Minimally invasive resin infiltration of white spot lesions: a clinical trial

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A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Science in Orthodontics

Oregon Health & Science University
Portland, Oregon

December 2012

Minimally invasive resin infiltration of white spot lesions: a clinical trial

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Acknowledgements

Thank you to all my committee members.

Thank you to Alex Vo, D.M.D. and Rachel Yamakawa, D.D.S. for all their hard work.

Thank you to Mansen Wang, Ph.D, M.S. for statistical analysis.

Thank you to my wife Brandy and my boys, Sjoren, Tobyn, and Josiah for all their love and support.

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Keywords: Resin Infiltration, White Spot Lesion, Demineralization, Minimally Invasive

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ABSTRACT

Background: The purpose of this randomized single-blind clinical trial was to assess the aesthetic improvement and changes in area of white spot lesions (WSL) restored with resin infiltration.

Materials & Methods: A total of 20 patients with WSL that formed during orthodontic treatment on maxillary anterior teeth were selected from the Oregon Health & Science University orthodontic clinic. Among teeth with a WSL, one tooth per patient was randomly assigned to the control group (n=20) and the remaining teeth assigned to the treatment group (n=46). Teeth in the treatment group were restored using a resin infiltration technique (ICON® Etch; DMG America, Englewood, NJ). Photographic images of the teeth were made at the start of the treatment appointment (T1), at the end of the appointment (T2), and 8 weeks later (T3). Orthodontists evaluated the photographs for WSL changes T1 to T2 and T1 to T3 using a visual analog scale (VAS; 0 = no change; 100 = complete disappearance). WSL area was also measured at each time point using morphometric software. VAS and area measurement data were analyzed using ANOVA.

Results: The mean VAS ratings for teeth treated with resin infiltration showed highly significant improvement relative to control teeth at T2 (67.7 vs. 5.2; $p<0.001$) and T3 (65.9 vs. 9.2; $p<0.001$). The mean percent reduction in area for WSL treated with resin infiltration was 61.8% at T2 and 60.9% at T3, highly significant reductions compared to control teeth (-3.3%; $p<0.001$).

Conclusions: Resin infiltration significantly improves the clinical appearance and reduces the size of the WSL.

Clinical Implications: Resin infiltration is an effective and minimally invasive treatment for WSL.

Key Words: Resin Infiltration, White Spot Lesion, Demineralization, Minimally Invasive

INTRODUCTION

Enamel white spot lesions (WSL), an outcome of enamel demineralization, are common sequela of poor oral hygiene. The presence of fixed orthodontic appliances makes oral hygiene more difficult increasing susceptibility to WSL formation. [1,2] Reported prevalence of WSL in orthodontic patients ranges from 4.9% [3] to 97% [4], with a recent study showing 72.9% of patients developing a new WSL during treatment. [5] Subsurface enamel porosities associated WSL are caused by a cyclical imbalance between demineralization and remineralization resulting from an acidic environment created by cariogenic bacteria. [6] With time, remineralization at the outer surface of the lesion decreases access of ions to deeper portions of the lesion resulting in an arrest of the remineralization process. [2,7,8] The lesion's opaque white appearance is due to scattering of light at the subsurface demineralized enamel. [6,9] WSL may naturally regress due to salivary remineralization and toothbrush abrasion, however complete regression does not occur for most lesions. [10,11] Regression following orthodontic appliance removal predominantly occurs in the first three months and lesions present after this time are likely to remain. [12]

Treatment options for WSL range from topical remineralization therapy to restoring the lesions. Improvements from remineralization therapy using casein phosphopeptide amorphous calcium phosphate (CPP-ACP), [13] low concentration fluoride, [14] or a combination , [15] are small and often clinically insignificant. [16] Bleaching results in limited aesthetic improvement and has been associated with tooth sensitivity and a reduction in microhardness of enamel. [17-19] In general, complete remineralization of WSL typically does not occur using topical applications of various products. [20]

Other treatment options for WSL include microabrasion and restoration. While microabrasion can remove WSL, the technique has the potential to remove large amounts of enamel. [16,21] Traditional composite restorations, veneers, and crowns require removal of enamel beyond the demineralized zone and into dentin. [22] Because orthodontic WSL predominantly affect a young patient population, the long-term prognosis of the restored teeth is a significant concern. Considering the invasiveness of microabrasion or traditional restorations compared to the relatively small amount of demineralized enamel in WSL, a less invasive restorative technique would be more ideal.

Resin infiltration is a minimally-invasive restorative treatment option involving penetration of a resin into the body of the WSL with minimal removal of enamel. [23] With this method, the outer layer of sound remineralized enamel is removed with an acid etchant exposing the demineralized lesion body, and the lesion is subsequently filled with a low viscosity resin. [23] *In vitro* studies have shown significant masking of white spot lesions using resin infiltration techniques. [24-26] Initial *in vivo* case reports have been promising, showing immediate significant improvement of WSL. [27,28] Although resin infiltration has been used for restoration of interproximal incipient caries, there are currently no randomized clinical trials evaluating resin infiltration of WSL.

