes a pH 6.5, 15% hydrogen peroxide gel in combination with a gas-plasma light or a metal halide light (BriteSmile light) to accelerate the whitening process. The BriteSmile process also offers a further advantage because both the maxillary and mandibular teeth can be whitened at the same time and the whitening process takes approximately one hour.

Laboratory evaluation of the BriteSmile 2000 system conforming to the guidelines set forth in Acceptance Program Guidelines for Home-Use Tooth Whitening Products (10) has already been completed. Results of these studies showed that the BriteSmile system will not soften enamel or composite restorations (11). Scanning electron microscopy studies confirmed these findings and demonstrated that the system will not cause surface changes in enamel and restorative materials (12).

Further a pilot clinical trial was performed to examine the safety and efficacy of the BriteSmile tooth whitening system. Thirty subjects with normal oral health status and stained teeth were selected to participate in this monadic clinical trial. The average baseline shade of the participants was B3. Teeth whitening was performed according to the standard BriteSmile procedure and the pre and post whitening tooth color was measured by using standard shade measuring techniques (13). The results of this study did not show significant adverse effects and the average shade change was calculated to be approximately 9 (14).

A field trial or a post-marketing study involving one thousand subjects was also performed to examine the safety and efficacy of the BriteSmile 2000 system. The results showed an average improvement of 8 tabs and approximately 96% of the patients were satisfied with the post-treatment color (15).

The safety and efficacy of peroxide containing tooth whitening products is well known. In-vitro studies have shown that specific lights enhance the stain bleaching effect however, the effects of light upon clinical efficacy remain to be investigated. Hence, the purpose of this study is to evaluate the safety and efficacy of the BriteSmile 2000 system and submit the results to the American Dental Association for consideration of an ADA seal of Acceptance.

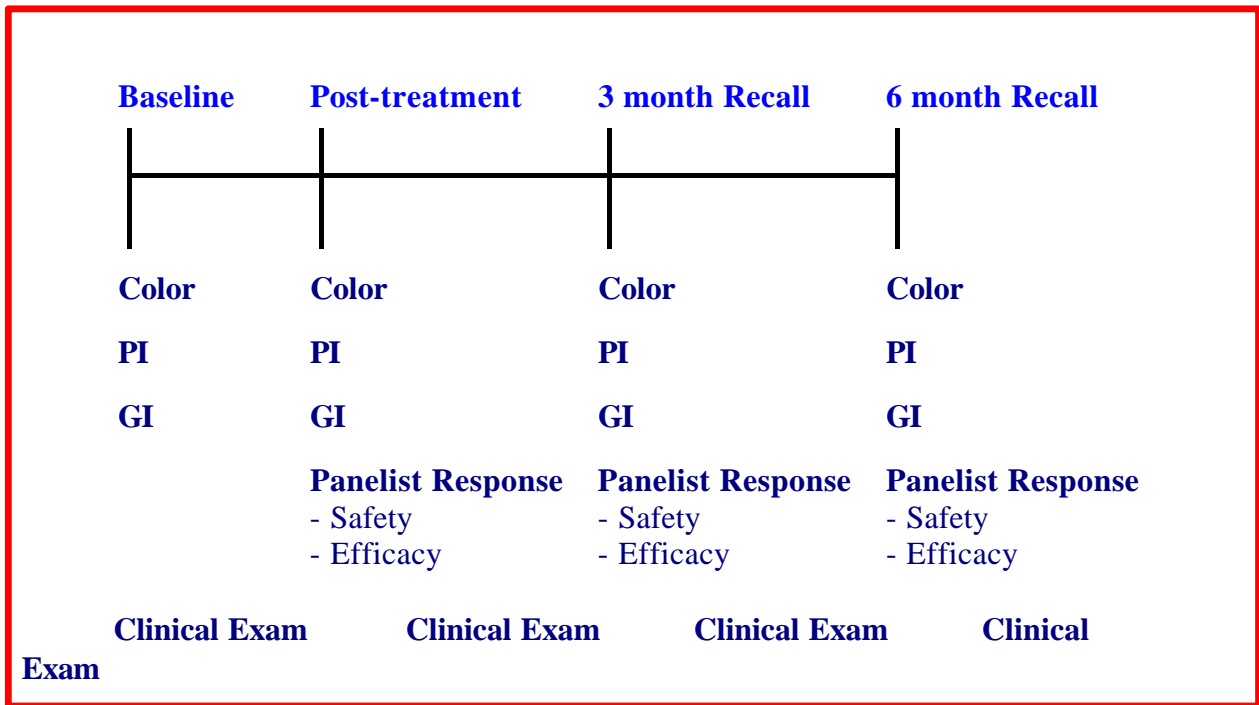
MATERIALS AND METHODS

Study Design

Seventy five healthy subjects with tooth discoloration equal to or darker than D4 on the Vita Shade Guide™ were selected to take part in this blind, randomized, three cell parallel clinical study. The groups were balanced according to shade with twenty five subjects assigned to each test regimen. The products were coded and neither the investigator nor the subjects were informed as to the identity of the product or to which group an individual belonged. The three groups were as follows:

- 1. Peroxide gel alone**
- 2. Placebo gel + BriteSmile Light**
- 3. Peroxide gel + BriteSmile Light**

The treatments were blinded with respect to the investigator by having the investigator leaving the room during the treatments. In accordance with the ADA guidelines for take home tooth whitening products the following measurements were obtained:



Subject Selection

Seventy five subjects were selected to participate in this clinical trial the inclusion/exclusion criteria were as follows:

Inclusion Characteristics

1. Signed informed consent form.
2. Good general health as evidenced by the medical history.
3. Ages 18 to 65 (male or female).
4. Availability for the 6 month duration of the study.
5. Have not undergone a professional whitening treatment.
6. Minimum shade of Vita A3/D4 or darker.

