ICON CARIES INFILTRANT RESIN AND MI PASTE PLUS
FOR THE TREATMENT OF WHITE SPOT LESIONS

by

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A THESIS
Submitted to the graduate faculty of The University of Alabama at Birmingham,
in partial fulfillment of the requirements for the degree of
Master of Science

BIRMINGHAM, ALABAMA

2010
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ABSTRACT

**Introduction:** Fixed appliances create new oral hygiene demands for orthodontic patients. Poor compliance with proper oral hygiene can lead to demineralization of enamel and cause unesthetic white spot lesions (WSLs). Most current treatment protocols for WSLs depend on patient compliance, which is frequently lacking in adolescent patients. A novel material “Icon” has recently been developed to treat WSLs through a minimally invasive procedure performed in the dental office. This material infiltrates a WSL and seals it in order to stop caries progression. The aim of this study was to investigate the efficacy of Icon on WSL progress and to compare it to treatment with MI Paste Plus (MIP+) and fluoride mouthrinse. **Methods:** Forty human teeth with WSLs were used in this study. The teeth were divided into four groups (n=10/gp) to receive treatment with the following materials: Icon caries infiltrant resin (DMG America, Englewood, NJ), Icon and MIP+ (GC America, Alsip, IL), MIP+ only, and fluoride mouthrinse. Teeth were sectioned in half through the WSL and examined using a digital microscope (Keyence VHX 600 Series) at 100x magnification. One half of each tooth was treated following the manufacturer’s instructions, while the other half served as a control. Then, both halves were submerged in an artificial caries solution for twenty-five days. MIP+ and fluoride treatments were applied daily during this time period. At the conclusion of the treatment time, the teeth were reimaged using the digital microscope. The images were placed side by side, and the WSL depths were measured at
the point of greatest change to determine the amount of demineralization or remineralization produced. The Icon group was compared with the MIP+ and fluoride groups, and each group was compared with its own control group. The results were statistically analyzed using a mixed model ANOVA (p<0.05). **Results:** Icon, Icon/MIP+, and MIP+ treated teeth had WSL depth changes of -0.68, 1.95, and 11.83nm, which were all significantly less than the depth change that took place with fluoride treated teeth. **Conclusions:** Icon effectively halted demineralization in teeth with WSLs.
ACKNOWLEDGEMENTS

The author thanks Drs. Burgess, Cakir, Jacobson, Browne, and Litaker, Ms. McNeal, Mr. Beck, and the faculty members and residents of the Department of Orthodontics, University of Alabama School of Dentistry, Birmingham, Alabama.
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<tr>
<td>CPP</td>
<td>casein phosphopeptide</td>
</tr>
<tr>
<td>CPP-ACFP</td>
<td>casein phosphopeptide-amorphous calcium fluoride phosphate</td>
</tr>
<tr>
<td>CPP-ACP</td>
<td>casein phosphopeptide-amorphous calcium phosphate</td>
</tr>
<tr>
<td>CPP-CP</td>
<td>casein phosphopeptide-calcium phosphate</td>
</tr>
<tr>
<td>MIP+</td>
<td>MI Paste Plus</td>
</tr>
<tr>
<td>PC</td>
<td>penetration coefficient</td>
</tr>
<tr>
<td>PPM</td>
<td>parts per million</td>
</tr>
<tr>
<td>RMGIC</td>
<td>resin-modified glass ionomer cement</td>
</tr>
<tr>
<td>TEGDMA</td>
<td>triethylene glycol dimethacrylate</td>
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<tr>
<td>WSL</td>
<td>white spot lesion</td>
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INTRODUCTION

White Spot Lesions and Orthodontics

One of the main goals of orthodontic treatment is to give the patient a healthy, esthetic smile. An orthodontist aims to reach this goal by aligning the teeth and correcting the bite. However, even if a perfect occlusion is obtained, a beautiful smile may not result if the patient has not complied with proper oral hygiene protocol throughout their treatment. Early carious lesions, sometimes called white spot lesions (WSLs) may form, compromising the health of the teeth and the esthetic result of the treatment. Once present, the white spot lesion is often resistant to remineralization and irreversible, leaving the patient with a permanent scar from the braces.

Fixed orthodontic appliances introduce new oral hygiene demands on patients. Brackets, bands, wires, and other auxiliaries turn smooth tooth surfaces into retentive sites for plaque accumulation. Areas that were once self-cleansing due to salivary flow and oral musculature become stagnant, plaque-collecting zones. Plaque removal becomes much more difficult too, since the appliances do not allow clear access to the tooth surface. Bacteria release lactic acid, which decrease plaque pH to a critical cariogenic pH. Without adequate plaque removal, the acid begins to demineralize or decalcify the enamel around the brackets. Subsurface mineral loss causes the normally translucent enamel to become opaque due to an optical phenomenon, producing a white spot lesion. This process can occur in just 4 weeks, which is typically the period of time between one orthodontic appointment and the next. When the appliances are removed
at the end of treatment, these lesions are seen as frosty white enamel opacities that often encircle the area where the bracket or band was located on the tooth during treatment. These white spots create an esthetic concern, especially when located on anterior teeth. Studies report a prevalence of white spot formation anywhere from 2% to 96%. \cite{1,3,5,6,8} Gorelick, Geiger, and Gwinnett\textsuperscript{5} reported that 49.6% of orthodontic patients and 10.8% of treated teeth had white spot formation during orthodontic treatment. In their study, the maxillary anterior teeth showed the highest incidence of white spot formation at 15.3%, with 23% of maxillary lateral incisors and 8.4% of maxillary central incisors developing white spot lesions. Mizrahi\textsuperscript{9} noted that the maxillary and mandibular molars showed the highest prevalence of white spot lesions after orthodontic treatment, but maxillary incisors were the next most affected teeth. Sites that are commonly affected are the cervical margins of the teeth, under loose bands, and at the junction of the bonding resin.\textsuperscript{7} Generally, they occur readily in any area that the patient cannot easily access with a toothbrush. These white spot lesions are relatively resistant to remineralization and are usually still present more than five years after treatment commences.\textsuperscript{5}