The purpose of this randomized single-blind clinical trial was to assess the aesthetic improvement and changes in area of WSL restored with resin infiltration. Patients that developed WSL during orthodontic treatment were treated with a commercially available resin infiltration system. Photographic images were made of WSL before (T1), immediately after treatment (T2) and eight weeks later (T3). The photographic images were rated by orthodontists for changes in WSL appearance and were used to measure changes in WSL area. Our hypothesis was that WSL restored with resin infiltration would have improved appearance and reduced area compared to untreated WSL.

METHODS & MATERIALS

Sample

Approval for this study was obtained from the Oregon Health & Science University (OHSU) Institutional Review Board. Power analysis, based on changes in WSL restored with resin infiltration as reported in a previous study,[28] showed a minimum sample size of 20 patients to show significance at a power of 80%. Patient allocation followed CONSORT guidelines (Fig. 1).[29] Twenty-three patients were selected from the OHSU orthodontic clinic, with three patients subsequently lost to attrition, resulting in a final sample of 20.

Initial screening for inclusion was based on WSL observed in intraoral photographs obtained immediately after removal of braces. Additional inclusion criteria included: white spots visible on at least two maxillary anterior teeth, absence of any pre-existing (before orthodontic treatment) white spots, patient age range from 12-30 years, no previous treatment of WSL, at least 3 months time elapsed since removal of appliances, International Caries Detection and Assessment Score (ICDAS)[30] code of 2-3 (enamel opacity with smooth enamel surface or some enamel roughness, respectively), and absence of caries. At a clinical examination, the presence of WSL was confirmed using the ICDAS and the presence of staining was recorded. Other information collected from the patient's chart included: gender, age, time in braces, and time elapsed since braces removal. For the 20 patients who completed the study, a total of 66 teeth met the inclusion criteria. Among the qualified teeth, each patient had one randomly selected to serve as a control (no treatment; n=20) and the remainder were assigned to the treatment group (n=46). Due to reports of variable treatment responses,[27,28] allocation of teeth was biased toward the treatment group to maximize the number of teeth treated.

Resin Infiltration

Resin infiltration protocol was slightly modified from manufacturer's (ICON®; DMG America, Englewood, NJ) instructions. Patients wore protective glasses and a dry field isolation system (NOLA™, Great Lakes Orthodontics, Tonawanda, NY) was placed. Teeth in both groups were cleaned with a rubber cup and plain pumice (Miltex, York, PA), rinsed for 30 seconds, air dried for 30 seconds, and photographs were made (T1).

WSL on teeth in the treatment group were abraded with a fine grit polishing disc (EP system; Brasseler, Savannah, GA). A 15% hydrochloric acid gel (ICON® Etch; DMG America) was placed on the WSL for 2 minutes. The etching gel was rinsed for 30 seconds and then air dried for 30 seconds. The etch, rinse, and dry steps were repeated, after which the lesions were desiccated using ethanol (ICON® Dry; DMG America) and air dried for 30 seconds. The resin infiltrant (ICON® Infiltrant; DMG America) was applied to the surface and allowed to penetrate the lesion for 3 minutes. Excess material was wiped away from the surface using a cotton roll, and then light curing (1600 mW/cm^2) was applied for 40 seconds. The resin infiltrant was re-applied for 1 minute, excess was removed and the material was again light cured for 40 seconds. Excess resin in the proximal spaces was removed using dental floss. The facial surface was polished using a polishing cup (Enhance®, Dentsply, York, PA). The teeth were evaluated by recording ICDAS and the presence of staining and any restoration irregularity. Photographic images were again made (T2).

Patients were given standard oral hygiene supplies (toothpaste, toothbrush, and dental floss) and instructions for homecare. After 8 weeks the patients returned, their anterior teeth were again isolated, cleaned with pumice, rinsed, air dried, evaluated and photographed (T3).

Photography and Orthodontist Evaluation of WSL

Standardized photographic images of each tooth were made at the three time points using a digital camera (Nikon D60, Nikon, Tokyo, Japan) with a macro lens (Macro Rokkor-X 100mm; Minolta, Tokyo, Japan) and a point-source flash (Maxwell 303H, Maxwell Technologies, San Diego, CA) positioned at a fixed focal distance from the subject. Tooth surfaces were dried immediately before the images were made to exclude the influence of moisture on WSL appearance. The photographic images of the teeth were cropped and placed into a series of PowerPoint™ slides. For each tooth, images were shown side by side to compare T1 to T2, or T1 to T3, with the image pairs being randomly ordered among the control and experimental teeth and time points. Raters (5 orthodontic faculty members) were calibrated through a series of 6 slides and then asked to rate aesthetic changes of the WSL for each tooth by marking a 100 mm visual analog scale (VAS), with a mark at 0 indicating no improvement and a mark at 100 representing complete disappearance of the WSL. Due to the large number of comparisons (152), raters were given one of two sequenced versions of the slides to avoid systematic bias associated with rater fatigue; each sequence included 20 repeat image pairs to assess intra-rater reliability.