Exclusion Characteristics

1. Presence of orthodontic appliances.
2. A soft or hard tissue tumor of the oral cavity.
3. Carious lesions requiring immediate treatment.
4. Restorations on all anterior teeth which will interfere with color measurement procedures.
5. Advanced periodontal disease (characterized by the presence of purulent exudate, tooth mobility and/or extensive alveolar bone loss).
6. Is participating in another clinical study or panel test.
7. Pregnant women or women who are breast feeding.
8. Congenital tooth stains or dental defects.

Clinical Procedures

After subject acceptance into the study, oral hard and soft tissues were examined and a polyvinyl siloxane (Impragum, ESPE, PA) impression was obtained for each subject. The impression was used to fabricate chroma-meter color measuring stents for teeth #s 7, 8, 9 and 10.

Tooth color measurements were performed by reflectance spectroscopy using the Minolta Chroma Meter with 45⁰/0⁰ illumination/ observation geometry (16). Readings were taken on the midfacial aspect of each maxillary central incisor and lateral incisors using custom fabricated positioning jigs to ensure repeatable positioning of the meter. Color parameters were recorded in triplicate in the tristimulus L*a*b* color space as established by the CIE (Commission Internationale de L'Eclairage) (17,18).

Tooth color was also measured using the Vita Shade guide. To ensure consistent measurements, all color measure measurement procedures were carried out by the same investigators under color corrected operatory light. The subjects were then randomized into three equal groups based on the shade guide color.

Plaque and gingivitis indices were measured using the method of Loe and Silness (19) as follows:

Gingival Index

- 0 = Normal gingiva.
- 1 = Mild; slight color change; slight edema.
- 2 = Moderate; Redness and Glazing.
- 3 = Severe; Marked redness and edema; ulceration; spontaneous bleeding.

Plaque Index

- 0 = No plaque.
- 1 = Film at gingival margin: remove plaque with probe.
- 2 = Moderate; seen with naked eye.
- 3 = Abundance of material

Tooth whitening was then performed by investigators not involved in tooth color measurements procedures. Investigator blindness was preserved by having the investigators measuring tooth color or tooth color evaluators leaving the operatory when tooth whitening was performed. The clinical whitening procedures were as follows:

Control - Peroxide gel alone

1. Supervise tooth brushing the subject for 30 seconds.
2. Measure Color, GI, PI and perform clinical soft and hard tissue examination.
3. Color evaluators leave the operatory.
4. Apply isolation materials to the maxillary and mandibular gingiva and extend approximately 1 mm onto the tooth surfaces.
5. Insert cheek retractor and cotton rolls in the vestibules.
6. Insert bite block.
7. Apply Vaseline Petroleum Jelly to the lips.
8. Apply whitening gel approx. 2 mm thick to the teeth using a bend-a-brush.
9. Wait 20 minutes.

10. Reapply gel.
11. Wait 20 minutes.
12. Reapply gel.
13. Wait 20 minutes.
14. Remove light, isolation materials and clean teeth with an air water syringe.
15. Color Evaluators Enter the Operatory
16. Measure color, GI, PI and perform clinical soft and hard tissue examination.

Control - light + placebo gel

1. Supervise tooth brushing the subject for 30 seconds.
2. Measure Color, GI, PI and perform clinical soft and hard tissue examination.
3. Color Evaluators Leave the Operatory
4. Apply isolation materials to the maxillary and mandibular gingiva and extend approximately 1 mm onto the tooth surfaces.
5. Insert cheek retractor and cotton rolls in the vestibules.
6. Insert bite block.
7. Apply Vaseline Petroleum Jelly to the lips.
8. Apply placebo gel approx 2 mm thick to the teeth using a bend-a-brush.
9. Place BriteSmile 2000 light in contact with the bite block.
10. TURN ON LIGHT.
11. Wait 20 minutes.
12. Remove light
13. Reapply placebo gel.
14. Place BriteSmile 2000 light in contact with the bite block.
15. TURN ON LIGHT.
16. Wait 20 minutes.
17. Reapply placebo gel.
18. Wait 20 minutes.
19. TURN OFF LIGHT.
20. Remove isolation material and clean teeth with an air water syringe.
21. Color Evaluators Enter the Operatory
22. Measure color, GI, PI and perform clinical soft and hard tissue examination.

Peroxide gel + light - BriteSmile 2000

1. Supervise tooth brushing the subject for 30 seconds.
2. Measure Color, GI, PI and perform clinical soft and hard tissue examination.
3. Color Evaluators Leave the Operatory

4. Apply isolation materials to the maxillary and mandibular gingiva and extend approximately 1 mm onto the tooth surfaces.
5. Insert cheek retractor and cotton rolls in the vestibules.
6. Insert bite block.
7. Apply Vaseline Petroleum Jelly to the lips.
8. Apply placebo gel approx 2 mm thick to the teeth using a bend-a-brush.
9. Place BriteSmile 2000 light in contact with the bite block.
10. TURN ON LIGHT.
11. Wait 20 minutes.
12. Remove light
13. Reapply placebo gel.
14. Place BriteSmile 2000 light in contact with the bite block.
15. TURN ON LIGHT.
16. Wait 20 minutes.
17. Reapply placebo gel.
18. Wait 20 minutes.
19. TURN OFF LIGHT.
20. Remove isolation material and clean teeth with an air water syringe.
21. Color Evaluators Enter the Operator
22. Measure color, GI, PI and perform clinical soft and hard tissue examination.

Panelist Assessment of Tooth Color and Product Safety

To obtain additional information concerning tooth color and the subjective incidence of adverse reactions, all panelists were required to answer the following questions after the treatment.

3. Did you feel any discomfort during the procedure?

Not at all Slightly Moderately Greatly

If yes, please explain _____

4. Did your teeth feel sensitive before the procedure?

Not at all Slightly Moderately Greatly

5. Did your teeth feel sensitive after the procedure?

Not at all Slightly Moderately Greatly

Three and Six Month Recall

Attempts were made to recall all panelists three months and six months after the whitening treatments. At these periods the following parameters were measured:

1. **Tooth Color – chroma meter and shade guide**
2. **Gingival Index (GI)**
3. **Plaque Index (PI)**
4. **Clinical Examination of Soft and Hard tissues**
5. **Panelist perception of tooth color and safety**

Panelist perception of color and panelist observations concerning product safety was also determined by the use of the questionnaire shown in the protocol.