The Caries Process

Several factors contribute to the formation of dental caries. Mutans streptococci and lactobacilli, which colonize tooth structure and thrive in an acidic environment, are frequently associated with dental caries. These organisms metabolize fermentable carbohydrates to form glucans and lactic acid. Together, the bacteria and its by-products make up a sticky substance known as plaque. This process is cyclic, as the presence of plaque creates retention for subsequent colonization of different bacteria which form
glucans and acid. Unless plaque is adequately removed from the teeth, bacterial produced acid penetrates into the enamel and causes the hydroxyapatite crystals that compose the mineralized tooth structure to release calcium and phosphate ions. As these ions diffuse out of the tooth, demineralization occurs. Remineralization, or the reverse process, can occur in the presence of calcium, phosphate, and fluoride ions and a neutral pH. When demineralization and remineralization rates are in equilibrium, the enamel remains essentially unchanged. However, when the demineralization process outweighs the remineralization process, caries development continues.

Demineralization of the enamel occurs in two sequential stages. The first is known as surface softening, where the mineral loss of the interprismatic substance is greatest at the enamel surface. The mineral loss occurs as ions are released into the plaque and saliva. With continued demineralization, the lesion can then progress to the second stage, where a subsurface lesion develops deeper in the enamel. In this phase, the body of the lesion may have lost up to 50% of its mineral content and therefore has an increased volume of space. The outer layer, known as the zone of remineralization, remains intact due to its higher mineral content produced by ions diffusing out of the tooth which are deposited in this zone. Remineralization occurs more readily with a surface softened lesion than with a subsurface lesion due to a difference in ability of ions to penetrate the outer surface.
White Spot Lesion Prevention

Manual Products

The first and most important step to preventing white spot lesions while wearing fixed orthodontic appliances is proper oral hygiene. Approximately 20% to 30% of adolescents do not adequately remove plaque during orthodontic treatment. Patients should be given thorough oral hygiene instructions at the beginning of treatment, and it should be reinforced at each appointment. Mechanical plaque removal is essential and can be achieved by daily brushing and flossing. While a manual toothbrush may be sufficient, some clinicians recommend a powered toothbrush, which removes plaque more effectively and efficiently for orthodontic patients.

Fluoride Products

Regular use of fluoride products during orthodontic treatment decreases the formation of white spot lesions. Fluoride has several mechanisms of action that allow it to be ideal for caries prevention. One mechanism of action is replacing the hydroxyl group in hydroxyapatite \( \text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2 \). The newly formed substrate, fluorapatite \( \text{Ca}_{10}(\text{PO}_4)_6\text{F}_2 \), is stronger than hydroxyapatite and is more resistant to dissolution. Furthermore, fluoride has been shown to increase the rate of remineralization. If fluoride is present in saliva, it will adhere strongly to the tooth surface and attract calcium and phosphate ions in saliva and plaque fluid. Then, the chemical reaction between these ions and the hydroxyapatite molecule can take place readily. Fluoride also exhibits caries protection through its properties of being
bacteriostatic at low concentrations and bactericidal at high concentrations. 200 ppm is the threshold.\textsuperscript{18}

Several systematic reviews have focused on finding the most effective fluoride protocol to prevent white spot lesions during orthodontic treatment. Chadwick\textsuperscript{17} identified 143 articles on this topic and reviewed 7 articles describing 6 studies in their final paper. After extensive comparisons among fluoride products, they concluded that all groups treated with fluoride were less susceptible to decalcification during orthodontic treatment than those who did not use fluoride. However, they also stated that it was not possible to recommend which preparation or schedule was the best to prevent demineralization. Derks\textsuperscript{19} also performed a review of previous studies on preventing white spot lesions during orthodontic treatment. While he concluded that fluoride was an effective preventative measure, he also stated that more randomized clinical trials are necessary to find the optimal defensive strategy.

Patients should brush their teeth with a toothpaste that contains fluoride. Most toothpastes contain 900 to 1100 ppm sodium fluoride and are appropriate for use by a low caries risk patient. Other fluoride toothpastes may contain stannous fluoride, monofluorophosphate, or amine fluoride.\textsuperscript{20} Prescription toothpastes, such as Prevident 5000, with 5000 ppm fluoride are recommended for higher risk patients. Orthodontists frequently advise patients to brush after each meal and before bedtime. The toothpaste is usually rinsed off of the teeth with water, but leaving a layer of residue on the teeth is one way to increase the fluoride concentration in the saliva.\textsuperscript{4} With any fluoride application, not eating or drinking for 30 minutes after the application is recommended.
Brushing with a fluoride toothpaste alone can still allow up to 15% mineral loss in enamel adjacent to orthodontic brackets.\textsuperscript{18} Accordingly, fluoride mouthrinse or gel is another essential item in the oral hygiene armamentarium and may be considered the standard of care in orthodontics.\textsuperscript{11} 50% of orthodontic patients had an increase in the number of white spot lesions when a fluoride preventative protocol was not used, according to a study by Gorelick, Geiger, and Gwinnett.\textsuperscript{5} They also found that 30% fewer orthodontic patients developed white spot lesions when they used a fluoride mouthrinse.\textsuperscript{21} Although there is little evidence of which fluoride delivery method is best, most orthodontists recommend daily use of a 0.05% neutral sodium fluoride mouthrinse. A study by Grobler, Øgaard, and Rolla\textsuperscript{22} showed that two weeks after a single application, calcium fluoride is still present on the enamel surface. Geiger, Gorelick, and Gwinnett’s results show that a combination of daily brushing with fluoride toothpaste and daily rinsing with a 0.05% (225ppm) neutral sodium fluoride mouthrinse can give the orthodontic patient full protection from demineralization.\textsuperscript{21} Alternative options that orthodontists may recommend are various concentrations of acidulated phosphate fluoride and stannous fluoride.