WSL Area Calculation

Image file names were encoded to ensure the investigator was blinded. WSL area was measured using an image analysis program (ImageJ, NIH, Bethesda, MD). Facial surfaces of the teeth and WSL were traced from each of the three time points. A photographic image of a ruler made at the fixed focal distance was used for calibration. The area (mm^2) of each tooth and corresponding WSL was used to calculate the percent change in WSL area at T2 and T3 by comparing T1 to T2 and T1 to T3. Measurements of 20 WSL were repeated to evaluate method error.

Statistical Analysis

Orthodontists' VAS ratings were averaged for each tooth and time point, and analyzed using Repeated Measures ANOVA. Percent area change in WSL was also analyzed using Repeated Measures ANOVA. The factors of age, gender, time elapsed since appliance removal, treatment duration, tooth type, and WSL initial severity were analyzed using Repeated Measures ANOVA for effect on VAS and percent area change for treatment teeth. Inter-rater reliability for VAS method was calculated using Pearson correlation coefficients for the 5 raters. [31] Pearson correlation coefficients were also used to measure intra-rater reliability for VAS and area calculation methods. [31] Method error for area measurements was calculated using the Dahlberg formula. [32]

RESULTS

Clinical Examination

A stippled surface texture was observed at T2 and T3 on most teeth restored with resin infiltration. No other irregularities in resin infiltration restorations were observed. ICDAS and staining data were not included in the final analysis due to low number of teeth having ICDAS score of 3 (n=4) and presence of staining (n=5). All teeth in the treatment group with ICDAS 3 at T1 were ICDAS 2 at T2 and T3. All teeth in the treatment group that had staining at T1 no longer had staining at T2 and T3.

Orthodontist Evaluation of WSL

Teeth that received treatment (Fig. 2-4) had significantly higher VAS ratings (Fig. 5) than control teeth. At T2 the mean VAS rating for teeth that received treatment was 67.7 compared to 5.2 for control teeth ($P<0.001$; Fig. 5) and at T3 the mean VAS rating for teeth that received treatment was 65.9 compared to 9.2 for control teeth ($P<0.001$; Fig. 5). Within treatment and control groups there was no significant difference in VAS ratings when comparing changes at T2 to those found at T3.

The factors of age, gender, tooth type, time in appliances, time elapsed since appliance removal, and initial severity did not have a significant effect on VAS ratings in treatment teeth (Table 1). Pearson correlation coefficients were high for intra-rater reliability, ranging from $r=0.97$ to $r=0.99$ for the 5 raters. Pearson correlation coefficient for inter-rater reliability was also strong ($r=0.97$) among the 5 raters. Standard deviations for the VAS ratings were relatively high at T2 (SD=22.3) and T3 (SD=26.6) for teeth treated with resin infiltration (Figs. 5, 6).

WSL Area Calculation

Treatment teeth had a highly significant greater percent reduction of POWSL area than control teeth (Fig. 7). At T2 the mean percent reduction for teeth receiving treatment was 61.8% compared to -3.3% for control teeth ($P<0.001$; Fig. 7). Similarly, at T3 the mean percent reduction for teeth receiving treatment was 60.9% compared to 1.0% for control teeth ($P<0.001$; Fig. 7). There was no significant difference in percent reduction when comparing changes found at T2 to those at T3 within treatment and control groups. Standard deviations were relatively high at T2 (SD=23.9%) and T3 (SD=24.2%) for teeth treated with resin infiltration. Method error for area measurement was 0.47 mm^2 relative to initial WSL areas that ranged from 1.1 mm^2 to 42.9 mm^2. The factors of age, gender, tooth type, time in appliances, time elapsed since appliance removal, and initial severity did not have a significant effect on WSL percent reduction in treatment teeth (Table 1).