Calculation of Color Change.

A.) Chroma Meter

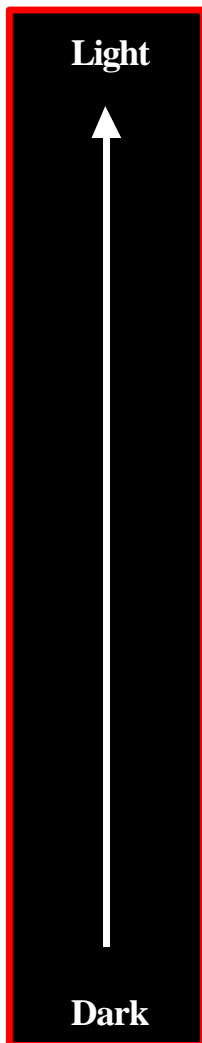
The objective change in tooth color was determined by averaging the color parameters for each tooth (i.e., #7, 8, 9 and 10) and color differences were calculated between the initial measurements and those measurements obtained post-treatment, three month recall and six month recall. This method has been shown to be related to human color perception and recommended by the American Dental Association for determination of color differences between various tooth shades (10, 17). In this method, the colors of teeth are compared using the CIELAB or the tristimulus color difference equation (17, 18):

$$DE = \{(DL^*)^2 + (Da^*)^2 + (Db^*)^2\}^{1/2}$$

Where ΔE is the difference in color, the more positive the value the whiter the color. ΔL^* is the change in lightness, the greater the ΔL^* the whiter the teeth. Δa^* and Δb^* are chromacity values i.e. the amount of redness and the amount of yellowness.

B. Shade Guide

Shade changes were measured by obtaining the shade of teeth numbers 7, 8, 9 and 10 under color corrected operatory light. The shade of each tooth was scored by arranging the Vita guide according to the degree brightness as shown below and recommended by the manufacturer and counting the number of tabs. The overall change in shade was then obtained by averaging the scores.



<u>Tab</u>	<u>Score</u>
B1	16
A1	15
B2	14
D2	13
A2	12
C1	11
C2	10
D4	9
A3	8
D3	7
B3	6
A3.5	5
B4	4
C3	3
A4	2
C4	1

C.) Panelist Perception

After treatment, at three months recall and at six month recall, the panelists were asked questions concerning the yellowness and whiteness of the teeth. The questions were as follows:

- How much did the product increase the whiteness of your teeth?
Not at all Slightly Moderately Greatly
- Did the test product reduce the yellowness of your teeth?

Not at all Slightly Moderately Greatly

Calculation of Gingival Index.

Gingivitis index was scored according to the method of Loe and Silness (19). Those teeth with cervical restorations and crowns were excluded from the scoring procedure. Whole-mouth (excluding second and third molars) mean scores were obtained by averaging the values recorded from all scorable surfaces as detailed in the protocol.

Calculation of Plaque Index.

Plaque index was scored according to the method of Loe and Silness (19). Those teeth with cervical restorations and crowns were excluded from the scoring procedure. Maxillary and mandibular second and third molars were excluded from scoring. Mean scores were obtained by averaging the values recorded from all scorable surfaces.

Assessment of Product Safety.

Product safety was evaluated by clinical examinations of the hard and soft tissues and panelist reported incidences of adverse reactions.

RESULTS.

All subjects completed the first phase of the study. A summary of the subject population is presented in the table 1.

Table 1.

<u>Group</u>	<u>Number of Subjects</u>	<u>% Female</u>	<u>Mean Age (\pm SD)</u>
Placebo gel + light	25	18	37.13(+/-12.3)
Peroxide Gel	25	15	36.64(+/-5.7)
BriteSmile	25	16	39.22(+/-12.7)

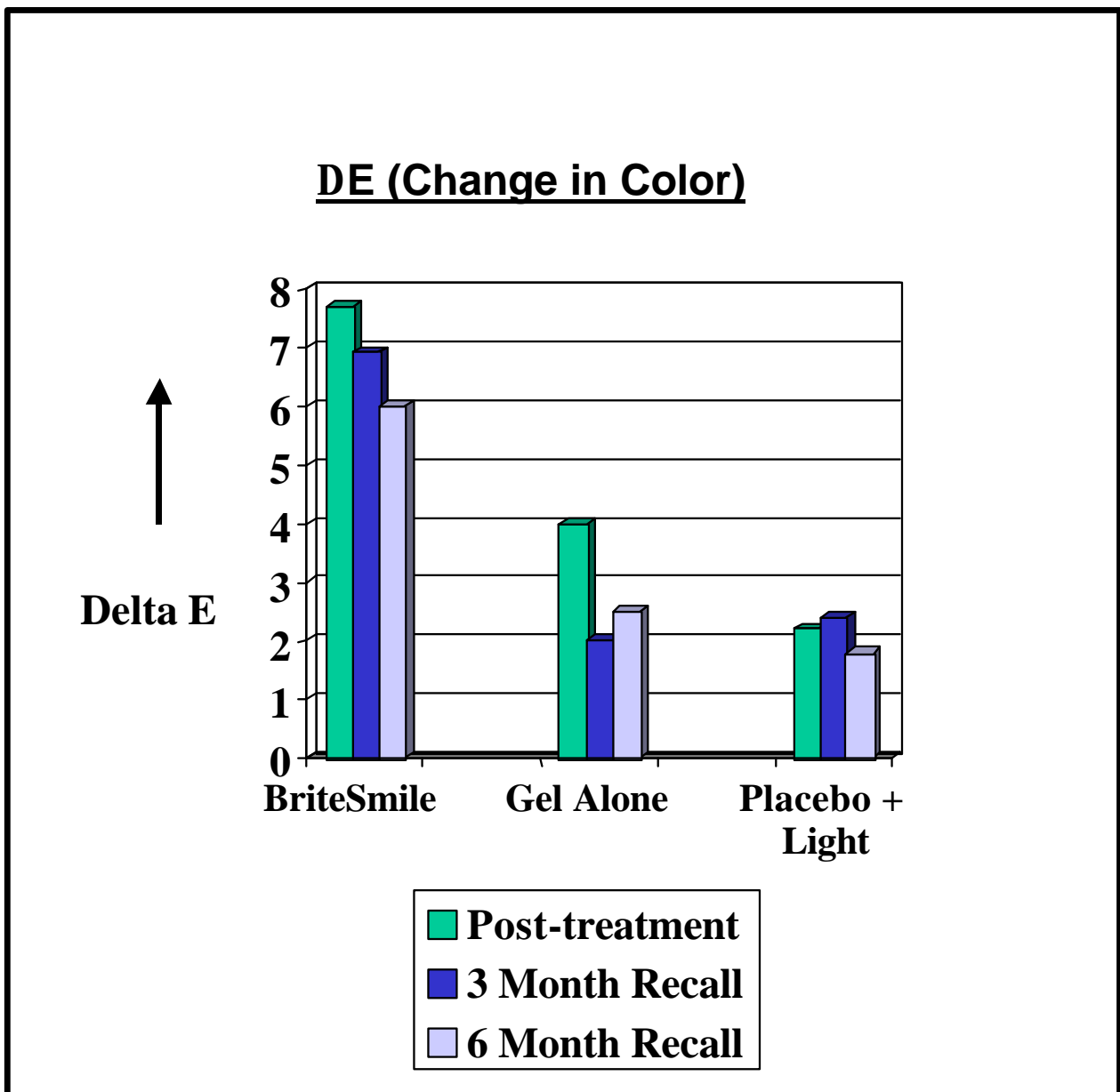
Statistical analysis by the F and the t tests did not show significant differences in the ages of the subjects indicating the subjects are from the same population.