In order for the topical fluoride treatment to be effective, it must be used as directed. For mouthrinses, patients must comply with daily usage to get maximum prevention of white spot lesions. Unfortunately, one study found that compliance with mouthrinising is poor, as 42% of patients rinsed every other day and only 13% rinsed every day as instructed.\textsuperscript{21} Noncompliance with this part of the oral hygiene regimen correlated with an increase in white spot lesions. 51% of noncompliant patients developed white spot lesions, whereas they occurred in only 21% of those who rinsed at
least every other day. Patients were more likely to prevent white spot lesions when they used the fluoride mouthrinse daily, even when their oral hygiene was considered poor throughout treatment.

Alternative fluoride delivery mechanisms that do not depend on patient compliance are available. Fluoride varnishes (5% NaF in a copal varnish) contain a high concentration of fluoride that is released slowly over time and can be applied by the orthodontist at the patient’s regular appointment. One study by Vivalidi-Rodrigues found that white spot lesions were reduced by 44.3% when fluoride varnish was applied every 3 months during orthodontic treatment. Farhardian et al performed a split mouth within-subject clinical trial designed to determine the effectiveness of a single dose of high-concentration fluoride varnish. One week after bonding, a fluoride varnish was applied to one of the two premolars scheduled for extraction, and then T-loops were placed on both premolars to cause more plaque accumulation. When the teeth were extracted 85-90 days after the fluoride application, the authors found that the fluoride varnish decreased the depth of the white spot lesion by about 40% in a three month timeframe. Therefore, they also recommended fluoride varnish application every three months during orthodontic treatment.

Another non-compliant based method of fluoride application is through primers and adhesives used to bond brackets. Glass ionomer cement contains fluoride that is released gradually, and this happens more readily in a low pH environment. This approach has the advantage of releasing fluoride around the bracket when and where it is needed most. Furthermore, glass ionomer cements can be recharged with fluoride when topical solutions are applied. Unfortunately, a study by Hallgren et al. also found that
glass ionomer bonding cements had lower bond strength and more bond failures than resin cements. In order to increase bond strength, resin particles were added and resin-modified glass ionomer cement (RMGIC) was formed. These cements maintain the ability to release fluoride and also have a bond strength that is adequate to bond orthodontic brackets to enamel, although early strength may still be problematic. In 2007, Sudjalim showed that RMGIC reduced occurrence of enamel demineralization, even when used without another source of fluoride treatment.

Orthodontic ties impregnated with fluoride are also available and offer a similar benefit. These ties contain stannous fluoride (SnF$_2$) that is released slowly over time around the bracket base. Often the initial release of fluoride is high, but the level quickly drops. In 1996 Wiltshire found that a burst of fluoride was released in the first two days, but a substantial decrease of 63% was seen after one week and 88% after two weeks. Although the ties can imbibe fluoride present in the mouth, Wiltshire reported in another study in 1999 that the level of fluoride is most likely below the threshold needed to prevent white spot lesions in the presence of plaque around the brackets.

Based on a review of the literature, fluoride-containing cements and ties should not be the primary source of fluoride for an orthodontic patient. They are best used as an adjunct to supplement the demineralization protection provided by fluoride mouthrinses and varnishes.

**Casein Phosphopeptide (CPP)**

Although fluoride treatment is considered the gold standard in orthodontics, it may not be enough to prevent white spot lesions in some susceptible patients.
Featherstone noted that supersaturation of the mineralizing ions (fluoride, calcium, and phosphate) is “the driving force for remineralization.”\textsuperscript{10} To convert one molecule of hydroxyapatite to one molecule of fluorapatite, ten calcium ions, six phosphate ions, and two fluoride atoms must come together and react.\textsuperscript{7,27} For a patient using a fluoride treatment alone, the process depends on the presence of other ions in the saliva.\textsuperscript{18} If they are not bioavailable, remineralization cannot occur.

Although it seems simple to deliver these ions to the tooth, the clinical application has been a challenge. Soluble forms of calcium phosphate do not adhere to the tooth surface well enough to diffuse into the enamel, while insoluble forms do not allow the ions to be bioavailable. After extensive research, the milk protein casein was found to have anticaries properties due to its ability to increase the calcium and phosphate content of plaque.\textsuperscript{30} It does so through multiple phosphoseryl residues that can bind twenty-five calcium ions, fifteen phosphate ions, and five fluoride ions per molecule, which is greater than one hundred times the amount that could be stabilized in a neutral or alkaline pH.\textsuperscript{30} These ions are sequestered in a way that does not allow them to reach the critical size needed for precipitation.\textsuperscript{30,32,33} Casein has a strong affinity for hydroxyapatite, and when the two are in contact the demineralization rate is decreased.\textsuperscript{34} It also promotes remineralization through localization and stabilization of these ions at the tooth surface and releasing them gradually.\textsuperscript{35} There are three different types of casein products available: casein phosphopeptide (CPP), casein phosphopeptide-amorphous calcium phosphate (CPP-ACP), and casein phosphopeptide-amorphous calcium fluoride phosphate (CPP-ACFP).
**Calcium Phoshopeptide-Amorphous Calcium Phosphate (CPP-ACP)**

GC America has used this technology to form a casein phosphopeptide-amorphous calcium phosphate trademarked Recaldent™. It is commercially available in sugar-free chewing gum, mints, lozenges, and a dental cream known as MI Paste. The version containing 900ppm sodium fluoride is known as MI Paste Plus. According to the manufacturer:\(^\text{36}\)

“Casein phosphopeptide (CPP) is a sticky protein that binds calcium and phosphate ions, stabilizing them in an amorphous state. When applied within the oral cavity, the CPP and amorphous calcium phosphate (ACP) readily bind to pellicle, plaque, and soft tissue, localizing bioavailable calcium and phosphate to the tooth surface.”