DISCUSSION

While resin infiltration was proposed as a restorative treatment for WSL nearly 40 years ago,[33] advances in technique and materials have resulted in a more effective approach that has been proposed as a treatment for WSL caused by demineralization.[23] Results of this study show that resin infiltration of WSL can predictably significantly improve the aesthetics of most teeth. Reduction in WSL VAS ratings and area measurements indicated a high level of WSL amelioration in treatment teeth compared to no change in control teeth. These results are similar to those found in a case series by Kim and associates where 17 out of 18 orthodontic WSL treated with resin infiltration were completely or partial masked.[28]

The resin infiltration method employed in our study used minor modifications to the manufacturer's instructions. We chose to use the NOLA™ isolation system because use of a rubber dam, as suggested by the manufacturer in order to prevent moisture contamination and protect the gingiva from the hydrochloric acid etchant, would have interfered with access to WSL near the gingival margins. We also abraded all WSL prior to etching to enhance effectiveness of the etchant. The variation in outcomes for teeth treated with resin infiltration may have been due to variations in lesion anatomy, with thickness of the superficial remineralized layer being the biggest factor.[25] The remineralized layer thickness has been found to vary considerably, with the majority of lesions having a surface layer thickness between 20 and 60μm.[34,35] It is possible that teeth in the treatment group that had better outcomes had more complete removal of this remineralized layer, while those with little WSL improvement had insufficient removal.

The WSL evaluation method was designed to give a subjective (VAS rating) and an objective (area measurement) means for measuring outcomes. Despite the availability of technology-based methods for WSL evaluation (e.g., quantitative light fluorescence), results of visual evaluation of photographs have been found to most closely match patients' perceptions of esthetic concerns.[36] The main disadvantages of orthodontists' rating WSL are bias and lack of validity,[36] however raters were blinded, reducing bias, and inclusion criteria were designed to increase validity by eliminating patients with WSL that had been treated or were present before orthodontic treatment. The investigator measuring WSL area was also blinded reducing any potential for bias. Reliability of the assessment methods employed were demonstrated by the relatively low method error ($0.47mm^2$) for the area measurements and by strong intra-rater (mean r= 0.98) and inter-rater (r=0.97) reliability for the VAS ratings.

Gender, age, time in braces, time elapsed since appliance removal, tooth type, and WSL initial severity had no statistically significant affect on outcomes for WSL restored with resin infiltration. The negative findings likely relate to the methods and in particular the selection criteria used in this study. For example, initial severity was defined as the percent of the tooth covered by WSL at T1 and did not take into account other anatomical factors such as lesion depth, a variable that could potentially influence the results.[25] Furthermore, it is known that enamel becomes less permeable with age[37,38] and that WSL surface layer thickness may increase with time elapsed since removal of appliances and subsequent improved oral hygiene.[34] Such factors could account in part for the somewhat high standard deviations found in our results, and present potential topics for future investigation. With broadened selection criteria, it may be possible to determine if age and duration of the WSL impact the results of resin infiltration restoration.

While WSL are often unaesthetic, previous studies have shown that they are stable long-term and normally do not progress to caries.[2,4] In the current study, differences in assessments of control teeth at all time points were negligible. With treated teeth, clinical examination at T2 and

T3 showed no staining, open margins, ledges, or wear with the resin infiltration restoration. While the stippled surface texture seen on close examination of the restorations could be viewed as a minor defect, we found that the texture could be easily removed at a later date with use of more aggressive polishing discs (data not shown). Studies have found that with interproximal incipient carious lesions, the defects can be predictably infiltrated,[23] caries progression rate is reduced,[25] and placement of more invasive restorations can be delayed.[39] Although in the present study the restored lesions were stable over the 8-week period, long-term outcomes of WSL resin infiltration restorations are unknown.

Results of the current study are consistent with previous reports showing that because resin infiltration is effective and relatively non-invasive, the approach holds advantages over other options for WSL treatment.[23,35,39] High concentration fluoride has been contraindicated as this approach enhances remineralization of the superficial layer of the lesion, accelerating the arrest of remineralization in the subsurface portion of the WSL.[40,41] Although micro abrasion has been shown to remove WSL, resulting in 83% to 97% reductions in area, the procedure inherently removes up to 360 µm of the demineralized enamel.[16,17,21,42] By comparison, the two rounds of etching with HCl used in our protocol have been shown to remove approximately 80 µm of enamel.[34] It has been demonstrated *in vitro* that resin infiltration can exceed a depth of 400 µm, making complete infiltration of deeper WSL possible.[43] Traditional composite restorations, veneers, and crowns require removal of enamel, and matching natural tooth shade and opacity can pose aesthetic challenges, especially in the anterior region. The resin used in this study (ICON® Infiltrant; DMG America) is unfilled and has optical properties similar to that of natural enamel, effectively transmitting the natural shade of the tooth.[44] Thus, based on current evidence, resin infiltration may be the treatment of choice for WSL that fail to regress naturally.

CONCLUSIONS

1. Resin infiltration significantly improves the clinical appearance and reduces the size of WSL.

2. The clinical appearance of WSL restored with resin infiltration is stable for at least 8 weeks.

REFRENCES

1. Geiger AM, Gorelick L, Gwinnett AJ, Benson BJ. Reducing white spot lesions in orthodontic populations with fluoride rinsing. *Am J Orthod Dentofacial Orthop.* 1992;101:403-407.