Chroma Meter

Color differences were calculated between the initial measurements and those after the first and second weeks. To obtain a quantification of a total change in color before, after treatment at three month recall and at six month recall, ΔE was calculated by the tristimulus color difference equation. The overall change in color was obtained by calculating the ΔE for teeth numbers 7, 8, 9 and 10 and then obtaining the average. The results of the average ΔE are shown in table 2 and graph 1 below.

Table 2 and Graph 1

<u>DE (Change in Color)</u>			
<u>Product</u>	<u>Post-Tx.</u>	<u>3 month recall</u>	<u>6 month recall</u>
BriteSmile	7.70 (+/-1.94)	6.94 (+/-2.72)	5.99 (+/-2.41)
Gel alone	4.04 (+/-1.44)	2.05 (+/- 1.07)	2.51 (+/-1.16)
Placebo +Light	2.19 (+/-0.64)	2.37 (+/- 1.36)	1.83 (+/-0.69)



Statistical Analysis

Statistical Analysis of the chroma meter data was performed using the F-test. The results showed significant differences ($p < 0.01$) between the three groups as outlined in table 3.

Table 3

<u>Sample</u>	<u>Post-Treatment DE</u>	<u>p</u>
BriteSmile	7.70 (+/-1.94)	<0.01
Gel alone	4.04 (+/-1.44)	
BriteSmile	7.70 (+/-1.94)	<0.01
Placebo +Light	2.19 (+/-0.64)	
Placebo +Light	2.19 (+/-0.64)	<0.01
Gel alone	4.04 (+/-1.44)	

The data shown above demonstrates that the BriteSmile System is significantly better when compared to the peroxide gel alone and the placebo gel plus light. As expected the placebo gel had a minimal effect upon tooth whiteness. The data also suggests that the light has a synergistic effect upon tooth whiteness. This is based upon the finding that the gel alone gave a mean ΔE of 4.04 and the placebo alone showed a mean ΔE of 2.19. Therefore, if the tooth whitening effect was additive then a mean ΔE

of $4.04 + 2.19 = 6.23$ would be expected. However, a mean ΔE of 7.70 was obtained therefore suggesting an activating effect of the light upon the 15% peroxide gel.

Color Reversion

The color reversion was measured by recalling the subjects at 3 and 6 months. A number of subjects dropped due to reasons unrelated to the clinical experience or adverse reactions. Notably, the drop outs are common for studies of this type because of the subjects desire to have white teeth rather than the compensation for participation in the study. In the BriteSmile group 2 subjects dropped out, in the placebo + light 5 subjects dropped out. None of the subjects dropped out in the peroxide alone group.

Color Reversion at 3 Months

Statistical analysis of the post-treatment ΔE *versus* 3 month ΔE by the F-test did not show significant difference between the post-treatment and the three month recall indicating that the tooth whiteness is maintained for the three month period. The results are summarized in table 4, below.

Table 4

<u>Sample</u>	<u>Post-Treatment DE</u>	<u>3 Month DE</u>	<u>p</u>
BriteSmile	7.70 (+/-1.94)	6.94 (+/-2.72)	>0.05

Gel alone	4.04 (+/-1.44)	2.05 (+/- 1.07)	>0.05
Placebo +Light	2.19 (+/-0.64)	2.37 (+/- 1.36)	>0.05

Color Reversion at 6 Months

Statistical analysis comparing the post treatment ΔE versus 6 month ΔE using the F-test did not show significant differences ($p < 0.01$) indicating that color will be maintained for at least 6 months. The results are shown in table 5 below:

Table 5

Mean changes in DE

<u>Sample</u>	<u>Post-Treatment DE</u>	<u>6 Month DE</u>	<u>p</u>
BriteSmile	7.70 (+/-1.94)	5.99 (+/-2.41)	>0.05
Gel alone	4.04 (+/-1.44)	2.51 (+/- 1.16)	>0.05
Placebo +Light	2.19 (+/-0.64)	1.83 (+/- 0.69)	>0.05

Shade Guide

To confirm chroma meter measurements, tooth shade was also measured at baseline, post treatment, 3 month recall and at 6 month recall. To obtain consistent measurements, all shade guide measurements were obtained by the same investigators.

The investigators involved in the shade measurement process were not aware as to the identity of the product or to the procedure the subject had undergone.