The clinical results of CPP-ACP are very promising. One study by Dr. Eric Reynolds\(^\text{37}\) determined that levels of CPP-ACP adequate to protect enamel could be detected in plaque up to three hours after chewing a piece of sugar-free gum containing Recaldent™. A study showed that the CPP-ACP is even able to bind to pellicle and provide a source of ions on plaque-free tooth surface.\(^\text{38}\) Using a rat model, Reynolds’ group reported that treatment with 1.0% CPP-CP preparation twice a day led to 55% fewer smooth surface carious lesions than in a control group.\(^\text{30}\) When the same protocol was applied to human subjects, Reynolds found that enamel mineral loss was reduced by 51%.\(^\text{39}\)

The formulation of CPP-ACP containing fluoride has also been shown to be successful. Reynolds used a rat model in one study and showed that the animals who were treated with casein phosphopeptide-calcium phosphate (CPP-CP) and 500 ppm
fluoride had a significantly lower caries rate than those treated with CPP-CP alone or fluoride alone.\textsuperscript{30}

**White Spot Lesion Treatment**

Although white spot lesion prevention is ideal, they unfortunately occur frequently in the orthodontic patient population. The methods and materials used for preventing these lesions are not the always the same as the approach that is needed to treat them. Treatment should start with the most conservative procedure and only progress to more invasive methods as needed.\textsuperscript{20}

**Fluoride Products**

Fluoride is considered the standard of care for white spot lesion treatment. While highly concentrated fluoride products may prevent the formation of white spot lesions, they are not ideal for treating them. In high amounts fluoride quickly remineralizes the enamel surface and creates a barrier preventing ion penetration to the subsurface lesion.\textsuperscript{20} Therefore, the internal part of the lesion cannot be repaired, and the white spot lesion persists.\textsuperscript{3} The current treatment recommendation for an existing white spot lesion is a mouthrinse with a low fluoride concentration.\textsuperscript{12} Featherstone reported that a minimum level of 0.03 ppm fluoride in the saliva enhanced the mineralization process, but the optimum concentration was achieved at 0.08 ppm fluoride.\textsuperscript{10} Accordingly, toothbrushing twice a day with fluoridated toothpaste and rinsing daily with a 0.05% sodium fluoride toothpaste should be recommended to the patient immediately when white spot lesions are noted following debonding of orthodontic brackets.\textsuperscript{40} This
frequent exposure to low levels of fluoride will keep enough fluoride in the saliva to allow optimal remineralization.

*Casein Phosphopeptide (CPP)*

In addition to preventing white spot lesions, casein phosphopeptide-amorphous calcium phosphate can be used to treat them. As previously discussed, CPP-ACP makes calcium and phosphate ions bioavailable. Since the ions are released slowly, they can penetrate deep into the enamel lesion and remineralize it completely. In 1997, Reynolds performed an *in vitro* study on human teeth with artificially created white spot lesions and showed that CPP remineralized white spot lesions at a rate of $3.9 \pm 0.8 \times 10^{-8}$ mol hydroxyapatite/m$^2$/s, which was significantly faster than a control group. He discovered that higher concentrations, such as 0.5% and 1.0% CPP, performed better than lower concentrations and also found the optimal performance pH to be 7.0. A clinical study performed by Andersson in 2007 demonstrated that CPP-ACP was capable of remineralizing the white spot lesions that formed naturally during orthodontic treatment. In this study, patients applied CPP-ACP cream daily to visible white spot lesions on incisors and canines for three months. This group was compared with a group using 0.05% sodium fluoride mouthrinse for six months, and both groups were also instructed to brush with a fluoride toothpaste for six months. Although each group showed dramatic improvement at twelve months, the CPP-ACP group had 63% fewer visible white spot lesions while the fluoride group had only 25% fewer lesions. The authors concluded that CPP-ACP treatment creates a more esthetic result than fluoride alone. Furthermore, a study by Lijima, Reynolds, and others using the CPP-ACP containing
chewing gum showed that the enamel remineralized by the MI Paste was actually more resistant to demineralization than normal enamel. Chewing gum also stimulates saliva flow which increases the calcium and phosphate orally.

*Bleaching*

One conservative method to make spot lesions less noticeable is by whitening the teeth. Bleaching can allow the white spot lesion to blend with the surrounding tooth structure, thereby camouflaging the problem. Patients may choose from a tray-based delivery system customized by their dentist or a polyethylene strip that can be acquired over-the-counter. Whitening gels contain either hydrogen peroxide or carbamide peroxide and can be obtained in various concentrations. While this procedure may create a more esthetic result, bleaching the teeth will not strengthen the demineralized tooth structure.\(^{40}\) Fluoride or another remineralizing treatment should be used along with bleaching in order to satisfy both the esthetic and health requirements.

