TREATMENT OF WHITE SPOT LESIONS WITH MI PASTE PLUS, WITH OR WITHOUT MICROABRASION:

A SPLIT-MOUTH, RANDOMIZED CLINICAL TRIAL

A Thesis

by

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ABSTRACT

Purpose

The purpose of this study was to determine whether the addition of microabrasion to MI Paste Plus provides significant added benefits over MI Paste Plus alone in reducing the amount of demineralization and restoring enamel lightness.

Materials and Methods

This prospective, randomized controlled split-mouth clinical trial involved 14 patients, recruited from the Texas A&M College of Dentistry, Department of Orthodontics, who completed fixed orthodontics at least six months prior to the study, and had at least one white spot lesion on both upper left and right anterior dentition. Teeth were randomized to the combined side (which received both microabrasion and MI Paste Plus) or the control side (which received only MI Paste Plus). The combined side underwent two applications of rubber dam-isolated microabrasion while patients applied MI Paste Plus to both groups twice daily throughout the study. Enamel lightness value was obtained using spectrophotometer analysis. Surface area of the lesion was obtained with photography software analysis.

Results

Lesion size as a percentage of surface area significantly decreased for both groups compared to baseline. The combined side exhibited significantly more reduction

in lesion surface area than the control side. Enamel lightness value improved significantly from baseline in the control side.

Conclusions

Microabrasion with MI Paste Plus, as a dual technique, should be considered as an effective and less-invasive option in the treatment of white spot lesions in post-orthodontic patients.

DEDICATION

This thesis is dedicated to Steve LeRoy, my father who recently and unexpectedly passed away, and whose love and support made this study possible. With his loving memory in mind, I hope that the findings of this study may improve the lives of many patients to come.

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NOMENCLATURE

WSL(s)	White spot lesion(s)
CPP-ACP	Calcium phosphopeptide amorphous calcium phosphate
L* value	Lightness value

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1. INTRODUCTION

White spot lesions (WSLs) represent an umbrella term of demineralized areas of smooth surfaces of teeth, whose subsurface porosities usually manifest in visibly opaque, chalky-white patches.[1] They fall under two main categories: carious white spot lesions, and non-carious white spot lesions. Carious WSLs occur when plaque accumulates and releases acid as a metabolic byproduct, resulting in demineralized enamel. This process is often associated with orthodontic patients because the presence of brackets, wires, and bands restricts normal hygiene access, with reports of WSLs forming as early as one month after appliance placement.[1,2] If left unchecked, the WSL may progress in severity to a cavitated lesion.[3]

Non-carious lesions, on the other hand, involve an etiology that is related to the development of enamel, often by interfering with the normal mineralization process. One salient example of non-carious lesions is dental fluorosis, which occurs in enamel development. The presence of excessive fluoride ions interferes with protein removal and mineral acquisition, resulting in porous and hypomineralized lesions.[4] While usually white in color due to the optical change in light refraction from the decalcification, in severe cases the lesions present a brown color due to staining of pits and mottled enamel. Fluorosis is a relatively common enamel disorder, with at least 40% of adolescents having at least mild fluorosis.[5]

The decalcified aspect of white spot lesions is often referred to as “subsurface”, because there tends to be hypermineralized surface layer above the inner porous region.

This hypermineralized surface layer arises when it is exposed to fluoride, particularly in higher concentrations.[6] The inner hypomineralized porous chamber results in the visual white opacity because it reflects more light, and yet is "trapped" by a hypermineralized surface layer. This outer layer effectively acts as a boundary to prevent the influx of calcium and phosphate to the inner porous chamber, preventing the needed mineralization to resolve the lesion.

WSLs are commonly produced during orthodontic treatment and form at a significantly higher rate than non-orthodontic patients.[7] One study reports that around 23% of patients will develop at least one white spot lesion, with a prevalence estimated to be as high as 96%.[8-11] Another study found that WSLs have a 26% prevalence in orthodontic patients,[12] adding to the evidence that WSLs are a significant concern in the field of orthodontics. The most commonly affected teeth appear to be the maxillary lateral incisors, as well as the molars, mandibular canines and premolars with no predilection of left versus right side of the maxilla.[1,7]

MI Paste Plus has been shown clinically to decrease the extent of WSLs from a clinical study by Robertson et al in 2011, and microabrasion has been shown to improve the outcome of WSLs when combined with MI Paste Plus versus microabrasion alone.[13,14] Recently, Ryan showed in an in vitro study that WSLs on extracted teeth can be significantly improved esthetically when MI Paste Plus was combined with microabrasion.[14] The results of her study provided the framework for clinical application: whether combining MI Paste Plus & microabrasion improve treatment outcomes for patients with white spot lesions.

1.1. Problem and Significance

The chalky-white areas of demineralization are an optical consequence of the lesion's subsurface porosity; since the resultant color is more opaque than natural enamel, these lesions may represent an esthetic concern of the patient. Treatment options to revert a WSL to natural-looking enamel tend to involve invasive techniques which eliminate tooth structure, are costly, and require replacements throughout a patient's lifetime due to restorative failure.

If the research hypothesis is supported by the evidence, then this study will help refine the clinical protocol for using MI Paste Plus. While the use of microabrasion when combined with MI Paste Plus has been shown to be effective on extracted teeth, it has yet to be demonstrated in a clinical trial. There also exists a gap in the literature regarding the clinical use of acid/abrasive particle immediately prior to application of MI Paste Plus. Ultimately, the study will enhance patient care by helping improve the efficiency of treating white spot lesions.

1.2 Specific Objectives/Aims

Quantifying the WSL:

- Take standardized photographs with photo analyzing software to measure area size of the lesion as a percentage of the total tooth.

- Use the Vita EasyShade spectrophotometer to measure changes in lightness values.

Clinical applications:

- Determine whether MI Paste Plus, with and without microabrasion, improves the lightness value and surface area percentage compared to baseline values.
- Determine whether there is a significant benefit to adding microabrasion to the application of MI Paste Plus.

1.3 Hypotheses

- Null hypotheses:
    - There is no difference in lightness value of the white spot lesion after treatment with MI Paste Plus and treatment with MI Paste Plus and microabrasion.
    - There is no difference in surface area percentage of the white spot lesion after treatment with MI Paste Plus and treatment with MI Paste Plus and microabrasion.

2 LITERATURE REVIEW

2.2 White Spot Lesions: Prevalence and Risk Factors

In modern orthodontics, patients increasingly demand a pleasing esthetic result and expect a satisfactory outcome upon removal of fixed appliances.[15] Small dental stains and discolorations previously tolerated by patients often become an esthetic concern after removal of braces.[16] Unfortunately, some patients face the unsightly result of decalcified, opaque areas on the teeth – more noticeable upon removal of fixed appliances – known commonly as white spot lesions (WSLs). Summitt et al define a white spot lesion as a subsurface enamel porosity from carious demineralization which presents as a milky white opacity when located on smooth surfaces.[17] Fejerskov includes a clinical element in the definition, explaining that a white spot lesion represents the first sign of a caries lesion on enamel detectable by the naked eye.[18] These areas of decalcification are a concern not only due to esthetics, but also because they pose the risk of progressing to cavitation if left untreated.[19]

WSLs are a very common issue as a result of orthodontic treatment – one study reports that around 23% of patients will develop at least one white spot lesion with a prevalence estimated to be as high as 96%.[8-11] Orthodontic patients have significantly more white spot lesions than non-orthodontic patients.[7] The teeth most commonly affected are the molars, maxillary lateral incisors, mandibular canines and premolars.[7] They have been found to develop as early as one month after placement of fixed orthodontic appliances.[2] There does not appear to be a difference in incidence between the right and left sides of the maxilla.[1] As mentioned, the prevalence of white spot lesions varies wildly, ranging from 0 to 97%.[8] Julien found that 23% of patients developed at least one white spot lesion while in treatment (noting the presence of obvious white spot lesions or worsening of existing lesions), which closely approximates the 26% prevalence of anterior teeth found by Lovrov et al.[8,12]

Fixed appliances in the oral cavity alter its ecology. Unfavorable changes which factor into the higher risk of demineralization include: the increased plaque retention from the irregular surfaces of brackets, and increased levels of mutans streptococci based on the type and frequency of retained fermentable carbohydrates.[9, 20,21] Orthodontic brackets block the usual movement of food and limit natural cleaning mechanisms, resulting in said increased accumulation of plaque, bacterial acid release, a decrease in pH and subsequent demineralization. Salivary factors play a role in the dynamics of demineralization, as saliva helps deliver calcium and phosphate ions to remineralize the enamel. Because the maxillary anterior teeth are a site with relatively little exposure to saliva, they experience a higher incidence of white spot lesions, with almost no lesions occurring on the saliva-rich lingual surfaces.[1] White spot lesions, therefore, are more likely to develop during fixed appliance therapy – and remain after their removal, due to the increased accumulation of plaque, acid-producing bacteria from retained carbohydrates, and the blocking of saliva, oral musculature, and normal hygiene access.[1,7] The presence of pre-existing white spot lesions also appears to be a risk factor for the development of new lesions.