The three groups of subjects were balanced according to tooth shade. Table 6, shows the baseline tooth shade.

Table 6

<u>Sample</u>	<u>Baseline Shade</u>
BriteSmile	B3 – D3
Gel alone	B3 – D3
Placebo +Light	B3 – D3

Table 7 shows the improvement in tooth color from the baseline i.e., baseline = 0 for the three groups. As in the case of the objective measurements, the improvement for each tooth was calculated i.e., teeth numbers 7, 8, 9 and 10 and the scores were averaged to get a mean improvement or change for that particular individual. The data shows an improvement of 8.24 tabs for BriteSmile, 5.4 tabs for the gel alone and 1.0 tab change for the placebo plus the light. The results confirm the chroma meter data and also support the hypothesis that the light and the peroxide gel synergize the whitening effect.

Table 7

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Mean Improvement in tooth color (Vita Tabs)

<u>Sample</u>	<u>Post-Treatment</u>	<u>3 month Recall</u>	<u>6 month Recall</u>
BriteSmile	8.24 (+/- 1.30)	7.70 (+/- 2.01)	7.18 (+/- 2.08)
Gel	5.40 (+/- 2.29)	3.84 (+/- 2.15)	3.12 (+/- 1.90)
Placebo Gel + Light	1.0 (+/- 1.98)	0.95 (+/- 2.74)	0.94 (+/- 2.08)

Statistical Analysis

Statistical analysis by the F-test showed significant differences between the groups ($p < 0.01$) indicating that the BriteSmile system has a greater efficacy compared to the peroxide gel alone or the peroxide gel plus the light.

Color Reversion

Color reversion was measured by recalling the subjects 3 months and 6 months after treatment. Again shade guide measurements were obtained by the same investigators in order to avoid inter-investigator variability.

Color Reversion at 3 Months

Statistical analysis of the post-treatment tab score *versus* 3 month tab score by the F-test did not show significant differences ($p > 0.1$) indicating that the tooth whiteness is maintained for the three month period. The results showing the reversion are summarized in table 8, shown below.

Table 8

<u>Mean Tab Changes</u>			
<u>Sample</u>	<u>Post-Treatment</u>	<u>3 month Recall</u>	<u>Reversion*</u>
BriteSmile	8.24 (+/- 1.30)	7.70 (+/- 2.01)	0.54
Gel	5.40 (+/- 2.29)	3.84 (+/- 2.15)	1.56
Placebo Gel + Light	1.0 (+/- 1.98)	0.95 (+/- 2.74)	0.05

*Color reversion was calculated by subtracting the mean three month tab change from the mean post-treatment tab change i.e., post-treatment minus 3 month recall.

Color Reversion at 6 Months

Statistical analysis of the post-treatment tab score *versus* 6 month tab score by the F-test did not show significant differences ($p > 0.1$) indicating that the tooth whiteness is maintained for the six month period. A summary of the results is shown in table 9.

Table 9

<u>Mean Tab Changes</u>			
<u>Sample</u>	<u>Post-Treatment</u>	<u>6 month Recall</u>	<u>Reversion*</u>
BriteSmile	8.24 (+/- 1.30)	7.18 (+/- 2.08)	1.06
Gel	5.40 (+/- 2.29)	3.12 (+/- 1.90)	2.28
Placebo Gel + Light	1.0 (+/- 1.98)	0.94 (+/- 2.08)	0.06

*Color reversion = post-treatment minus 6 month recall.

Post Treatment Panelist Perception of Color Change

In addition to the chroma meter and shade guide measurements, panelist perception of tooth color was also evaluated post-treatment, at three months recall and at six month recall. The data is summarized in table 10 below and shows the percentage of the population responding to the particular question.

Question: How much did the product increase the whiteness of your teeth?

Table 10

Post treatment Response

<u>Group</u>	<u>Not at all</u>	<u>Slightly</u>	<u>Moderately</u>	<u>Greatly</u>
Britesmile	0 %	0 %	16 %	84 %

Gel alone	0 %	28 %	56 %	16 %
Placebo + light	36 %	28 %	28 %	8 %

Tooth yellowness has also been related to the perception of tooth whiteness and yellow teeth are considered stained and usually unattractive hence, the panelists were also questioned regarding the reduction of yellowness. The following question was asked:

Question: Did the test product reduce the yellowness your teeth?

The post treatment responses have been tabulated in table 11.

Table 11

Post treatment Response

<u>Group</u>	<u>Not at all</u>	<u>Slightly</u>	<u>Moderately</u>	<u>Greatly</u>
Britesmile	0 %	0 %	12 %	88 %
Gel alone	12 %	28 %	52%	8 %
Placebo + light	36 %	24 %	20%	20 %

The data shown confirms the results of the chroma meter measurements, shade evaluations and shows that a majority of the subjects (84%) in the BriteSmile group achieved the greatest whitening as far as their own perception is concerned. This compares with 16% with the hydrogen peroxide gel alone and 8% with the placebo plus the gel. Similarly, 88% of the subjects reported the greatest yellowness reduction with

the BriteSmile product compared to 8% with the gel alone and 20% with the placebo gel plus the light.

3 Month Post Treatment Panelist Perception of Color Reversion

Panelist perception of color reversion was also determined at three month post treatment. In order to evaluate the amount of color reversion the panelists were asked the question: Compared to after treatment, has the whiteness of your teeth decreased? The data tabulated (table 12) below shows the percentage of responses to the question above.

Question: Compared to after treatment, has whiteness of your teeth decreased?

Table 12

Response at 3 Month Recall

<u>Group</u>	<u>Not at all</u>	<u>Slightly</u>	<u>Moderately</u>	<u>Greatly</u>
Britesmile	35 %	60 %	5 %	0 %
Gel alone	40 %	40 %	20 %	0 %
Placebo + light	75 %	15 %	5 %	5 %

The data shown above indicates and confirms the finding of the chroma meter and shade guide measurements that none to a slight amount of regression is expected and is perceived by the panelists. However, the utility of the data obtained above is questionable since only 16% of the panelists treated with hydrogen peroxide alone and 8% with the placebo plus the gel reported a significant whitening effect.