*Microabrasion*

When a white spot lesion is limited to the enamel surface, a treatment known as microabrasion may be appropriate. Microabrasion removes a thin layer of enamel (about 50-150 microns) so that demineralized tissue can be reduced without sacrificing much healthy tissue in the process.\(^{43}\) The teeth needing treatment are isolated, then 18% hydrochloric acid and a fine-grit silicon carbide abrasive are applied via a high torque-low rpm contra-angle in a slow speed handpiece for about 30 seconds before being rinsed off with water. The process is gradual and can be repeated as needed until the white spot
lesion is no longer apparent. Five to ten applications will usually produce the desired result.\textsuperscript{40} A four minute sodium fluoride treatment is recommended after the procedure.\textsuperscript{40} However, no restoration is needed because the calcium and phosphate that is removed is redeposited and compacted into the remaining enamel.\textsuperscript{43} The enamel appears shiny and polished and blends well with natural enamel.\textsuperscript{40} Studies have shown that the new layer is more resistant to demineralization.\textsuperscript{40,43-35} For shallow lesions, this approach generally works well, but some white spot lesions are too deep to remove this way.

\textit{Restoration}

With a deeper white spot lesion, the appearance of the tooth may be improved with a tooth-colored restoration, such as a composite resin or glass ionomer. In cases where the white spot lesion has progressed to a frank cavitation, this treatment approach is absolutely necessary. However, if the surface of the lesion is still intact, this method is less than ideal and should only be considered after all other strategies have been exhausted.\textsuperscript{23} Any dental restoration involves irreversible removal of tooth structure. In addition to removing the decalcified enamel, healthy enamel will have to be sacrificed to fulfill the requirements of proper restoration design. If the patient desires more esthetic results, a veneer or crown can be placed. The dentist must inform the patient that once this approach is initiated, he or she will have to maintain the restoration throughout their lifetime and have it replaced as needed.
**Infiltrant Resins**

In recent years, an approach known as microinvasive or minimum intervention dentistry has evolved. Its aim is "maximum conservation of demineralized, noncavitated enamel and dentin." White spot lesions fall within this realm, and should therefore be treated without removal of tissue if possible. Previous limitations in dental materials and procedures made this approach difficult, but developing technology is making it a reality today.

In 1975, Davila first published a study on the use of adhesives to penetrate white spot lesions. He used both artificially created and naturally formed white spot lesions. In one test group, the adhesive was placed directly on the white spot lesion without etching first. In the other test group, the white spot was prepared with 50% phosphoric acid for 60 seconds, and then the adhesive was applied. The teeth were sectioned, and the treatment group was placed in 10% hydrochloric acid in 10 to 15 minute intervals to allow rapid demineralization. The enamel dissolved quickly, except for the area surrounding the adhesive. The authors credit this effect to protection from the resin tags in the enamel. Although both treatment groups displayed an adequate resin penetration depth in the artificially created lesions, only the etchant group allowed resin to occlude the pores and offered defense from demineralization. The authors termed this procedure plastification.

Others further developed the procedure. In 1976, Robinson authored an article on arresting naturally formed carious lesions using a resorcinol-formaldehyde resin. He determined that treatment with this resin led to a reduced rate of demineralization. Unfortunately, the resin was a dark-red color and is obviously a problem for treating
white spot lesions in an esthetic area. There were also some concerns that it may be toxic. Years later in 2001, Robinson sought to find a commercially available dental adhesive that would be appropriate for caries infiltration. He reported that most dental adhesives were able to occlude up to 60% of the enamel pores. By doing so they reduced further demineralization, especially when more than one treatment was performed. He concluded that the available materials have potential for treating white spot lesions but that modifications were needed, such as added fillers, antibacterial products, or materials that encouraged remineralization. In 2004, Schmidlin examined the ability of an unfilled resin, Heliobond, to penetrate into demineralized and remineralized enamel. His group discovered that unfilled resins have good infiltration ability. Unfortunately, however, they also reported that these resins are highly solubility in saliva and do not hold up well under mechanical stress. Although many studies showed that treatment of white spot lesions could be possible through an infiltration technique, further research was needed to refine the material and the procedure.

Recently, Dr. Hendrick Meyer-Lueckel and Dr. Sebastian Paris have contributed extensively to the knowledge pool on this concept. In 2006, their group compared five different adhesives and a fissure sealant and their effects on the progression of demineralization of artificially created white spot lesions in bovine enamel. They also examined two different penetration times: 15 seconds and 30 seconds. The lesions were created by coating the teeth with nail varnish and leaving three windows of enamel exposed to a demineralization solution for 14 days. Then, two of the three windows were treated with the test material, each one with one of the two designated penetration times, while the third window served as the control. After etching with 20% phosphoric acid for
5 seconds and drying thoroughly, the material was applied for the desired time and light-cured for 30 seconds. Half of each lesion was then coated with nail varnish to provide a baseline control. After a 14 day exposure to a second round of demineralization solution, the specimens were cut perpendicularly to the surface, and the lesion depths were measured and increase in depths calculated. The authors found that filling the pores with three of the five adhesives or the sealant material can completely inhibit demineralization. A complete and homogenous resin layer was necessary for maximum prevention, and these qualities were better attained with the longer penetration time of 30 seconds.51

In a later study in 2007, Meyer-Lueckel, Paris, and Kielbassa52 examined three different etching gels applied for various times. Some previous studies showed that the highly mineralized surface layer of enamel does not allow access to the depth of the demineralization and that better remineralization was attained by removing it.53,54 Meyer-Lueckel et al52 applied this concept to the action of their resin and sought to remove the outer enamel layer for better penetration. They noted that artificially formed carious lesions had a surface layer with a mean thickness of 15-30 µm and a mineral content of 63-76 vol%. However, due to a constant demineralization-remineralization cycle that occurs in the mouth, natural lesions had a surface layer with a mean thickness of 40 µm and a mineral content of 85%. The acid etchants used in this study included 37% phosphoric acid, 5% hydrochloric acid, and 15% hydrochloric acid. Each etch was applied for 30, 60, 90, or 120 seconds. Using confocal microscopy and transversal microradiography, they determined that etching with 15% hydrochloric acid for 90-120
seconds removed nearly all of the surface layer while the other etchants and application times did not.\textsuperscript{52}