The prevention of WSLs throughout fixed appliance therapy is an important element of orthodontic treatment. Undesirable decalcifications may result along tooth surfaces less privy to salivary exposure, particularly when oral hygiene is poor, as is often the case amongst most adolescent patients.[7] Therefore, an excellent hygiene regimen which emphasizes the mechanical disruption of acid-producing plaque represents a critical step in the prevention of white spot lesions during fixed appliances. Additional preventive measures include resin sealants placed on tooth surfaces susceptible to decalcification. Several studies testing the effectiveness of sealants in white spot prevention have shown their ability to prevent white spots, with those of higher filler content demonstrating higher retention rate.[22-25] Despite these preventive measures, treatment techniques to heal white spot lesions are important to explore and refine, given the persistent incidence of decalcification.

Treatment options tend to involve invasive techniques, which eliminate tooth structure, can be costly, and will likely require replacements throughout a patient's lifetime. MI Paste Plus has been shown clinically to prevent white spot lesions and decrease their surface area[13], and microabrasion has been shown to improve the outcome of WSLs when combined with MI Paste Plus versus microabrasion alone.[14] Both topical remineralization products and microabrasion are alluring treatment options, because they entail zero to minimal reduction in tooth structure compared to more aggressive restorative techniques.

2.3 White Spot Lesions: Formation & Distribution

White spot lesions of the teeth represent areas of imbalanced remineralization and demineralization.[9] They are characterized by a hypermineralized surface layer, and an underlying region of demineralization exhibiting relatively higher porosity. Because this porosity affects light refraction, the lesions appear opaque, with a chalk-white color compared to the adjacent sound enamel. The outer hypermineralized layer essentially acts as a barrier for minerals to access the porous inner region, which itself lacks mineral density. The lesions are particularly noticeable after drying the teeth, though they are also seen in the presence of moisture in more advanced cases.[26] During active appliance treatment, they tend to occur gingival to the bracket with a dull, pitted surface. The additional presence of plaque suggests an active lesion.[3]

Throughout the day, teeth are constantly subjected to alternating cycles of demineralization and remineralization, depending on the local pH level. Demineralization occurs when sufficiently acidic ($pH < 5.5$), calcium and phosphate ions are dissolved from the enamel.[8] Conversely, when pH rises, ions from the saliva (or other sources) remineralize the enamel. A disturbance in the balance of mineralization, such as a prolonged exposure of acidic pH, can result in decalcification of teeth because there is a net loss of enamel mineral content, which is the underlying basis of dental caries.[8,27] Reasons for drops in pH vary from lack of saliva, poor oral hygiene leading to increased acid-producing bacteria, a highly acidic diet, and orthodontic appliances which harbor more plaque. This initial step in the carious process – the demineralization of enamel – results in a white spot lesion. Visually it is distinct because of the altered absorption and refraction of light, as well as the greater porosity and mineral loss due to demineralization.[26] Because porous enamel scatters more light than sound enamel, the lesion is seen as more opaque with a distinct white coloration.[1,7]

Patients generally become more concerned about their dental appearance once fixed appliances are removed.[16] Esthetically, these lesions are of concern to patients because the most susceptible enamel surfaces are those in the esthetic smile zone – in particular, the labial enamel of the maxillary incisors, with one study finding the highest incidence at the labio-gingival aspect of the maxillary lateral incisors (as discussed previously, the relatively less frequent exposure to mineral-carrying saliva helps explain the greater occurrence of white spot lesions on the labial aspect of the maxillary incisors).[1] The association between anterior dental esthetics and psychosocial domain has been well documented, particularly among younger subjects.[28] One study found that amongst patients aged 9 to 15, the self-perceived level of dental attractiveness was more strongly related to self-concept than the actual severity of malocclusion via PAR score.[29] Given the likelihood that white spot lesions occur in esthetic regions of the dentition, it is important for the dental profession to investigate better preventive measures, as well as treatment approaches when preventive measures fail.

2.4 White Spot Lesions: Quantitative & Qualitative Assessment

White spot lesions are dental opacities which have specific characteristics depending on their etiology (either carious or non-carious). It is important to distinguish carious WSLs from another commonly observed non-carious dental opacity: dental fluorosis.

A.L. Russell found several key differences that distinguish fluorotic lesions from non-fluoride enamel opacities.[30] Fluorotic lesions are usually seen on cusp tips or incisal edges, they have blended margins that shade off imperceptibly into surrounding normal enamel, they occur symmetrically, and they have no gross hypoplasia, absent of any pitting. Non-fluoride enamel opacities, on the other hand, may affect the entire crown, are often round or oval with a clearly differentiated margin from adjacent enamel, and usually contain a pitted, etched, or rough surface.[30]

Classifying the severity of a white spot lesion clinically is often done using the Gorelick scale, based on an ordinal scale from 1-4, indicating “none”, “slight”, “severe”, and “cavitation” respectively.[1] The shortcoming of this system is that it overlooks mild and moderate changes in the lesions and lacks the quantitative precision of an interval variable, such as that provided by quantitative light-induced fluorescence (QLF).[31] Several modifications of the Gorelick scale have been published, which further specify the fraction of surface area the lesion encompasses,[32] and the enamel decalcification index modified to include a tooth with a bonded bracket,[33] all of which remain ordinal variables. Another ordinal measure is the International Caries Detection and Assessment System (ICDAS), which scores the severity of carious lesions from 0 to 6. However, the ICDAS lacks sufficient power to distinguish white spot lesion changes within code 2, compared to QLF assessments.[34]

Several researchers have used various photographic analysis software to trace the demineralized surface area of the tooth and calculate it as a percentage of the total surface area of the labial aspect of the tooth.[35,36] In one study by Livas et al, photographs were taken with a Nikon D1x camera (Nikon Corporation, Tokyo, Japan) with a 105 mm/2.8 AF Micro Nikkor lens and Nikon SB-29s Macro flash. The camera was set to manual with an aperture of f9 and a shutter speed of 1/125 of a second. The image quality was set as fine and ISO sensitivity 200. They concluded that this type of software image analysis provides a reproducible and reliable method for quantification of artificial enamel demineralization around orthodontic brackets.[35]

There is further precedent to validate the usage of photo-tracing software to analyze white spot lesion surface area. A study by Bock et al used photograph-analyzing software, Image Pro Plus (Version 7.0, Media Cyberkinetics, Santa Clara, CA), to determine area of the lesion. Here, the software calculated the pixel size to determine the total area of each tooth. Afterwards, the software calculated the size of the WSL by automatically detecting the brightest area of the tooth surface. To exclude all areas that were not part of the WSL (such as reflections being caused by the flash light), the borderlines of the WSL were corrected manually.[36] Bock et al used Adobe Photoshop CS5 Extended (Version 12.0x64, licensed for medical use) to detect the changes in luminance.

Quantitative light-induced fluorescence (QLF) is a means of assessing the degree of mineralization, in which images of teeth are taken by the machine with high-intensity blue violet light. Areas that are more demineralized will scatter more light and emit less fluorescence, altering the output number.[37,38] Micro CT analysis is an in vitro technique to assess mineralization of dental samples, as it generates mineral density and produces three-dimensional reconstructed images for regions of interest.[14]

Spectrophotometric evaluation is a technique used to evaluate the color properties of a tooth, utilizing the CIELAB system, which is the most frequently utilized system for color analysis in dentistry.[26] The CIELAB system calculates the colorimetric distance between two samples (ΔE) using an equation with three variables: lightness value (L*; 0-100), green-red chromacity (a*; -150 to +100), and blue-yellow chromacity (b*; -100 to +150). The equation to differentiate the colorimetric distance between two samples is:

$$\Delta E = [L_1{*}-L_2{*})^2 + (a_1{*}-a_2{*})^2 + (b_1{*}-b_2{*})^2]^{1/2}$$

Changes in color measurements using a spectrophotometer are advantageous over visual color assessments because they are more objective, quantifiable, and faster to obtain.[39] A study by Tolcachir et al in 2015 used the CIELAB system to assess the color changes of demineralized extracted teeth after application of CPP-ACP, and found significant decreases in lightness value and hue value, signifying a return to a color similar to natural enamel.[26] Ryan utilized a Vita spectrophotometer to analyze color changes in extracted teeth with artificial white spot lesions treated with microabrasion, with and without CPP-APP. She found a significant improvement in lightness value in the experimental teeth, reflecting their greater enamel translucency.[14]