2. Øgaard B, Rølla G, Arends J, Ten Cate J. Orthodontic appliances and enamel demineralization part 2. prevention and treatment of lesions. *Am J Orthod Dentofacial Orthop.* 1988;94:123-128.

3. Boersma J, Van der Veen M, Lagerweij M, Bokhout B, Prahl-Andersen B. Caries prevalence measured with QLF after treatment with fixed orthodontic appliances: Influencing factors. *Caries Res.* 2005;39:41-47.

4. Gorelick L, Geiger AM, Gwinnett AJ. Incidence of white spot formation after bonding and banding. *Am J Orthod Dentofacial Orthop.* 1982;81:93-98.

5. Richter AE, Arruda AO, Peters MC, Sohn W. Incidence of caries lesions among patients treated with comprehensive orthodontics. *Am J Orthod Dentofacial Orthop.* 2011;139:657-664.

6. Chang H, Walsh L, Freer T. Enamel demineralization during orthodontic treatment. aetiology and prevention. *Aust Dent J.* 1997;42(5):322-327.

7. García-Godoy F, Hicks MJ. Maintaining the integrity of the enamel surface the role of dental biofilm, saliva and preventive agents in enamel demineralization and remineralization. *J Am Dent Assoc.* 2008;13:25S-34S.

8. Øgaard B. White spot lesions during orthodontic treatment: Mechanisms and fluoride preventive aspects. *Semin Orthod.* 2008;14:183-193.

9. Benson P, Shah A, Millett D, Dyer F, Parkin N, Vine R. Fluorides, orthodontics and demineralization: A systematic review. *J Orthod.* 2005;32:102-114.

10. Årtun J, Brobakken BO. Prevalence of carious white spots after orthodontic treatment with multibonded appliances. *Eur J Orthod.* 1986;8:229-234.

11. Øgaard B. Prevalence of white spot lesions in 19-near-olds: A study on untreated and orthodontically treated persons 5 years after treatment. *Am J Orthod Dentofacial Orthop.* 1989;96:423-427.

12. Al-Khateeb S, Forsberg CM, de Josselin de Jong, E., Angmar-Månsson B. A longitudinal laser fluorescence study of white spot lesions in orthodontic patients. *Am J Orthod Dentofacial Orthop*. 1998;113:595-602.

13. Bailey D, Adams G, Tsao C, et al. Regression of post-orthodontic lesions by a remineralizing cream. *J Dent Res*. 2009;88:1148-1153.

14. Bishara SE, Ostby AW. White spot lesions: Formation, prevention, and treatment. *Semin Orthod.* 2008;14:174-182.

15. Beerens M, Van Der Veen M, Van Beek H, Ten Cate J. Effects of casein phosphopeptide amorphous calcium fluoride phosphate paste on white spot lesions and dental plaque after orthodontic treatment: A 3□month follow□up. *Eur J Oral Sci*. 2010;118:610-617.

16. Akin M, Basciftci FA. Can white spot lesions be treated effectively? *Angle Orthod.* 2012; 82:770-775

17. Basting RT, Rodrigues AL, Serra MC. The effects of seven carbamide peroxide bleaching agents on enamel microhardness over time. *J Am Dent Assoc*. 2003;134:1335-1343.

18. Haywood VB, Leonard RH, Nelson CF, Brunson WD. Effectiveness, side effects and long-term status of nightguard vital bleaching. *J Am Dent Assoc*. 1994;125:1219-1226.

19. Knösel M, Attin R, Becker K, Attin T. External bleaching effect on the color and luminosity of inactive white-spot lesions after fixed orthodontic appliances. *Angle Orthod.* 2007;77:646-652.

20. Reynolds E. Remineralization of enamel subsurface lesions by casein phosphopeptide-stabilized calcium phosphate solutions. *J Dent Res*. 1997;76:1587-1595.

21. Murphy TC, Willmot DR, Rodd HD. Management of postorthodontic demineralized white lesions with microabrasion: A quantitative assessment. *Am J Orthod Dentofacial Orthop*. 2007;131(1):27-33.

22. Summitt JB, Robbins JW, Schwartz RS, dos Santos J. *Fundamentals of operative dentistry: A contemporary approach.* Quintessence Pub. 2006.

23. Kielbassa AM, Muller J, Gernhardt CR. Closing the gap between oral hygiene and minimally invasive dentistry: A review on the resin infiltration technique of incipient (proximal) enamel lesions. *Quintessence Int*. 2009;40:663-681.

24. Paris S, Meyer-Lueckel H. Masking of labial enamel white spot lesions by resin infiltration--a clinical report. *Quintessence Int*. 2009;40:713-718.

25. Gray G, Shellis P. Infiltration of resin into white spot caries-like lesions of enamel: An in vitro study. *Eur J Prosthodont Restor Dent*. 2002;10:27-32.