Meyer-Lueckel and Paris continued to refine the caries infiltration procedure by examining the influence of the penetration coefficient (PC), the infiltrant composition, and application time on the penetration depth and prevention of further demineralization. Some of their preliminary studies showed that resins with a higher PC and longer application time allowed better penetration, but these investigations only involved a shallow carious lesion that did not require much infiltration.\textsuperscript{55-57} Using twelve low-viscosity resins that were allowed to infiltrate for 10, 22, or 40 seconds, they found that lesions did not progress as readily when the resin had a high PC and a long infiltration time. Resins with this property frequently have a high concentration of triethylene glycol dimethacrylate (TEGDMA). Some porous areas were observed and were attributed to a high ethanol content, which helps raise the PC.\textsuperscript{58} Robinson et al suggested that a second application might make the resin more homogenous.\textsuperscript{49} Paris and Meyer-Lueckel confirmed this idea in their own research. They determined that the progression of lesions was halted when they were infiltrated twice.\textsuperscript{59}

DMG America has used these findings to develop a product called Icon, which is short for infiltration concept. It is a caries infiltrant resin designed to bridge the gap between prevention and restoration of white spot lesions.\textsuperscript{60} Icon is a low viscosity substance that treats white spot lesions by penetrating to the depth of the demineralization. The manufacturer says that Icon is ideally suited for lesions that extend as far as the outer one third of dentin.\textsuperscript{61} It can treat any smooth surface lesions, including interproximal lesions when a special tip is used. The teeth are cleaned and isolated, and
Icon etch (15% hydrochloric acid) is applied for two minutes. After thoroughly rinsing and drying the tooth, Icon is applied and allowed to infiltrate for four minutes before being light cured. A second coat is allowed to infiltrate for one minute before being light cured. Once Icon is placed, the pores that were previously pathways for the acid to diffuse become occluded. Thus, the demineralization process is arrested. Icon is also capable of producing an esthetic result. Wayne Flavin, who is the director of scientific affairs for DMG, says that Icon has a refractive index similar to enamel and this property allows a highly cosmetic effect.

Studies on infiltration resins are ongoing in order to perfect the product. Paris and Meyer-Lueckel completed an in situ study designed to assess how well caries infiltration resins can prevent further demineralization. They used bovine enamel specimens that were embedded into an appliance that was then worn by a human volunteer. Although their results are not yet published, they concluded that the resin was able to arrest the lesion. Paris and Meyer-Lueckel are currently working on a project that compares the progress of lesions treated with infiltration radiographically. Studies being performed at Case Western Reserve University and the University of Alabama at Birmingham are focusing on the color stability of infiltrant resins. The caries infiltration concept has recently become popular, and several more published studies should be expected in the near future.

Present Study

Caries infiltrant resins have been shown to be effective in reducing the progression of demineralization of enamel carious lesions. No reports have been
conducted to compare a caries infiltrant resin (Icon) to other commercially available products used to treat white spot lesions. The specific aim of this study was to determine how well Icon prevents further demineralization of white spot lesions and to compare its results with those of MI Paste Plus and fluoride. Icon was also used with MI Paste Plus to determine if adjunct remineralization products improve or interfere with Icon’s success.
MATERIALS AND METHODS

Study Design

Forty recently extracted human teeth with naturally formed white spot lesions were collected and stored in a 10% solution of sodium hypochlorite. Approximately one month prior to the study, the teeth were transferred to distilled water. The teeth were polished with fluoride-free pumice for ten seconds to remove any surface debris. Four groups of ten teeth were established and randomly assigned to a treatment group. The teeth were sectioned occlusogingivally through the white spot lesion using a 0.14” blade in an Isomet™ low-speed saw (Model 1180, Buehler, Lake Bluff, IL) into two halves. Each half was assigned at random to be either a treated half or a control half. The study design is shown in table 1.

Table 1

<table>
<thead>
<tr>
<th>Study design</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment group</strong></td>
</tr>
<tr>
<td>Group 1: Icon</td>
</tr>
<tr>
<td>Group 2: Icon and MI Paste Plus</td>
</tr>
<tr>
<td>Group 3: MI Paste Plus</td>
</tr>
<tr>
<td>Group 4: 0.2% sodium fluoride</td>
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</tbody>
</table>
Each half was imaged under 100x magnification using a digital light microscope (Keyence, VHX-600 series, Woodcliff Lake, NJ). Figure 1 shows the images of both halves of one tooth after being sectioned.

Figure 1

A tooth was sectioned through the white spot lesion into two halves and imaged using a digital light microscope at 100x magnification.

Under magnification, two coats of clear acid-resistant nail varnish (Sally Hansen, Morris Plains, NJ) were applied to the outer part of the tooth, excluding the white spot lesion, and to the entire cut surface of the tooth. Group one teeth were treated with a caries infiltrant resin, Icon (DMG, Hamburg, Germany), according to the manufacturer’s instructions. The teeth were etched for two minutes using Icon-Etch 15% hydrochloric acid (DMG) and rinsed for 30 seconds with sterile water and dried for another 30 seconds with oil/moisture-free air. Icon-Dry (DMG) was applied for 30 seconds, and then the teeth were dried again. Icon-Infiltrant (DMG) was placed and allowed to infiltrate for 3 minutes before light-curing for 40 seconds using an Elipar™ S10 LED curing light (3M ESPE, St. Paul, MN) with an intensity of 1200mW/cm². A second coat of Icon-Infiltrant
(DMG) was applied for 1 minute and light-cured for 40 seconds. Group two teeth were also treated with Icon in the same manner, but a product containing ACP-CPP, MI Paste Plus (GC America, Alsip, IL), was applied to the white spot lesions on a daily basis after the initial treatment with Icon. Group three teeth received daily application of MI Paste Plus (GC America) only. Group four teeth were rinsed for sixty seconds each day with 10 mL of 0.2% neutral sodium fluoride mouthwash.