2.5 White Spot Lesions: Prevention

The concept of minimally invasive dentistry behooves dental professionals to first emphasize preventive measures when possible and reduce the need for restorative therapy.[40] . O'Reilly and Featherstone showed that WSLs occur as early as one month after placement of fixed appliances, even among patients brushing with fluoride toothpaste, suggesting that additional preventive measures, such as a daily fluoride mouthrinse, are key.[2] Ogaard et al reported similar results, identifying WSLs within four weeks in the absence of any fluoride supplementation; they emphasized the need for anti-caries measures including professional cleanings and fluoridation.[41,42] Protective measures such as oral hygiene, fluoride application and sealants represent attempts to prevent white spot lesions. Preventing lesions from forming in the first place is clearly the best outcome esthetically and least costly for the patient.[19]

2.5.1 Education

An excellent oral hygiene regimen, involving mechanical disruption of plaque biofilm, is essential during fixed orthodontic appliances, given how the brackets and wires create an increased opportunity for cariogenic flora to flourish. The lack of home-care compliance has been associated with increased levels of WSL formation among male and female patients of multiple age groups.[43] Toothbrushing should be performed at least twice daily, with mixed reports regarding the benefits of electric dentrifices.[44] Electric toothbrushes appear to produce better hygiene results for those with poor oral hygiene compared to manual brushes.[45,46] Praising the patient for good oral hygiene and reminders about the consequences of poor oral hygiene has also been shown to be effective.[47] Dietary counseling is advisable to the extent that it may encourage the patient to consume less frequent cariogenic food, including fermentable carbohydrates.

However, the consistent use of at-home fluoride toothpastes does not completely prevent white spot lesions, highlighting the need for additional preventive measures.[48]

2.5.2 Fluoride

Fluoride serves as a preventive measure against demineralization because it replaces the hydroxy group of the crystalline unit hydroxyapatite, thereby becoming fluorapatite. Whereas hydroxyapatite has a pK_a of 5.5, fluorapatite has a lower pK_a of 4.5, meaning that fluorapatite can withstand even more acidic conditions before dissolution, thus forming a stronger enamel that is more resistant to the caries process.[47,49] Calcium fluoride is the major product formed from topical therapy, which may serve as a reservoir capable of remineralization and inhibiting demineralization during acid challenges.[50]

Topical fluoride is applied to the dentition in multiple ways. High-concentration fluoride such, as varnishes applied professionally, have the potential to reduce the incidence of demineralization during active orthodontic appliance therapy.[2,41] Caution must be taken when applying high-concentration fluoride, however. Visible white spots should not be treated with high-concentration fluoride; doing so may create a hypermineralized surface layer, which inhibits remineralization of the underlying porous region, arresting the lesion and potentially leading to enamel staining.[41,51] High-concentration fluoride applied to white spot lesions not only inhibits remineralization, but increases the risk of staining the lesion as well.[3]

2.5.3 Sealants

Resin-based sealants have been used extensively in general and pediatric dentistry, primarily to prevent occlusal groove caries. They represent an important aspect of preventive dentistry as they are a non-invasive attempt at preventing caries in susceptible pits and fissures.[52] Benham et al, who completed a split-mouth trial in which incisors and canines received sealants, showed a significant reduction in enamel demineralization during fixed appliance therapy compared to the contralateral control teeth.[22]

However, concerns regarding longevity have limited the use of sealants among some practitioners, in part due to the hydrophobic nature of resin-based sealants and the dry, isolated field they require.[53] Another major factor that affects sealant longevity is their resistance to mechanical abrasion. Erosion of the material occurs during daily mastication and tooth brushing, with unfilled sealants displaying more erosion than sealants with a higher resin filler content.[22,25] Since sealants are prone to wear abrasion and do not fully provide enamel coverage as teeth continue to erupt, they do not prevent all white spot lesions for the full duration of treatment, highlighting the need for a multi-pronged approach to prevention and treatment strategies when prevention fails.[24]

2.6 White Spot Lesions: Treatment Options

The ideal result after removal of fixed appliances is to have healthy enamel with no areas of demineralization. This is best achieved with an effective prevention strategy, including a good oral hygiene regimen to remove plaque and topical fluoride application, as mentioned previously. In the event that prevention efforts fail, it behooves the clinician to treat the white spot lesion in the most conservative way possible, only increasing the level of invasiveness if the treatment did not resolve the problem and the patient is interested.[19]

2.6.1 Remineralization

The strategy of remineralization represents the most conservative approach to dealing with WSLs, and is usually the first attempt at treatment.[19] It is widely acknowledged that after removal of fixed orthodontic appliances, white spot lesions have a limited ability to heal on their own through natural remineralization.[54] The observed reduction of white spot lesions post-orthodontic treatment can also be explained by removal of the etiologic agent: without orthodontic brackets and wires, less acid-producing plaque is likely to accumulate and cause demineralization. Abrasion of the surface enamel during tooth brushing[18], removal of the etiology, and remineralization seem to help explain the observed reduction in post-orthodontic white spot lesions.[31]

The degree to which post-orthodontic WSLs may heal on their own via natural remineralization, and by what point in time, varies somewhat in the literature. Guzman et al, for example, found that within the first few weeks of debanding, there is a generally a natural improvement of the WSLs due to remineralization, and that by 6 months, about half of lesions will have remineralized without any additional specific treatment.[3] Sonesson et al advocated at least 3 to 6 months post-debond with at-home brushing prior to further treatment but did not cite a source to support this recommendation.[54] Mattousch et al looked at 370 post-orthodontic carious surfaces and found that only 2.7% of lesions completely remineralized after two years, whereas 40% of the lesions showed overall improvement, most of which occurred during the first 6 months after debonding.[55] His conclusions are in contrast with the general belief that WSLs tend to improve on their own after debonding, ostensibly due to the natural process of remineralization with at-home fluoride brushing. Willmot found that small lesions improve rapidly during the first 6 weeks after debonding, with a 50% further improvement of larger lesions after 6 months, with no specific treatment.[56] In general it appears that the majority of natural remineralization of white spot lesions will occur during the first 6 months after appliance removal, and thus any residual lesions after six months may require additional treatment to resolve.

Plaque removal and natural remineralization is limited and does not always reduce the white spot lesions to an acceptable level. Cochrane explains that salivary remineralization is a process driven by a low concentration gradient, which therefore tends to improve the esthetics of superficial white spots while showing little improvement to deeper lesions.[57] Given the superficial nature of salivary remineralization, additional remineralizing agents are recommended for lesions which do not heal naturally.[68] Remineralization agents involve multiple applications of low-concentration topical fluoride to the enamel in several forms, ranging from toothpastes to mouthwash and varnishes, to allow calcium and fluoride to slowly penetrate the lesion. As stated previously, high-concentration fluoride is not recommended to treat white spot lesions, because it hypermineralizes the outer layer and creates a barrier of diffusion, thereby blocking access to heal the deeper porous layer. This hypermineralized layer also tends to stain with an unsightly organic debris, worsening the esthetic issue.[42,56,58-60] Denis et al advocate the usage of fluoride creams, rinses, and CPP-APP products to treat lesions of an ICDAS code of 0 or 1, but to consider more invasive approaches like microabrasion, bleaching, and erosion-infiltration if the lesion is a 2 or beyond.[61]

2.5.2 Casein Phosphopeptide Amorphous Calcium Phosphate

Scientists have isolated a purified version of milk protein, casein, known as casein phosphopeptide amorphous calcium phosphate (CPP-APP). Several studies have shown that CPP-APP has an anti-cariogenic effect, inhibits demineralization, and enhances remineralization, in both animal and human studies.[62,63] In addition, several studies and clinical trials have established that the use of MI Paste Plus during orthodontic treatment helps both prevent and reduce the size of white spot lesions.[13,64-67] The chemical basis of MI Paste Plus is such that its active compound, CPP-APP, stabilizes high concentrations of calcium and phosphate at the enamel surface. The CPP complexes thus provide a more available source of ionic calcium and phosphate, creating a larger concentration gradient in the process of remineralization[66,68,69], as demonstrated in vitro.[70] MI Paste Plus thus facilitates remineralization of the lesion throughout its entire body, rather than just at the surface as seen with fluoride treatment alone.[62]

In 2019, Ryan showed that MI Paste application significantly increased the mineral density of white spot lesions, which had a synergistic effect when combined with the effects of microabrasion.[14] The two mechanisms behind this treatment effect is that microabrasion removes the hypermineralized layer of the lesion (which helps provide enhanced diffusion of ions in solution), and that the acidic gel helps create more porous enamel (which are more easily infiltrated by the ions). Her split-tooth study showed that teeth which received both microabrasion and MI Paste Plus displayed superior translucency and mineral density than those which received microabrasion alone.