26. Torres CRG, Borges AB, Torres LMS, Gomes IS, de Oliveira RS. Effect of caries infiltration technique and fluoride therapy on the colour masking of white spot lesions. *J Dent*. 2011;39:202-207.

27. Neuhaus KW, Graf M, Lussi A, Katsaros C. Late infiltration of post-orthodontic white spot lesions. *J Orofac Orthop.* 2010;71:442-447.

28. Kim S, Kim Euny, Jeong Taes, Kim JW. The evaluation of resin infiltration for masking labial enamel white spot lesions. *Int J Paediatr Dent*. 2011;21:241-248.

29. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: Updated guidelines for reporting parallel group randomized trials. *Open Med*. 2010;4:e60.

30. Ormond C, Douglas G, Pitts N. The use of the international caries detection and assessment system (ICDAS) in a national health service general dental practice as part of an oral health assessment. *Prim Dent Care*. 2010;17(4):153-160.

31. Rodgers JL, Nicewander WA. Thirteen ways to look at the correlation coefficient. *Am Stat.* 1988;42:59-66.

32. Harris EF, Smith RN. Accounting for measurement error: A critical but often overlooked process. *Arch Oral Biol.* 2009;54:S107-S117.

33. Dayila JM, Buonocore MG, Greeley CB, Provenza DV. Adhesive penetration in human artificial and natural white spots. *J Dent Res*. 1975;54:999-1008.

34. Meyer-Lueckel H, Paris S, Kielbassa A. Surface layer erosion of natural caries lesions with phosphoric and hydrochloric acid gels in preparation for resin infiltration. *Caries Res*. 2007;41:223-230.

35. Meyer-Lueckel H, Paris S. Improved resin infiltration of natural caries lesions. *J Dent Res*. 2008;87:1112-1116.

36. Benson P. Evaluation of white spot lesions on teeth with orthodontic brackets. *Semin Orthod.* 2008;14:200-208.

37. Kotsanos N, Darling A. Influence of posteruptive age of enamel on its susceptibility to artificial caries. *Caries Res*. 1991;25:241-250.

38. Park S, Wang DH, Zhang D, Romberg E, Arola D. Mechanical properties of human enamel as a function of age and location in the tooth. *J Mater Sci Mater Med.* 2008;19:2317-2324.

39. Paris S, Meyer-Lueckel H. Infiltrants inhibit progression of natural caries lesions in vitro. *J Dent Res*. 2010;89:1276-1280.

40. Willmot D. White lesions after orthodontic treatment: Does low fluoride make a difference? *J Orthod.* 2004;31:235-242.

41. Ogaard B. The cariostatic mechanism of fluoride. *Compend Contin Educ Dent.* 1999;20:10-17.

42. Tong L, Pang M, Mok N, King N, Wei S. The effects of etching, micro-abrasion, and bleaching on surface enamel. *J Dent Res.* 1993;72:67-71.

43. Paris S, Meyer-Lueckel H, Kielbassa AM. Resin infiltration of natural caries lesions. *J Dent Res.* 2007;86:662-666.

44. Paris S, Meyer-Lueckel H. Masking of labial enamel white spot lesions by resin infiltration--a clinical report. *Quintessence Int.* 2009;40:713-718.

Figure Legends

Figure 1: CONSORT Flow Diagram

Figure 2: Example of an above average response to resin infiltration. T1 left image, T3 right image, Mean VAS: 89, Percent reduction: 81%

Figure 3: Example of an average response to resin infiltration. T1 left image, T3 right image, Mean VAS: 70, Percent reduction: 58%