An artificial caries solution was prepared by first combining 500 mL 1M lactic acid with 10 mL K$_2$HPO$_4$ stock solution. The pH of the solution was brought up to 4.7 using 1M NaOH. Then, 10 g hydroxyethyl cellulose (Sigma-Aldrich Co., St. Louis, MO) was added, and the entire solution was mixed in a blender until a semi-gel solution formed. The solution was titrated to pH 4.8, which was verified using a calibrated sensION 4 pH/ISE meter (Hach Company, Loveland, CO).

Each group of teeth was placed in a separate container of the artificial caries solution and then stored at 37° C. Each day all teeth were removed from the demineralization solutions for treatment. During this time, groups two and three received daily application of MI Paste Plus, while group four was rinsed with fluoride mouthwash for sixty seconds. Group one and the control group were not treated during this time but were removed from the demineralization solution for the same duration as the other groups. All groups of teeth were allowed to remain on the bench top for thirty minutes following treatment. The pH of the demineralization solutions was checked daily and replaced whenever the pH reached 4.9. The teeth were then placed back into the demineralization solutions and stored at 37°C. This process was repeated daily for three
weeks. After three weeks, the pH of the demineralization solution was adjusted to 3.8, and the process continued for four more days.

At the conclusion of the treatment, the nail varnish was removed and all teeth were re-imaged under 100x magnification using the digital light microscope (Keyence VHX-600 series, Woodcliff Lake, NJ). The initial and final images were placed side by side, lines were drawn perpendicular to the white spot lesion, and the depth of the white spot lesion was measured at the point of greatest change. The difference between the final depth and the initial depth was calculated to determine the amount of demineralization or remineralization that occurred.

**Statistical Analysis**

Unadjusted means and standard deviations were calculated for the initial and final demineralization depths and the change in demineralization depth. A Mixed model Analysis of Variance (ANOVA) was used to compare the initial and final demineralization depths of the white spot lesion. It was also used to compare the change in demineralization depth between the four treatment groups, as well as between each treatment group and its control. Statistical significance was determined at p<0.05. All analysis was performed using SAS version 9.2 (Cary, NC).
RESULTS

Two teeth were excluded due to chipping of the nail polish from the cut surface: one tooth in the MI Paste Plus group and one tooth in the sodium fluoride group. The results for these two groups are based on nine teeth, while the other two groups are based on the original ten teeth.

The mean initial and final depths of the white spot lesions for the treated halves are listed in Table 2. There was no statistical difference between the initial and final depth for the Icon group, the Icon and MI Paste Plus group, and the MI Paste plus group. However, the initial lesion depth was statistically less than the final lesion depth for the sodium fluoride group (p =0.0003).

Table 2

Mean lesion depths of treated halves(µm)

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Initial lesion depth</th>
<th>Final lesion depth</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1: Icon</td>
<td>825.87 (± 264.35)</td>
<td>825.19 (± 261.15)</td>
<td>0.9799</td>
</tr>
<tr>
<td>Group 2: Icon and MI Paste Plus</td>
<td>658.62 (± 352.68)</td>
<td>660.56 (± 348.98)</td>
<td>0.9427</td>
</tr>
<tr>
<td>Group 3: MI Paste Plus</td>
<td>667.35 (± 267.43)</td>
<td>679.14 (± 269.42)</td>
<td>0.6789</td>
</tr>
<tr>
<td>Group 4: 0.2% sodium fluoride</td>
<td>597.08 (± 298.13)</td>
<td>711.87 (± 305.51)</td>
<td>0.0003</td>
</tr>
</tbody>
</table>

The mean difference between the initial and final lesion depths for the treated halves and the control halves are listed in Table 3. Teeth treated with Icon had a mean decrease in white spot lesion depth of 0.68µm, while those treated with both Icon and MI
Paste Plus had a mean increase in lesion depth of 1.95 µm. MI Paste Plus and fluoride treated teeth had increases in lesion depth of 11.83µm and 114.79µm, respectively.

Table 3

Mean increase in lesion depths (µm)

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Treated half</th>
<th>Control half</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1: Icon</td>
<td>-0.68 ( ± 31.17)</td>
<td>81.50 ( ± 94.04)</td>
</tr>
<tr>
<td>Group 2: Icon and MI Paste Plus</td>
<td>1.95 ( ± 32.59)</td>
<td>64.90 ( ± 67.62)</td>
</tr>
<tr>
<td>Group 3: MI Paste Plus</td>
<td>11.83 ( ± 19.16)</td>
<td>39.07 ( ± 33.56)</td>
</tr>
<tr>
<td>Group: 0.2% sodium fluoride</td>
<td>114.79 ( ± 167.55)</td>
<td>116.01 ( ± 179.70)</td>
</tr>
</tbody>
</table>

Teeth treated with Icon, Icon and MI Paste Plus, and MI Paste Plus had statistically less progression of the white spot lesion than teeth treated with fluoride (p=0.0136, 0.0157, and 0.0302, respectively). However, there was no statistical difference of the increase in lesion depth between the first three treatment groups.

In the Icon group and Icon and MI Paste Plus group, treated halves had statistically less progression of the white spot lesion than control halves (p =0.0115 and 0.0486, respectively). There were no statistically significant differences between the progression of the lesion in treated halves and control halves of the MI Paste Plus and fluoride groups.
DISCUSSION

Every orthodontic patient hopes to have a beautiful smile the day the braces are removed. Even if the teeth are perfectly aligned and the occlusion is ideal, the patient may be disappointed with the results if there are white spot lesions on his or her teeth. Once these lesions form, restoring the teeth to a normal appearance through remineralization is very difficult. Most methods of treating white spot lesions depend on patient compliance and work slowly over time, if at all.