A double-blind, randomized controlled trial by Robertson et al in 2011 compared sixty patients in active orthodontic treatment, allocated to receive either MI Paste Plus or a placebo paste. The study concluded that MI Paste Plus has two significant benefits: it helped prevent the development of new white spot lesions, and decreased the number of white spot lesions already present. They found a 53.5% decrease in the enamel decalcification index (EDI) for the experimental group.[13]

In 2012, Pliska concluded that MI Paste Plus alone does not significantly improve the fluorescence value (mineral content) of WSLs in extracted bovine incisors, whereas microabrasion with-or-without MI Paste Plus did.[71] However, the study was under-powered, lacked an esthetic improvement variable, and the methodology involved acid-etching and mechanical abrasion as two separate steps rather than combining them.

Several recent studies have tested the effect of MI Paste Plus on WSLs both during and after fixed orthodontic appliances. However, none of them explicitly utilized microabrasion on their subjects, nor did they use any acid etch. Ebrahimi's randomized clinical trial in 2017 allocated patients into 4 groups of 20 patients each (MI Paste Plus, Remin Pro, 2% NaF, Control) and did not etch in any group. All three treatment groups were equally effective in reducing the area of WSLs, more-so than the control, which did not improve.[72] An in vitro study by Leila et al examined 30 extracted teeth (15 permanent, 15 primary), sectioned them, and subjected them to remineralization and demineralization cycles. They found that MI Paste Plus produced a more favorable fluorescence than ReminPro, though no acid etch was used for any tooth.[73] Beerens evaluated 65 post-orthodontics patients with at least 2 WSLs, in which half were given MI Paste Plus and half a placebo paste. No etching was performed. Based on QLF, microbial composition, and photographs using ICDAS, there were no significant differences.[74]

Rechmann randomized 40 patients into an MI Paste Plus & Fl varnish group and standard home care group, looking at improvement in EDI (enamel decalcification index) during orthodontic treatment. They did not etch the patients' teeth and they did not find any significant differences.[75] Bakry & Abbassey had 50 extracted third molars split in half, and separated into 4 groups of 25 specimens, and then stored in artificial saliva for 7 days. The teeth were subjected to 4 days of demineralization and remineralization cycles. They were not etched. The MI Paste and bonding group and MI varnish group showed statistically significant decreases in lesion depth and mineral loss of the subsurface lesions.[76] Kau compared three groups of 40 patients each, undergoing orthodontic treatment, who were given one of three creams: ClinPro 5000, MI Paste Plus, or Clinpro Tooth Creme 0.21% NaF. The selected product was brushed on for two minutes twice daily for four months. No etch was used. The study found that ClinPro 5000 performed better than MI Paste Plus and ClinPro Creme.[77]

2.5.3 Microabrasion

Microabrasion refers to the technique of burnishing an acid agent (usually 18% HCl) and abrasive particle onto a discolored dental surface with a slow-speed rotating handpiece, to restore the natural color of the lesion by allowing for proper mineralization. Historically it has been recommended to be used to treat fluorotic enamel[78-82], though more recently the technique has been expanded to address post-orthodontic demineralization.[83] Enamel microabrasion has been demonstrated to provide no additional risk to the pulp, nor does it make the treated surface more susceptible to caries; in fact, one study showed that microabrasion-treated enamel accumulates less plaque than untreated surfaces.[84, 85]

In her study on extracted teeth, Ryan et al showed that microabrasion significantly improved the lightness value and mineral density, with an even greater benefit when combined with CPP-ACP.[14] Gu, who compared microabrasion versus resin infiltration, showed that microabrasion alone significantly improves the appearance of white spot lesions, with a reduction of mean surface area percentage from 36% to 12% after six months.[86] Murphy confirmed the cosmetic benefit of treating white spot lesions with microabrasion.[87] A study in 2012 randomized patients to receive either microabrasion, fluoride rinses, or CPP-APP (no etch).[88] They found that all three groups experienced significant reduction in WSL surface area. The specific technique of the microabrasion application varies. A case report by Balan recommends three separate applications of the slurry for 30 to 40 seconds each.[89]

2.5.4 Restorative Options

More invasive dental procedures to eliminate white spot lesions include resin infiltration, in which composite resin is bonded to the affected enamel. In 2013, Knösel investigated the durability of esthetic improvement following Icon resin infiltration of white spot lesions over 6 months. The WSL color was assessed to be stable in relation to adjacent enamel after infiltration, displaying no significant changes over a 6 month period.[90] Similar to microabrasion, resin infiltration relies on acid etch to allow resin to penetrate through the hypermineralized surface into the porous layer of the lesion, while also preventing further acid entry to worsen the lesion.[91] The most aggressive end of the treatment option spectrum includes direct restorations with composite resin, veneers, and full-coverage crowns of a variety of ceramic materials. These options require removal of healthy tooth structure and are of considerable cost to the patient.[19]

2.6 Product Selection

Various factors determine which acid silica particle would best reach the goals of microabrasion. Croll argued for a lower concentration of acid and greater silica size particle, to help prevent accidental splashing of the acid.[82] Gu showed that the microabrasive agent OpaLustre, which has a lower acid concentration of 6.6% HCl and a larger sized silica particle of 20-260 microns, was used effectively to treat white spot lesions.[86] Opalustre and MI Paste Plus also represent the microabrasion and CPP-ACP products used by Ryan et al in her study showing an improved lightness value and mineral density on extracted teeth.[14]

The current GC America manufacturer instructions for MI Paste Plus do not include the use of acid (etch) nor mechanical abrasion, as the product's on-label usage is restricted to the treatment of hyper-sensitivity.[92] Robertson's study showed, however, a therapeutic benefit of CPP-ACP in the treatment of post-orthodontic white spot lesions.[13] A study by Leila also demonstrated the therapeutic benefit of CPP-ACP to treat WSLs, with MI Paste Plus showing superior mineralization over the product ReminPro.[73]

To date there remains a lack of clinical studies examining the combined treatment of WSLs with microabrasion and CPP-APP. Microabrasion itself has been performed successfully to treat carious and fluorotic decalcification as seen in various case studies,[78-82] but there remains a need for standardized protocol. Similarly, CPP-APP has been shown to improve WSLs clinically,[13] but no study appears to have combined CPP-APP with microabrasion on human subjects.

In her study, Ryan demonstrated that while microabrasion alone has a significant effect on WSLs, there is a synergistic benefit to incorporating CPP-APP on WSLs created on extracted teeth.[14] By showing a significant treatment effect on extracted teeth, her findings – along with the results of past studies – reveal the need to explore the next step in WSL treatment research using both microabrasion and CPP-APP with human subjects. Testing our hypothesis in the form of a clinical trial will ideally further our current understanding of how best to treat WSLs with less invasive techniques.

3 MATERIALS AND METHODS

The experimental design of this study was a prospective, split-mouth randomized-controlled trial. It was reviewed and approved by the IRB of Texas A&M University (Approval #: IRB-2019-1405-CD-FB). Patients recruited for the study age ranged from 15 to 20 years old. They were recruited from a patient pool of Texas A&M Department of Orthodontics.

To be included in the study, patients had to have bilateral WSLs - at least one lesion on the left side and at least one lesion on the right side of the maxillary canine-to-canine region (#6 to #11/upper 3-3). In addition, they had to have been out of treatment for at least six months, as previous studies have suggested that the majority of natural WSL improvement occurs within the first 6 months after braces removal.[3,54-56] Patients were excluded from the study if they presented with any of the following:

- Did not have all 6 upper anterior teeth
- Presence of cavitation: ICDAS 3 or more, or Gorelick scale of 4
- Milk allergies
- Hyperplastic gingiva within 1 mm of the lesion
- Any patient who has had professional fluoride treatment or increased-level fluoride toothpaste between braces removal and the start of the study.

Based off of a power level of 0.80, an alpha of 0.05 and an effect size of 0.50, 17 patients were required. The photographic records of approximately 200 patients were visually examined to identify those with post-treatment WSLs who had been out of treatment for at least six months. 48 patients were contacted after confirming the inclusion criteria, and 16 enrolled in the study. Two of these patients were dropped, one due to carious lesions and the other due to lack of cooperation with the study's protocol (did not want comply with no eating/drinking for 30 minutes after MI Paste Plus application).

Of the remaining 14 patients, seven were male and seven were female. The average patient age was 17.5, ± 2.5 years. The study included: 1 South Asian, 1 East Asian, 8 Hispanics, 1 African American, 2 Caucasians, and 1 undisclosed.