Panelist data concerning the decrease in yellowness was also obtained. This data is presented table 13:

Question: Compared to after treatment, has the yellowness of your teeth increased?

Table 13

Response at 3 Month Recall

<u>Group</u>	<u>Not at all</u>	<u>Slightly</u>	<u>Moderately</u>	<u>Greatly</u>
Britesmile	60 %	35 %	0 %	5 %
Gel alone	56 %	36 %	8 %	0 %
Placebo + light	80 %	15 %	0 %	5 %

As in the case above, a majority of the population reported a none to slight increase in tooth yellowness. Again, the utility of the data obtained above is questionable since only 16% of the panelists treated with hydrogen peroxide alone and 8% with the placebo plus the gel reported a significant whitening effect.

6 Month Post Treatment Panelist Perception of Color Reversion

As at the three post-treatment recall and six month post treatment recall, panelist perception of color reversion was also determined by the use of questionnaires. The data tabulated in tables 14 and 15 and the percentage of responses to the questions indicated below

Question: Compared to after treatment, has whiteness of your teeth decreased?

Table 14

Response at 6 Month Recall

<u>Group</u>	<u>Not at all</u>	<u>Slightly</u>	<u>Moderately</u>	<u>Greatly</u>
Britesmile	48 %	48 %	4 %	0 %
Gel alone	40 %	28 %	32 %	0 %
Placebo + light	58 %	42 %	0 %	0 %

Question: Compared to after treatment, has the yellowness of your teeth increased?

Table 15

Response at 6 Month Recall

<u>Group</u>	<u>Not at all</u>	<u>Slightly</u>	<u>Moderately</u>	<u>Greatly</u>
Britesmile	71 %	29 %	0 %	0 %
Gel alone	56 %	28 %	16 %	0 %
Placebo + light	82 %	18 %	0 %	0 %

The data shown above is very similar to the results obtained at the three month recall and again shows that a slight regression is expected after six months of treatment. Notably, as shown above especially, the BriteSmile group none of the panelists had reached their baseline tooth color and the average regression is approximately 1.0 tab.

Gingival Index

Gingival index was scored according to the method of Loe and Silness. Those teeth with cervical restorations and crowns were excluded from the scoring procedure. Whole-mouth (excluding maxillary and mandibular second and third molars) mean scores were obtained by averaging the values recorded from all scorable surfaces. The data are tabulated (table 16) below:

Table 16

	<u>Gingival Index</u>			
<u>Sample</u>	<u>Pre-Treatment</u>	<u>Post-Treatment</u>	<u>3 month Recall</u>	<u>6 month Recall</u>
BriteSmile	0.88 (+/- 0.43)	0.87 (+/- 0.42)	0.66 (+/- 0.41)	0.62 (+/- 0.36)
Gel	0.81 (+/- 0.33)	0.90 (+/- 0.32)	0.77 (+/- 0.33)	0.65 (+/- 0.33)
Placebo Gel + Light	0.78 (+/- 0.36)	0.75 (+/- 0.34)	0.70 (+/- 0.36)	0.72 (+/- 0.36)

Statistical Analysis

Statistical analysis was performed by the two tailed, type two t-test. The data showed significant differences ($p < 0.05$) in the BriteSmile group when the baseline GI data was compared with the 6 month recall data. Similar statistical significant differences were not found in the gel alone group or the light plus the gel. The significant reduction in the gingivitis score for the BriteSmile group is not understood but may be related to

the fact that the subjects become more aware of their oral health status. Further investigation is necessary to examine this phenomenon.

Plaque Index

Plaque index was scored according to the method described above. Those teeth with cervical restorations and crowns were excluded from the scoring procedure. Whole-mouth mean scores (excluding second and third molars) were obtained by averaging the values recorded from all scorable surfaces. The data are tabulated below:

Table 17

	<u>Plaque Index</u>			
<u>Sample</u>	<u>Pre-Treatment</u>	<u>Post-Treatment</u>	<u>3 month Recall</u>	<u>6 month Recall</u>
BriteSmile	1.04 (+/- 0.33)	0.24 (+/- 0.25)	0.46 (+/- 0.27)	0.47 (+/- 0.23)
Gel	0.58 (+/- 0.37)	0.13 (+/- 0.23)	0.52 (+/- 0.43)	0.42 (+/- 0.37)
Placebo Gel + Light	0.84 (+/- 0.39)	0.21 (+/- 0.11)	0.54 (+/- 0.27)	0.49 (+/- 0.25)

Statistical Analysis

Statistical analysis was performed by the two tailed, type two t-test. The data showed significant differences ($p < 0.05$) in the BriteSmile group when the baseline PI data was compared with the post-treatment, 3 month and 6 month recall. Similar statistical significant differences were also found in the placebo gel + light group.

However, significant differences ($p > 0.05$) were not found in the gel alone group at the 3 month recall and the six month recall. The significant reduction in the plaque scores in all three groups after treatment is easy to understand because the subject is required to brush the teeth two times and further the teeth are cleansed with during and after the procedure. The significant reduction in the plaque scores at 3 months and 6 month after recall is not understood and warrants further investigation.

Product Safety

Clinical Examinations

Clinical examinations did not show any differences in the placebo plus the light group or the gel alone group. However, in the BriteSmile group blanching of the gingival margin of tooth #10 was observed in Subject #9. A similar effect was observed in Subject # 36's maxillary central incisors Subject #9 did not complain of any discomfort while subject # 36 complained of "burning gums". This condition resolved within 30 minutes and did not need any intervention. At three and six month recall the tissues were within normal limits.

The blanching of the tissues is thought to be related to the contact with the peroxide gel with the tissues, a phenomenon commonly observed in tray whitening systems.

Dental hypersensitivity

One of the most common side effects of teeth whitening treatment is dental hypersensitivity. The tray whitening treatments are known to cause hypersensitivity in

approximately 50-60% of the subjects (20, 21) which is thought to be related to the concentration of the peroxide and the length of the therapy (22). Since, the length of therapy in this study is considerably shorter when compared to take home systems and the concentration of peroxide is greater, it was important to measure the subjective level of dental hypersensitivity.