A caries infiltrant resin, Icon, offers a unique approach to treating white spot lesions that does not depend on patient compliance and can be completed in one office visit to restore the natural appearance of the teeth. Icon penetrates the white spot lesion and seals it in order to prevent the lesion from progressing to cavitation. Previous studies have shown that Icon is able to halt the demineralization process when used to treat white spot lesions. However, no published studies have reported results that compare the effectiveness of Icon to other commercially available products used to treat white spot lesions. The aim of this study was to compare the progression of lesion depth of teeth treated with Icon, Icon and MI Paste Plus, MI Paste Plus, and fluoride mouthrinse.

In the present study, teeth treated with Icon and Icon and MI Paste Plus had a mean increase of white spot lesion depth of \(-0.68 \pm 31.17\mu m\) and \(1.95 \pm 32.59\mu m\), respectively. Furthermore, the initial lesion depths were not significantly different from the final lesion depths in these two groups. Both results indicate that Icon was able to halt progression of the white spot lesions. These results are similar to those reported by
Paris in 2006, who determined that infiltration with a fissure sealant and several adhesives inhibited further demineralization, and Meyer Lueckel in 2008, who reported that lesion progression of infiltrated lesions was reduced compared to untreated controls. Although the lesions in teeth treated with Icon and MI Paste Plus did not progress, these teeth did not have any less demineralization or any more remineralization than those treated with Icon alone. Therefore, using MI Paste Plus on white spot lesions that have been treated with Icon does not confer any additional benefit.

In this study, MI Paste Plus treated teeth had a mean lesion progression of 11.83 ± 19.16µm, which was less than the progression of its control teeth but not statistically less. Therefore, the effect of MI Paste Plus on stopping demineralization of white spot lesions is inconclusive. Reynolds previously reported that in an in vitro study on human teeth with artificially created white spot lesions, CPP complexes remineralized the lesions at a rate of $3.9 \pm 0.8 \times 10^{-8}$ mol hydroxyapatite/m²/s, which was faster than a control group. This study differed from ours in that its conditions were set for remineralization using a potassium phosphate buffer with a pH of 7.0, while the present study used demineralization conditions. Andersson performed an in vivo study and reported that CPP-ACP was capable of remineralizing 63% of the white spot lesions that formed during orthodontic treatment. His study was based on the demineralization-remineralization cycle that occurs intraorally. It has been suggested that MI Paste Plus performs better when allowed to interact with human saliva, which may explain why more remineralization occurred in the Andersson study than the present study.

Previous studies have shown that fluoride is ideal for preventing white spot lesions and is also useful for treating them. Øgaard reported that daily rinsing with
0.2% neutral sodium fluoride mouthrinse retarded lesion progression significantly in a clinical study using teeth with white spot lesions that were scheduled for extraction. He also noted that surface softened lesions remineralize quicker and more completely than subsurface lesions, where remineralize often only occurs in the surface layer. In this study, the depth of the lesions treated with fluoride increased by an average of 114.79 ± 167.55µm, while the control teeth for this group had mean lesion progression of 116.01 ± 179.70µm. The results are not statistically different and suggest that fluoride mouthrinse did not prevent demineralization from progressing, as did previous studies. One possible explanation is the difference in the contents of the solutions where the teeth are immersed. Human saliva contains calcium and phosphate ions that react with fluoride ions to form fluorapatite in order to remineralize the enamel. On the other hand, the artificial caries solution used in this study contained phosphate but no calcium. As the enamel demineralized, calcium and phosphate ions were released from the tooth structure and into the solution, which was replaced frequently. The teeth treated with fluoride were not able to remineralize since calcium was limited.

The critical pH where demineralization below is about 5.5 in most patients and may be even higher in children.\textsuperscript{65} In the mouth, the pH decreases when the individual eats or drinks and then rises again as neutralization takes place through salivary flow. There is a continuous cycle of demineralization and remineralization taking place throughout the day and night. These intraoral conditions are very different from the conditions set forth in this study, which were constantly below the critical pH and only promoted demineralization. One should expect that demineralization would not occur as rapidly in a patient with normal salivary flow and a healthy diet as it did in this study. An
in situ or an in vivo testing protocol would more accurately demonstrate the amount of demineralization that would occur for a patient.
CONCLUSIONS

Under the conditions of the present study, the following conclusions are made:

1. Icon infiltrant resin halted progression of white spot lesions when subjected to demineralizing conditions.

2. Icon infiltrant resin prevented progression of demineralization better than fluoride mouthrinse.

3. MI Paste Plus did not reduce demineralization or increase remineralization when used in conjunction with Icon.

4. The results of MI Paste Plus alone are inconclusive.

5. Fluoride mouthrinse did not prevent progression of demineralization.
REFERENCES


APPENDIX A

INSTITUTIONAL REVIEW BOARD FOR HUMAN USE APPROVAL FORM

DATE: 9/7/94

MEMORANDUM

TO: J. Nathan Bergdoll

Research Investigator

FROM: Susan Moore

Director, LAB/DSP

RE: Request for Determination Human Subjects Research

IRB Proposal No. 89-0101: Uses Cyclosporine, Bismuth, Resin and MT Protease for Treatment of White Spot Lesions

An IRB Member has reviewed your application for the Investigation of Not Human Subjects Research for a change in research proposal.

The reviewer has determined that the proposal is not subject to FDA regulations and is not Human Subjects Research. Note that any changes to the project should be resubmitted to the Office of the IRB for determination.

Signature