3.1 Study Flow

3.1.1 Informed Consent & Baseline Records (T_0)

Based off of a power level of 0.80, an alpha of 0.05 and an effect size of 0.50, 17 patients were required. The photographic records of approximately 200 patients were visually examined to identify those with post-treatment WSLs who had been out of treatment for at least six months. 48 patients were contacted after confirming the inclusion criteria, and 16 enrolled in the study. Two of these patients were dropped, one due to carious lesions and the other due to lack of cooperation with the study's protocol (did not want comply with no eating/drinking for 30 minutes after MI Paste Plus application).

Of the remaining 14 patients, seven were male and seven were female. The average patient age was 17.5, ± 2.5 years. The study included: 1 South Asian, 1 East Asian, 8 Hispanics, 1 African American, 2 Caucasians, and 1 undisclosed.

3.1.2 Treatments (T_1, T_2, T_3)

At the first treatment appointment, the patient was seated and the custom putty stent was fitted to confirm full seating. All teeth with qualifying lesions were dried with a cotton roll. The Vita spectrophotometer (VITA Easyshade® Compact, Germany) was calibrated on the calibration block and placed into the custom putty stent for each tooth. Three separate measurements of the L* value were recorded per tooth.

For the first microabrasion treatment, a non-latex rubber dam (Dental Dam, Latex-Free, Henry Schein, Melville, NY) was applied to ensure isolation from soft tissue and to reveal only the treatment group teeth. The rubber dam was secured between contacts with Wedgets (Patterson Dental). Then, a 1 mm thick layer of the microabrasion material, Opalustre (UltraDent Products, Inc., South Jordan, UT) was placed over each lesion in the treatment group. The microabrasion material contained 6.6% hydrochloric acid slurry with silicon carbide microparticles. Using a timer, the slurry was then burnished into each lesion with a prophy cup on a slow-speed handpiece with medium to heavy pressure for one minute, followed by copious aqueous rinse. This process was repeated for each lesion three times.

After microabrasion treatment, the rubber dam was removed and the Essix tray was seated with MI Paste Plus (CPP-ACP, calcium phosphopeptide amorphous calcium phosphate with 900 ppm sodium fluoride, GC America) loaded into the anterior wells, covering the maxillary anterior dentition and held in place for 5 minutes. The patient was then given the Essix tray with MI Paste Plus tubes. Their instructions were to inject MI Paste Plus into the anterior wells of the tray and wear at home twice daily for 5 minutes.

They were also informed to not rinse/eat/drink for 30 minutes afterward, and to brush with the provided OTC fluoride toothpaste (Colgate Total, Colgate-Palmolive, New York, NY) and manual toothbrush (Class 1 medical device, does not require FDA premarket notification nor approval) per manufacturer instructions, and avoid any additional fluoride treatment. To help with compliance, patients received automatic text updates twice per day as a reminder to wear the MI Paste Plus trays twice a day (Orthodontext software). As an attempt to track compliance, patients were asked to log a checklist for each time they wore their MI Paste Plus trays.

Four to six weeks after T1, progress clinical photographs and spectrophotometer readings were obtained in a manner consistent with the process described at the first clinical appointment. The experimental and control treatment protocol was performed by reapplying the microabrasion and MI Paste Plus as described in T1 to any lesion still present. The patients were furnished with additional tubes of MI Paste Plus and asked to continue wearing the MI Paste Plus trays twice daily. Finally, four to six weeks after T2, final clinical photographs and spectrophotometer readings were obtained. The daily log checklist was obtained, the patient was dismissed and the clinical portion of the study was over.

3.2 Data Collection

3.2.1 Photography: Surface Area of Lesion

Images of the enamel surfaces were captured at 3 time points (T0 as baseline, T2, at 6 weeks after initial treatment, and T3 as the final check at 3 months after initial treatment), with a Canon Rebel T4i camera using a 60 mm macro lens and ring flash, under standard fluorescent ceiling lighting. The camera settings used were: 1/250 shutter speed, F32 aperture, ISO100 at a distance of Orange 3 and flash ring power of ¼. Teeth were dried with a cotton roll immediately prior to photography. Six images were taken for each patient at each time point, with a photograph taken perpendicular to each of the six maxillary anterior teeth.

There were cases in which the perpendicular photograph was not ideal due to unwanted ring flash on the teeth. In that situation, a "best fit" angle approach was used: the angle which showed the least amount of ring flash on each of the three time points was chosen. After uploading the JPG file into Adobe Photoshop, the image was magnified by 100%, brightness setting was adjusted to a level of –100 and contrast increased to +100 for more accurate visual distinction between decalcified and healthy enamel.

To generate the surface area percentage, the facial aspect of the clinical crown for each tooth was first traced, with the operator stabilizing one hand over the other while dragging the mouse. The total pixel count was recorded. Then, the white spot lesion was traced, and the subsequent pixel count was used as the numerator. The quotient of these pixel counts, times one hundred, represent the percentage of surface area covered by the WSL.

This process was repeated for both treatment teeth and control teeth. The change in percentages over the three appointments was then studied statistically both in terms of within-group changes (from baseline) and between-group differences from baseline records through T2.

3.2.1 Spectrophotometry: Lightness Value

Lesion color was evaluated quantitatively using a spectrophotometer: Vita Easyshade Compact. This was used to record and compare lightness (L*) values to track color changes with treatment. This system utilizes the Commission Internationale de l'Eclairage system[93], and is regarded as one of the most accurate means to assess color.[94] Lightness value ranges from L* = 0 (pure black) to L* = 100 (pure white). As white spot lesions tend to be more opaque than sound enamel, they are expected to have relatively higher L* values. This phenomenon was confirmed in a study by Choi et al.[95] Consequently, treating the white spot lesion should display a decrease in L* value as it approximates healthy enamel.

The Vita spectrophotometer itself has a 5 mm diameter probe, which operates based on a halogen light which illuminates individual interior bundles. Light that is emitted from the spectrophotometer is deflected from the enamel surface, and returning light is analyzed within the unit. The spectrophotometer processes the refracted light with resultant display components using the CIELAB system.

A custom putty stent was used for each patient to ensure consistent placement of the spectrophotometer upon the lesion, as described previously. Vita spectrophotometer readings were taken at the pre-treatment appointment T0 for baseline values. They were also collected one month after the first round of microabrasion and MI Paste Plus, and a final time one month after the second round of microabrasion and MI Paste Plus. After confirming the fit of the putty stent, calibrating the Vita spectrophotometer, and drying the teeth with cotton roll, readings were taken in a manner consistent with the user manual. Measurements were taken three times for each lesion to gauge accuracy. The average of the three values was computed and used for statistical analysis. Lightness value change (ΔL) was calculated from T0 through T2.

3.3 Statistical Analysis

Surface area percentage and spectrophotometer lightness value variables were assessed for normality. The data related to surface area were determined to be normally distributed. Data related to L* values, however, were not normally distributed and displayed significant skew and kurtosis. Between-group differences for both variables were evaluated using the Wilcoxon signed-ranks test. Operator reliability for surface area tracing was assessed based on 10 randomly reanalyzed tracings.

4 RESULTS

4.1 Surface Area Percentages

There were no statistically significant between-side differences in lesion size percentage of the total facial surface) at baseline or after one month of treatment (Table 2). The initial mean lesion size (as a percentage of the entire labial tooth surface) was 24.6% and 20.2% for the treatment and control sides, respectively, with decreases to 17.5% and 14.6% after one month of treatment, respectively. The combined microabrasion and paste side, however, displayed significantly smaller lesions after two months of treatment compared to the paste only side. After two months of treatment, the lesions on the combined treatment side covered 9.7% of the total tooth area and 12.6% of the area on the paste-only side (Figure 1). The combined side showed almost twice as much reduction in WSL size as a percentage of the total tooth than the paste-only group (15% vs 7.6%).

The combined treatment side showed statistically significant changes both from start to 1 month and from 1 month to 2 months (Table 2), with each interval showing approximately the same amount of reduction (7.1% and 7.9% respectively) in WSL size as a percentage of the total tooth. The paste-only side, while also showing significant changes at all time points, experienced almost twice as much reduction during the first month than the second month (5.6% and 2.9% respectively).

During this first month of treatment, the WSLs on the combined treatment side decreased by 28.8%, to 71.1% of their initial sizes. The paste only side decreased by 27.8%, with no statistically significant between-side difference. There was a significant difference, however, in the amount of change from T2 to T3, with the combined side decreasing by 44.7% compared to the control side's decrease of 13.7%. There was also a significant between-group difference in the amount of change from T1 to T3, with the combined side showing a total of 60.6% reduction of the initial lesion size compared to a 37.6% reduction on the control side (Figure 2).

Compared to initial WSLs size there were statistically significant ($p < .01$) changes for both groups at all time points (Table 3). The combined side showed significant changes both during the first and second months, with each interval showing approximately the same amount of reduction (28.8% and 32.8%, respectively). The paste-only side, while also showing significant changes at all time points, experienced nearly three times as much reduction in the first month than the second month (27.8% and 9.8% respectively).