The rates of hypersensitivity in this study were measured by the use of questionnaires. As soon as the treatment was completed the subjects were asked the following question:

Did your teeth feel sensitive at any time after the procedure?

The subjects were then required to rank the hypersensitivity as follows:

Not at all Slightly Moderately Greatly

The results of the above question are shown in table 18 below:

Table 18

Hypersensitivity Post treatment Response

<u>Group</u>	<u>Not at all</u>	<u>Slightly</u>	<u>Moderately</u>	<u>Greatly</u>
Britesmile	76 %	20%	4 %	0 %

Gel alone	68 %	24 %	4 %	4 %
Placebo + light	84 %	16 %	0 %	0 %

None of the subjects who reported the occurrence of sensitive teeth required intervention or medications. The levels of hypersensitivity were found to be similar in all three groups of subjects tested. It is interesting to note that the levels of hypersensitivity obtained in this study are less when compared to the results reported for tray whitening systems (21, 22). The reason for this is unknown but it is possible that hypersensitivity is less in this technique because the gingival tissues are isolated and the length of therapy is much shorter.

In certain cases it was difficult to determine if the hypersensitivity was real or occurred as a result of under going the whitening procedure. To examine this further the subjects were questioned if their teeth were sensitive anytime including post-treatment and at anytime during the past 3 months and during the past 6 months. The results are shown in tables 19 and 20.

Table 19

Hypersensitivity 3 month Post Treatment Response

<u>Group</u>	<u>Not at all</u>	<u>Slightly</u>	<u>Moderately</u>	<u>Greatly</u>
Britesmile	63 %	32 %	4.5 %	4.5 %
Gel alone	68 %	24 %	4 %	4 %
Placebo + light	60 %	36 %	0 %	4 %

Table 20

Hypersensitivity 6 month Post Treatment Response

<u>Group</u>	<u>Not at all</u>	<u>Slightly</u>	<u>Moderately</u>	<u>Greatly</u>
Britesmile	76 %	20%	4 %	0 %
Gel alone	52 %	40 %	8 %	0 %
Placebo + light	82 %	16 %	0 %	0 %

The results shown above indicate that there is a chance of hypersensitive teeth after the treatment. In general, the overall extent of hypersensitivity is none to slightly. To examine this phenomenon further and to evaluate if in the subjects opinion if the risks of having hypersensitive teeth outweighs the benefit of having whiter teeth, the subjects were asked if they would recommend this procedure to their friends. The results are shown in tables 21, 22 and 23.

Table 21

Post-Treatment Whitening Procedure Recommendation

<u>Group</u>	<u>Not at all</u>	<u>May-be</u>	<u>Yes</u>
Britesmile	0 %	4 %	96 %
Gel alone	0 %	16 %	84 %
Placebo + light	24 %	12 %	64 %

Table 22

3 Month Post-Treatment Whitening Procedure Recommendation

<u>Group</u>	<u>Not at all</u>	<u>May-be</u>	<u>Yes</u>
Britesmile	4 %	8 %	88 %
Gel alone	0 %	16 %	84 %
Placebo + light	48 %	4 %	48 %

Table 23

6 Month Post-Treatment Whitening Procedure Recommendation

<u>Group</u>	<u>Not at all</u>	<u>May-be</u>	<u>Yes</u>
Britesmile	0 %	9 %	91 %
Gel alone	8 %	16 %	76 %
Placebo + light	47 %	0 %	53 %

The data shown above shows a trend between the whitening efficacy and product recommendation. For example the BriteSmile group has the greatest tooth whitening efficacy and has the highest rates of procedure recommendations. In contrast, the lowest recommendations were found in the placebo plus the light group yet, the levels of hypersensitivity were similar. It is also interesting to note, that the majority of the people in all three groups who reported hypersensitivity would recommend the product to their friends e.g., as shown above 91% of the subjects would recommend the BriteSmile procedure to their friends while 24 % reported of hypersensitivity.

To examine if the whitening treatments give rise to long term hypersensitivity, the subjects were questioned if they had hypersensitivity at the 3 month and the six month

recall. The subjects were also questioned if they had sensitive teeth before the procedure.

The questions were as follows:

Did your teeth feel sensitive before the procedure?

Did your teeth feel sensitive now ?

The results are tabulated in table 24.

Table 24

Comparison of the Pre and Post Procedure Hypersensitivity

Subjects reporting hypersensitivity			
<u>Group</u>	<u>Pre-Procedure</u>	<u>3 month</u>	<u>6 month</u>
Britesmile	16 %	9 %	9 %
Gel alone	19 %	4 %	8 %
Placebo + light	12 %	9 %	9 %

None of the subjects who reported post treatment hypersensitivity reported that they had sensitive teeth at the recall periods. Indicating that the whitening treatments investigated in this study will not give rise to long term hypersensitivity. It is also

interesting to note, that there is a trend towards lower hypersensitivity when the pre-procedure levels are compared to the three and six month recall levels. The reasons for the reduction in hypersensitivity is unclear but may be related to the reduction in plaque and improvement in the gingival condition of the panelists.

CONCLUSIONS

Human perception of tooth color is very complex and consists of both subjective and objective components. As every dentist knows, the subjective component of color is highly variable and dependent upon factors such as ambient lighting, the color of a person's skin, make-up or clothing, the distribution and appearance of nearby teeth, etc. In order to overcome these variables, tooth color in this study was measured using both the shade guide and the chroma-meter. The Minolta™ chroma meter was used because it gives a more objective and consistent method of measuring and detecting changes in tooth color. In contrast, the shade guide gives a measurement which is more understandable to the consumer. Hence, both methods were to examine the whitening efficacy of the BriteSmile system.