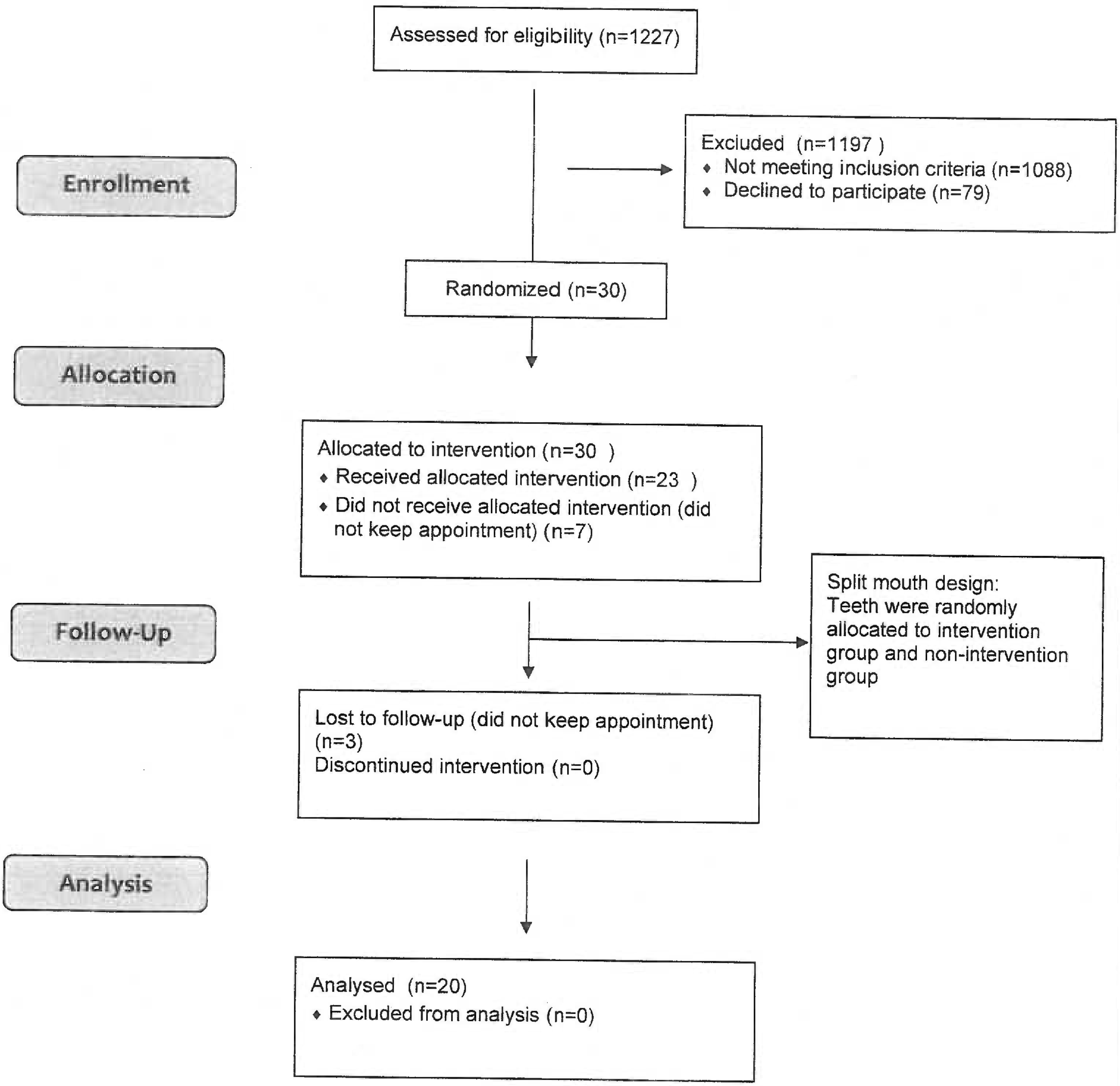
Figure 4: Example of a below average response to resin infiltration. T1 left image, T3 right image, Mean VAS: 19, Percent reduction: 23%

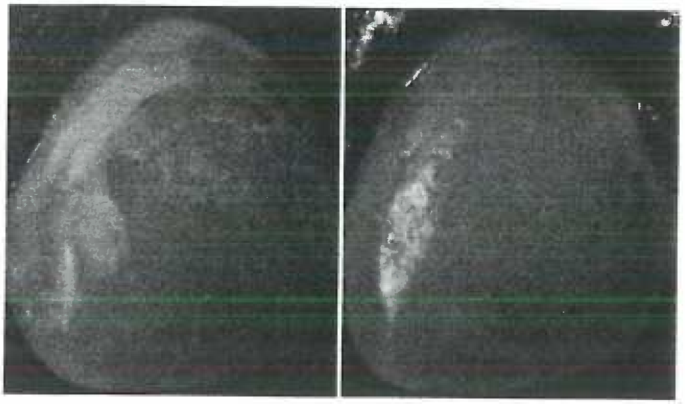
Figure 5: VAS results (means and standard deviations) by group and time: Treatment teeth showed statistically higher VAS ratings than control teeth at T2 and T3 (both $p<0.001$). Within control teeth group and within treatment teeth group there was no statistical difference in VAS ratings between T2 and T3.

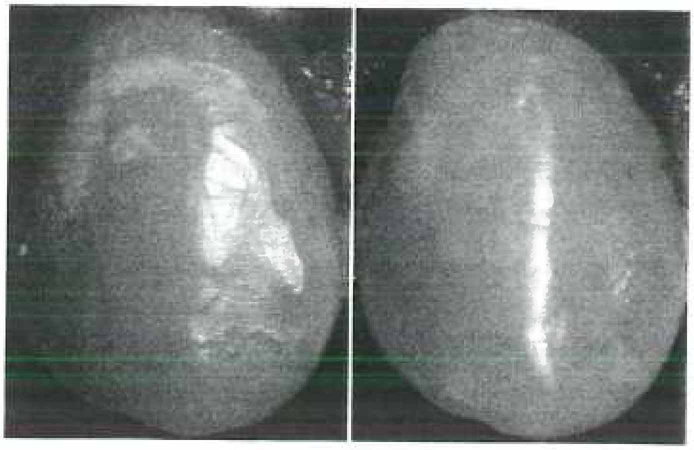
Figure 6: Mean VAS results T1 to T3 for each treated tooth, by patient. Note that with some patients treatment results were relatively consistent among teeth, whereas with other patients there was variability.