There were moderate to high positive correlations between the amount of lesion reduction and the size of the initial lesion (Figures 3,4). They follow a quadratic pattern, with greater reductions occurring for the larger than smaller WSLs. Comparing the quadratic graphs of both groups shows that the larger the initial WSL is, the more it benefits from combined treatment as opposed to paste-only (Figure 5A,B). Correlations at all six time intervals were found to be significant with the exception of the control group between T2-T3. The highest correlation between lesion size and lesion reduction was seen in the treatment group from T1 to T3, with a correlation of $r2 = .941$ and $p < .001$.

4.2 Lightness Values

There was no statistically significant between-side difference in L* values at baseline (Table 4). After one month of treatment, the combined side's median L* value was 78.2, which was statistically less than the control group median L* value of 80.4 (Figure 6). After two months of treatment, there was no significant difference between sides, with the combined side showing a median L* value of 79.6, compared to the control side's L* value of 79.4 ($p = .710$). The medians and IQRs for L* values at all time points are illustrated in box-and-whisker plots in Figure 6.

The combined treatment side showed a statistically significant decrease in L* values during the first month (from 80.3 to 78.2), while the control group (81.2 to 80.4) did not (Table 4). The control side showed a significant reduction in L* value compared from baseline to two months (81.2 to 79.4), whereas the combined treatment side showed no difference from its baseline (80.3 to 79.6).

The combined side showed twice the amount of reduction than the paste-only side (1.9 and 0.9, respectively) during the first month of treatment (Figure 7). There also were statistically significant between-side differences after 2 months. The L* values on the paste-only side decreased during the second month of treatment and increased on the combined treatment side (-0.4 compared to +0.2, respectively). There was no significant between-group difference in the changes of L* values that occurred from start to the end of the second month.

4.3 Compliance Measures: OrthodonText Software & MI Paste Plus Checklist

All 15 patients enrolled received twice daily automated text messages to wear the MI Paste Plus for 5 minutes. At each appointment, the patients confirmed that they had been receiving the text reminders. Patients were also given a printed checklist, and asked to mark a box every time they wore the MI Paste Plus. Of the patients who remembered to return their checklists after two months, 97.5% affirmed wearing the MI Paste Plus. One patient who forgot the checklist -reported missing just three times (97%). The other three patients forgot their checklists and could not remember their failure rates.

5 DISCUSSION

The application of MI Paste Plus alone significantly reduced the surface area of WSLs as a percentage of labial tooth surface area. Teeth that received MI Paste Plus showed a decrease in labial surface area percentage from 20.2% to 7.6%, and a 37.6% reduction relative to initial lesion size. A study by Robertson et al showed a 53.5% reduction in EDI for teeth in current orthodontic treatment receiving MI Paste Plus over a period of three months.[13] These results are not necessarily comparable because EDI is an ordinal variable in which quadrants of the tooth surrounding the bracket are assigned a number from 0-4 based on approximate amount of demineralization, although approximating the surface area represented by the reported data appears to give a reduction consistent with the current study's findings. In addition, another major difference was that the teeth being treated had fixed appliances (braces) on during the study. Brochner et al showed a 58% decrease in WSL surface area for teeth treated with MI Paste Plus for four weeks.[67] However, this decrease may be inflated because the treatment was performed immediately after braces removal; thus, it did not control for the natural reduction in lesion size normally seen in the months following braces removal. The proposed mechanism by which MI Paste Plus remineralizes the lesions, and thus restore the enamel's natural optic properties, is by increasing the bioavailability of calcium and phosphate through creation of a higher concentration gradient.[66,68,69]

Adding microabrasion to MI Paste Plus significantly reduced the surface area WSLs as a percentage of labial tooth surface area. Teeth that received the combined treatment showed a reduction in labial surface area percentage from 24.6% to 9.7%, and a 60.6%

reduction relative to initial lesion size. This reduction in surface area is less than the findings from Murphy et al,[87] whose study involved 16 teeth that showed an initial average surface area percentage of the labial aspect of 19.7%. After one session of 10 rounds of 10-second microabrasion, the teeth showed a decrease to 2.9% of the labial surface, representing an 83% reduction relative to initial lesion size. However, Murphy used a stronger acid (18% HCl compared to 6.6% HCl). In addition, they performed all of the microabrasion treatments once, whereas the current study waited a month between treatments, which could allow for a hypermineralized barrier layer to form between appointments. Microabrasion serves as an adjunct to remineralization because it pierces through the hypermineralized surface layer of the lesion through its acid-abrasion slurry. By allowing greater access of minerals into the lesion's underlying porous region, microabrasion effectively provides synergy with the remineralization potential of CPP-ACP.

Combining MI Paste Plus and microabrasion causes significantly greater reductions in WSL size than MI Paste Plus alone after months of treatment. These results are consistent with the in vitro study by Ryan et al,[14] whose survey showed a more favorable response to teeth with combined treatment than with microabrasion alone. This was an in vitro study which, in addition to the survey, measured L* values and mineral density using micro-CT. To date, it appears that no other researchers have quantified the effect of combining microabrasion with CPP-ACP on lesion size.

The combination of microabrasion and MI Paste Plus showed a greater reduction in lesion size for WSLs of greater initial size. This is consistent with the study by Murphy et al,[87] who also found that larger lesions showed a significantly greater reduction in surface area than smaller lesions. The explanation for why larger lesions respond better to combined treatment may be twofold. As a sphere increases in size, the ratio of surface area relative to its volume decreases. This may suggest that larger lesions have a relatively smaller hypermineralized surface layer compared to its inner porous chamber. Thus, the remineralization of larger lesions may be easier to achieve because there is a relatively smaller superficial barrier. This may also be consistent with why the paste-only group did not show a greater benefit for larger lesions. Also, with very small lesions (less than 1 mm), it becomes impractical and difficult to trace and report significant decreases.

MI Paste Plus alone significantly decreased the lightness value after two months. Teeth that received MI Paste Plus for two months showed a reduction in L* value from 81.2 to 79.4, a decrease of 1.8 units. These results are consistent with the study by Tolcachir et al, whose in vitro study of 5 extracted third molars with artificial WSLs showed a 1.64 decrease in L* value after 60 days of daily three-minute MI Paste Plus application.[26] Combining MI Paste Plus with microabrasion, however, did not show a significant difference in L* value compared to the paste alone. These results are in contrast with those found by Ryan et al, who found a greater enamel translucency in the combined group.[14] A likely explanation for this discrepancy is in the initial size and opacity of the lesions. Those in the current study were considerably smaller in diameter and included more diffuse fluorotic enamel lesions of mixed opacity, whereas Ryan created lesions of well-demarcated, solidly opaque lesions of a larger dimension (6.0 mm^2).

A limitation of the present study was the recruitment and enrollment of a sufficient number of subjects. Despite contacting 80+ subjects, only 14 enrolled, which was less than the projected minimum sample size of 17. Although significant differences were found, the resultant number of subjects limited the generalizability of the data. In addition, the quality of the lesions was not ideal given the aim of the study. The majority of the lesions of the subjects in the study were fluorotic and existed prior to starting braces. Because of this, lesions were smaller and more diffuse with mixed opacity, which made accurate tracing more difficult. Given the tendency for larger lesions to show more improvement, the study may have shown an even greater benefit had it treated larger lesions. A smaller diameter probe of the Vita spectrophotometer would have also been beneficial given the smaller lesions. The photography, while standardized, would have benefitted from advanced photography in which specialized light sources remove the interference of light flash artifacts on the enamel surface.

6 CONCLUSIONS

1. MI Paste Plus alone significantly reduced the surface area of WSLs from 20.2% to 7.6% of the total facial surface of the tooth, with nearly two-thirds of the reduction occurring during the second month of treatment.
2. Combining MI Paste Plus and microabrasion significantly reduced the surface area of WSLs from 24.6% to 9.7%, with similar amounts of reduction occurring during the first and second months of treatment.
3. Combining MI Paste Plus and microabrasion causes significantly greater reductions in WSL size than MI Paste Plus alone after 2 months of treatment. Relative to facial surface, the difference was approximately 2X; relative to initial WSL size, the difference was 1.6 times.
4. WSLs of larger initial sizes showed greater reduction in size with combined treatment than smaller lesions.
5. MI Paste Plus alone significantly reduced the L* value of WSLs from 81.2 to 79.4, with double the amount of reduction occurring in the first month of treatment.
6. Combining microabrasion and MI Paste Plus did not show a significant difference in L* value after two months compared to baseline, nor did it show a significant improvement in L* value after two months compared to MI Paste Plus alone.

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APPENDIX A

FIGURES

Figure 1. Change in WSL as a percentage of the entire facial surface of the tooth.