The results of this study showed that the BriteSmile 2000 system is more effective at whitening teeth when compared to the gel alone or the placebo gel plus the light. The data also indicate that the light and the gel combination may have a synergistic effect upon tooth whitening rather than an additive effect e.g., gel alone gave a mean ΔE of 4.04 and the placebo alone showed a mean ΔE of 2.19. Therefore, if the tooth whitening effect were additive then a mean ΔE of $4.04 + 2.19 = 6.23$ would be

expected. However, a mean ΔE of 7.70 was obtained therefore suggesting an activating effect of the light upon the peroxide gel. Similarly, the data shows an improvement of 8.24 tabs for BriteSmile, 5.4 tabs for the gel alone and 1.0 tab change for the placebo plus the light. This phenomenon deserves further investigation but it is thought to occur as a result of the result of the light dependent activation of peroxide (24).

Currently, one of the major issues concerning the use of whitening products is that of hypersensitivity. This study shows that the BriteSmile has a similar or even better hypersensitivity profile compared to current ADA approved products. The maximal level of hypersensitivity was obtained immediately following treatment, 76% of the subjects reported no hypersensitivity, 20% reported slight hypersensitivity and 4% reported moderate hypersensitivity. The discomfort arising as a result of hypersensitivity also appears to be low because all subjects completed the one hour treatment procedure and did not require analgesics. Further, the advantage of the whitening treatment seems to outweigh the disadvantage because 95-96% of the subjects who underwent the treatment would recommend the procedure to their friends.

Clinical examination of the oral cavity did not show any significant product related adverse reactions. Two subjects in the BriteSmile group showed a minor localized blanching of the gingiva which resolved within 30 minutes. The panelists in question did not complain of significant discomfort. The blanching of the tissues is common in take home tray applied products and is thought to occur either due to the leakage of the peroxide through the light cured liquid dam or due to incomplete curing of the material. Hence, in order to avoid similar problems it is recommended that the light cured material checked for curing e.g., the hardness should be checked with an explorer. To prevent leakage it is recommended that the gingival margins checked with an explorer to ensure complete seal.

An interesting out come of this study was an observation that a significant

reduction in plaque occurs in the subjects treated with the light. A statistically significant reduction in gingivitis was also observed in the BriteSmile group. The reasons for this find remain unknown but it is possible that the light has an effect on the plaque bacteria or alternatively, the desire to keep white teeth white may have played a role in the reduction in gingivitis in the BriteSmile group. Further studies are necessary to further examine this phenomenon.

REFERENCES

1. Darnell DH. and Moore WC. Vital tooth bleaching: the White and Brite Technique. *Compend. Cont. Educ. Dent.* 1990, 11:86-93
2. Arens D. The role of bleaching in Esthetics. *Dental Clinics of North America.* 1989; 33: 319-336
3. Feinman RA, Goldstein RE and Garber DA. *Bleaching Teeth.* Quintessence Publishing, Chicago. 1987; 18-33
4. Fletcher M, Farina M, Smyth M and Woodbury S. Bleaching of discolored teeth. *Penn Dental Journal* 1992: Winter: 9-29
5. Croll TP and Cavanaugh RR. Enamel color modification by controlled hydrochloric acid-pumice abrasion. *Quintessence Int.* 1986; 17:81-87
6. Haywood VB and Heyman HO. Nightguard Vital Bleaching. *Quintessence Int.* 1989; 20: 173-176
7. Haywood VB. Nightguard vital bleaching: Current information and research. *Esthet. Dent. Update* 1990; 1: 20-25
8. Haywood VB and Heyman HO. Nightguard vital bleaching. *Quintessence Int.* 1991; 22: 515-523
9. Stindt DJ, Quenette L: An Overview of Gly-oxide Liquid in Control and Prevention of Dental Disease. *Compend Contin Educ Dent* 1989;10:514-520
10. American Dental Association's Acceptance Program Guidelines for Home use Tooth Whitening Products (ADA Council on Scientific Affairs, May 1998).
11. Nathoo SA and Vaidyanathan TK. Effect of a Light Activated Tooth Whitening System upon Microhardness of Enamel and Composite. *J. Dent. Res.* 2000; 79: 966
12. Vaidyanathan TK. Nathoo SA. and Vaidyanathan J. Effect of Gas Plasma Light Activated Whitening: Surface Morphology. *J. Dent. Res.* 2000; 79: 1129
13. Nathoo SA. and Chmielewski MB. Clinical Evaluation of Colgate Platinum Professional Toothwhitening System and Rembrandt Lighten Bleaching Gel. *Compend. Contin. Educ. Dent. Suppl* 1994; 17: S640-645

14. Nathoo SA, Mascolo MM, and Warner JW Clinical Evaluation of a Light Activated Tooth Whitening System. *J. Dent. Res.* 2000; 79: 2358
15. Data on File, BriteSmile Inc.
16. Minolta Corp. Technical Manual for Minolta Chroma Meter CR- 200/CR-210/CR-221/CR-231
17. O'Brien WJ, Groh CL and Boenke KM. A New, Small-color-difference Equation for Dental Shades. *J. Dent. Res.* 1990; 9: 1762-1764
18. CIE. Recommendations on uniform color spaces. Color difference equations. Psychometric color terms. Suppl. 2 to CIE publication 15 (E-13.1) 1971/(TC-1.3), 1978, Paris: Bureau Central de la CIE.
19. Loe H and Silness J. Periodontal Disease in Pregnancy. *Acta Odontol. Scand.* 1963; 21:533-537
20. Matis BA, Cochran MA, Eckert G, and Carlson TJ. The Efficacy and safety of a 10% carbamide peroxide gel. *Quintessence Int.* 1998 29:555-563
21. Tam L. Clinical Trial of Three 10% Carbamide Peroxide Bleaching Products. *J. Can. Dental Assn.* 1999; 4:201-205
22. Rotstein I, Torek Y and Lewinstein I. Effect of Bleaching Time and Temperature on the Radicular Penetration of Peroxide Endod Dent Traumatol 1991; 7:196-198
23. Van Der Zee J, Krootjes BBH, Chigness CF et al. Hydroxyl Radical Generation by a light-dependent Fenton reagent. *Free Radical Biology and Medicine* 1993; 14:105-113