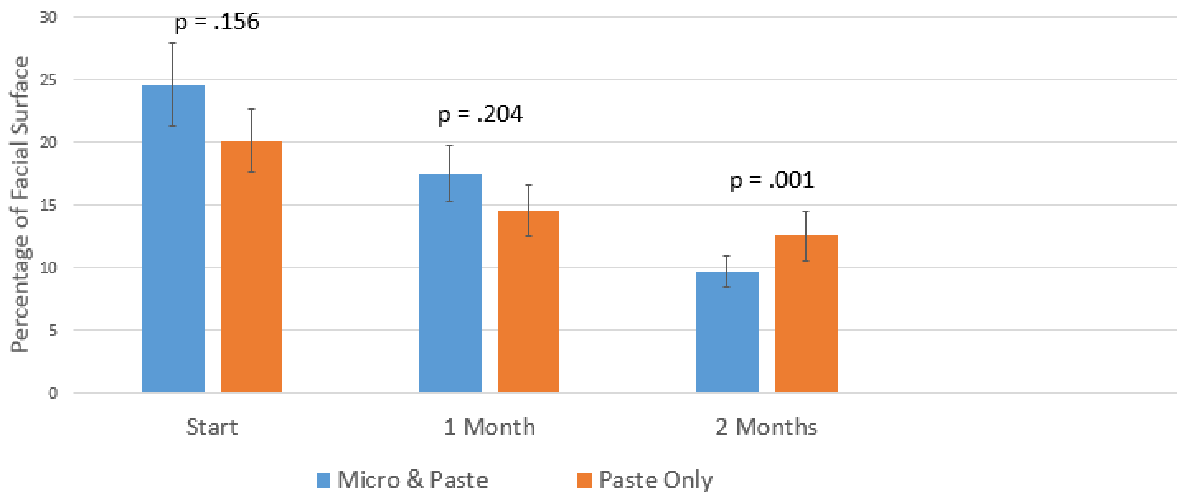


Figure 2. Reduction in WSL as a surface area percentage, relative to initial lesion size.

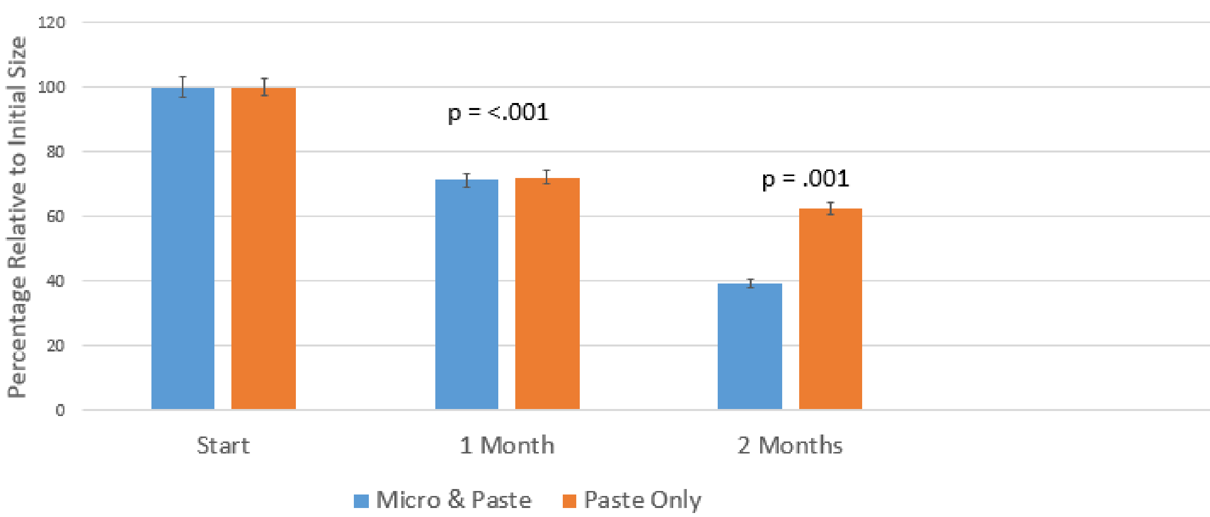


Figure 3. Percent change in WSL surface area based on initial lesion size for the combined group from start to 2 months.

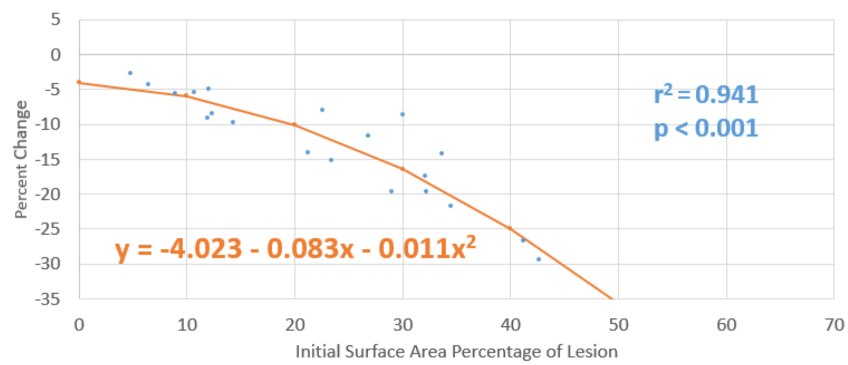


Figure 4. Percent change in WSL surface area based on initial lesion size for the paste-only group from 1 month to 2 months

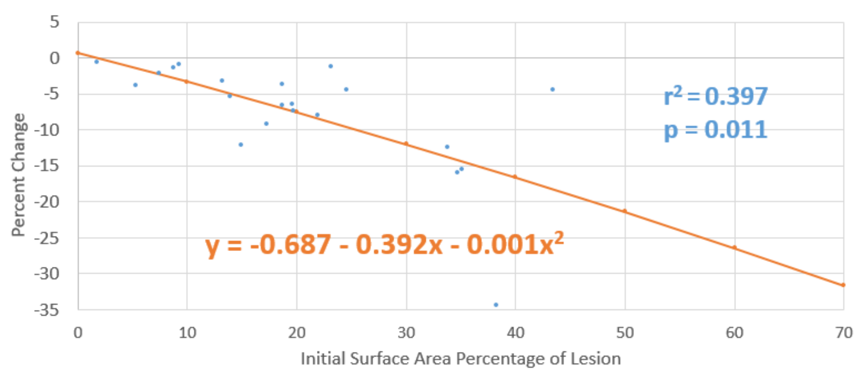


Figure 5A. Comparison of WSL surface area change (%) from start to 2 months based on initial lesion size: combined vs. Paste-only

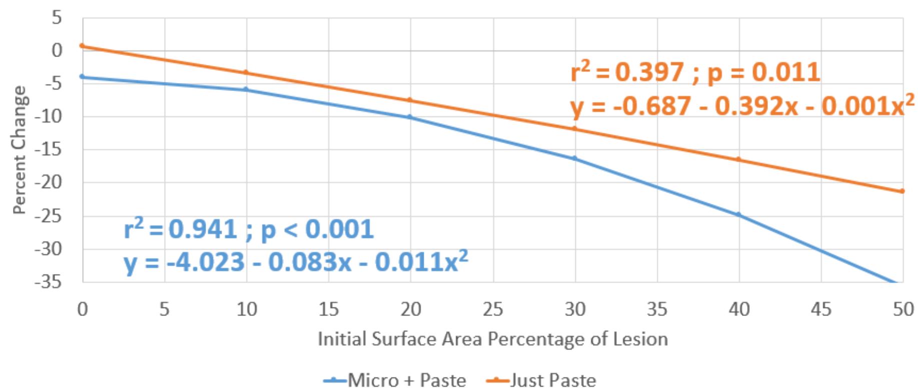


Figure 5B. Comparison of WSL surface area change (%) from start to 2 months based on initial lesion size: combined vs. Paste-only overlapped with percent change for each 10% size increase

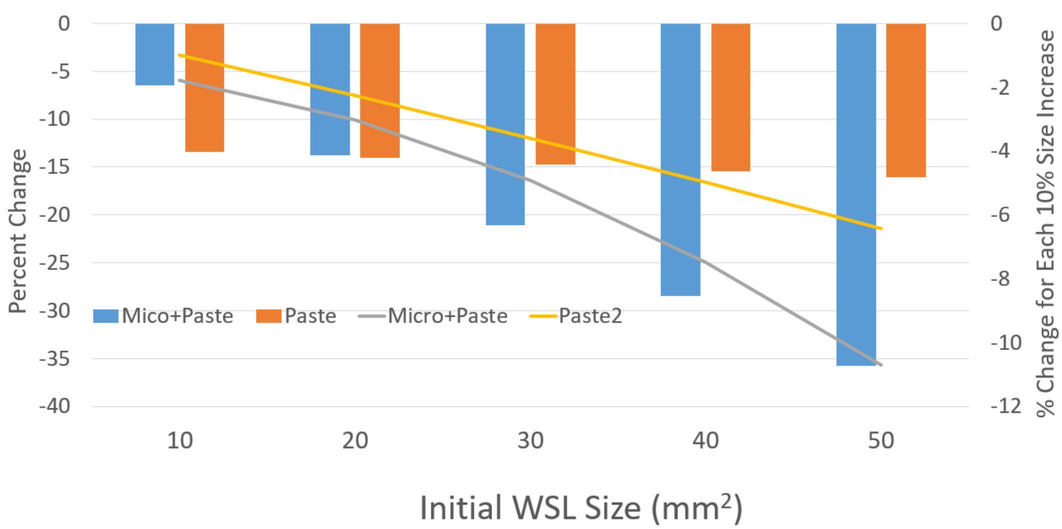


Figure 6. Medians and IQRs for L* values at baseline, 1 month, and 2 months for WSLs in both combined group and paste-only group.

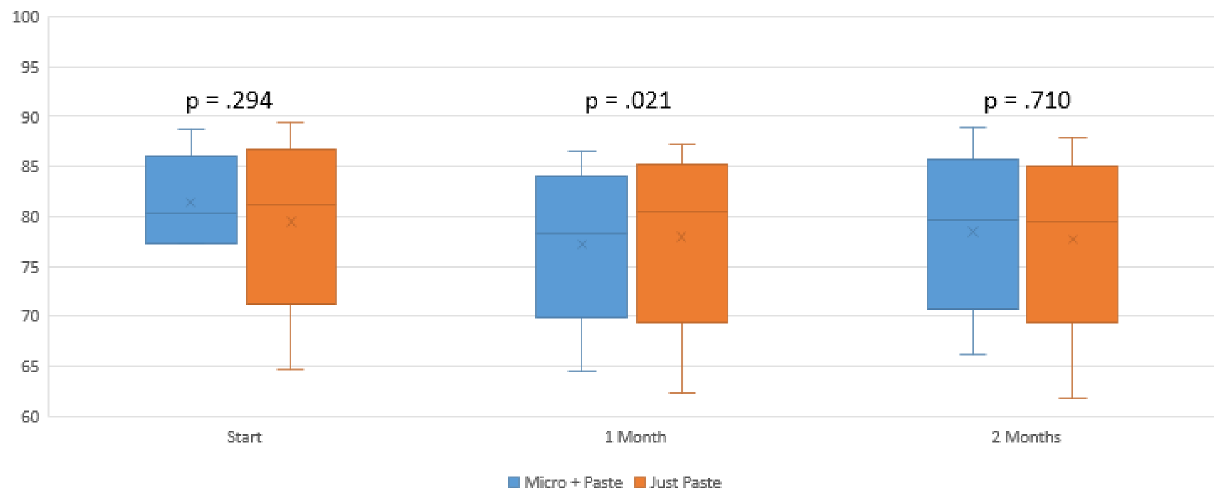
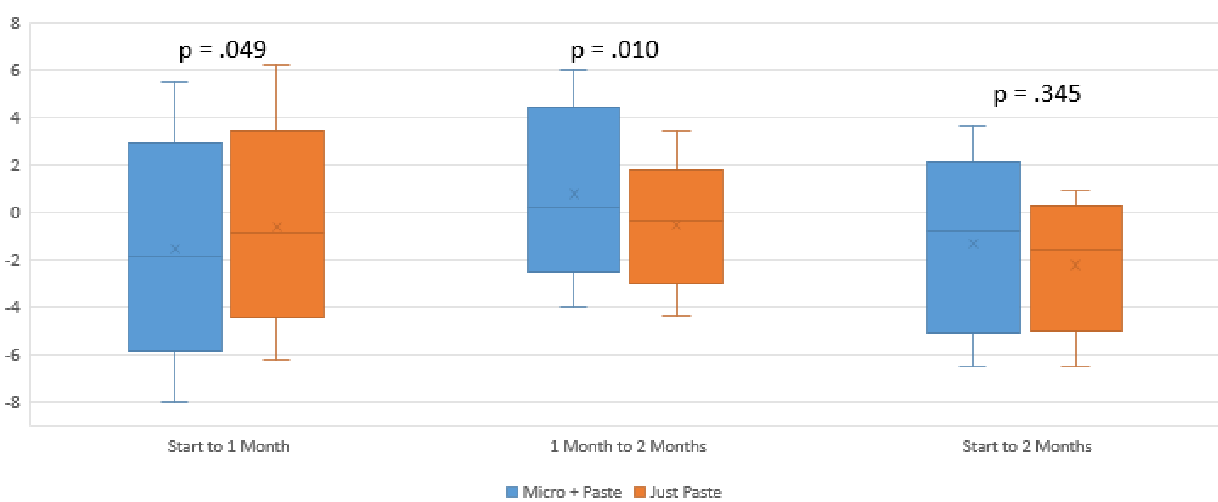


Figure 7. Change in medians and IQRs for L* values at baseline, 1 month, and 2 months for WSLs in both combined group and paste-only group.



APPENDIX B

TABLES

Table 1. Order and description of patient appointments in the clinical study.

Time Point	Appointment	Duration	Description
T_0	Initial Visit	30 mins	• Informed Consent • Baseline records
T_1	First Treatment (1-2 weeks later)	1 hour	• Spectrophotometer (spec) reading • Microabrasion: combined group only • MI Paste Plus: all teeth; send patient home with clear retainer with cream, wear twice daily for 5 min
T_2	Second Treatment (6-8 weeks later)	1 hour	• Spec & photograph records • Microabrasion: combined group only • MI Paste Plus: continue both groups
T_3	Final Visit (6-8 weeks later)	30 mins	• Spec & photograph records • End of study

Table 2. Means and standard error (S.E.) for WSL surface area (as a percentage of the total facial surface) at the start of treatment, 1 month after the start and 2 months after the start for all of the 48 teeth evaluated.

	Experimental (Micro + Paste) Side		Control (Paste) Side		
Times	Mean	Standard Error	Mean	Standard Error	Probability
Size of WSL as a Percentage of Total Tooth (%)					
Start	24.6	3.2	20.2	2.5	.156
Start to 1 Month	17.5	2.3	14.6	2.0	.204
Start to 2 Months	9.7	1.3	12.6	1.9	.001
Reduction in WSL Size as a Percentage of the Total Tooth (%)					
Start to 1 Month	**7.1**	1.5	**5.6**	1.4	.204
1 Month to 2 Months	**7.9**	1.5	**2.9**	0.6	<.001
Start to 2 Months	**15.0**	2.6	**7.6**	1.7	.001

Bold = statistically significant ($p < .01$) changes

Table 3. Means and standard error (S.E.) for WSL surface area as a percentage relative to its initial size at the start of treatment, 1 month after the start and 2 months after the start for all of the 48 teeth evaluated.

	Experimental (Micro & Paste) Side		Control (Paste) Side		
Times	Mean	Standard Error	Mean	Standard Error	Probability
Size of WSL as a Percentage Relative to its Initial Size (%)					
Start to 1 Month	71.1	0.7	72.3	0.8	.630
Start to 2 Months	39.4	0.4	62.4	0.8	<.001
WSL Reduction Relative to its Original Size (%)					
Start to 1 Month	**28.8**	3.8	**27.8**	4.4	.881
Start to 2 Months	**60.6**	3.1	**37.6**	5.0	.001

Bold = statistically significant (p < .01) changes

Table 4. Medians and inter-quartile ranges (IQR) for Vita spectrophotometer Lightness (L*) value comparing WSLs in combined group to WSLs in control group at the start of treatment, 1 month after the start and 2 months after the start for all of the 48 teeth evaluated.

	Experimental (Micro + Paste) Side		Control (Paste) Side		
Times	Median	IQR	Median	IQR	Probability
L* Value					
Start	80.3	77.1 to 83.5	81.2	78.0 to 84.1	.294
After 1 Month	78.2	75.3 to 81.3	80.4	76.4 to 83.3	.021
After 2 Months	79.6	75.1 to 82.5	79.4	77.1 to 82.3	.710
Change in L* Value					
	Median	IQR	Median	IQR	Probability
Start to 1 Month	**-1.9**	-3.7 to +0.4	-0.9	-2.7 to +0.6	.049
1 Month to 2 Months	+0.2	-1.1 to +2.8	-0.4	-1.6 to +0.2	.010
Start to 2 Months	-0.7	-3.7 to +0.6	**-1.6**	-3.6 to -0.6	.345

Bold = Bold = statistically significant (p < .01) changes