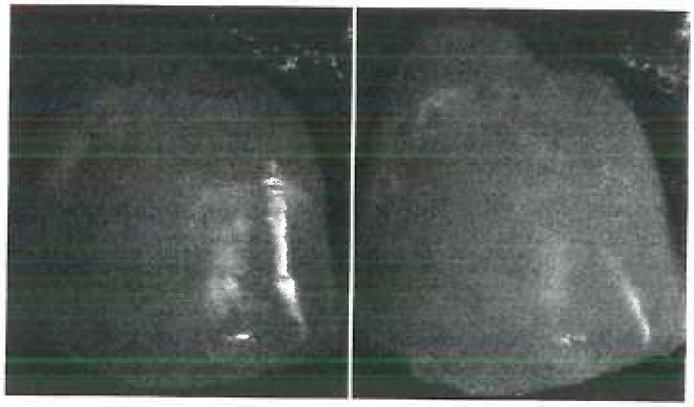
Figure 7: Percent change in area of WSL T1 to T2 (**T2**), and T1 to T3 (**T3**). Treatment teeth showed a high percent reduction compared to control teeth at T2 and T3 (both $p<0.001$). Comparisons within control and treatment teeth groups showed no differences between T2 and T3 measurements.

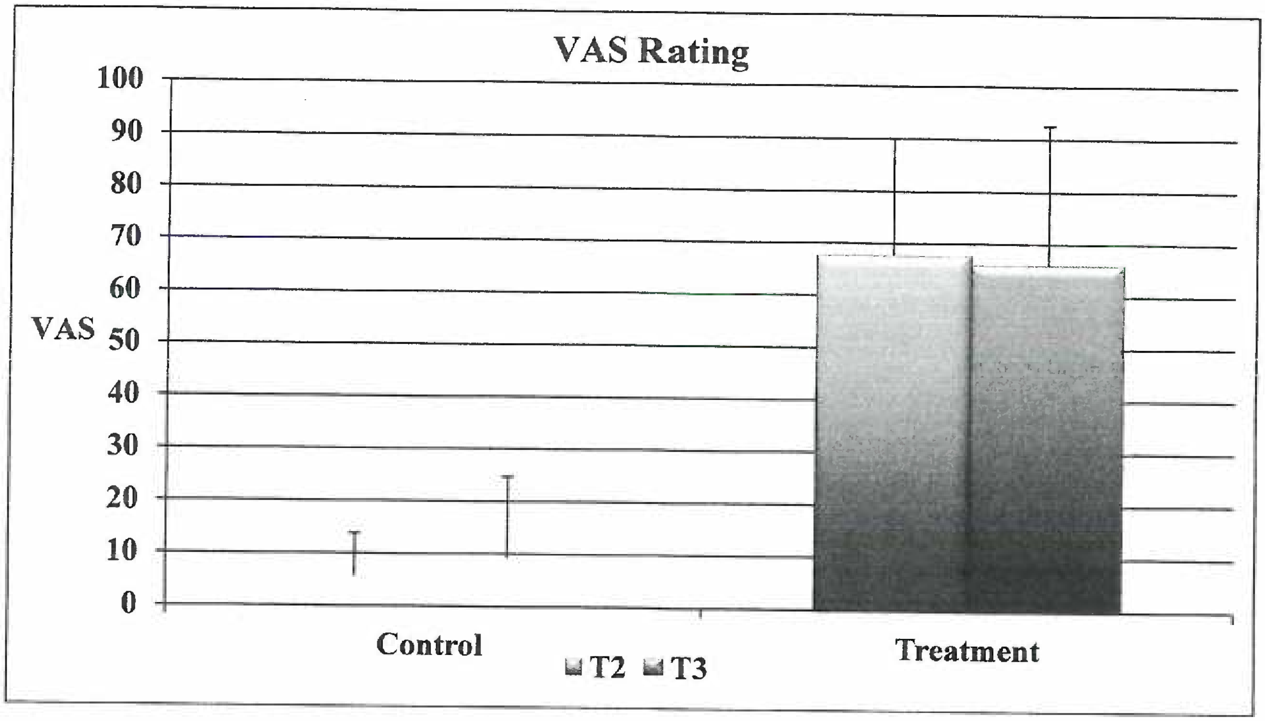
CONSORT 2012 Flow Diagram

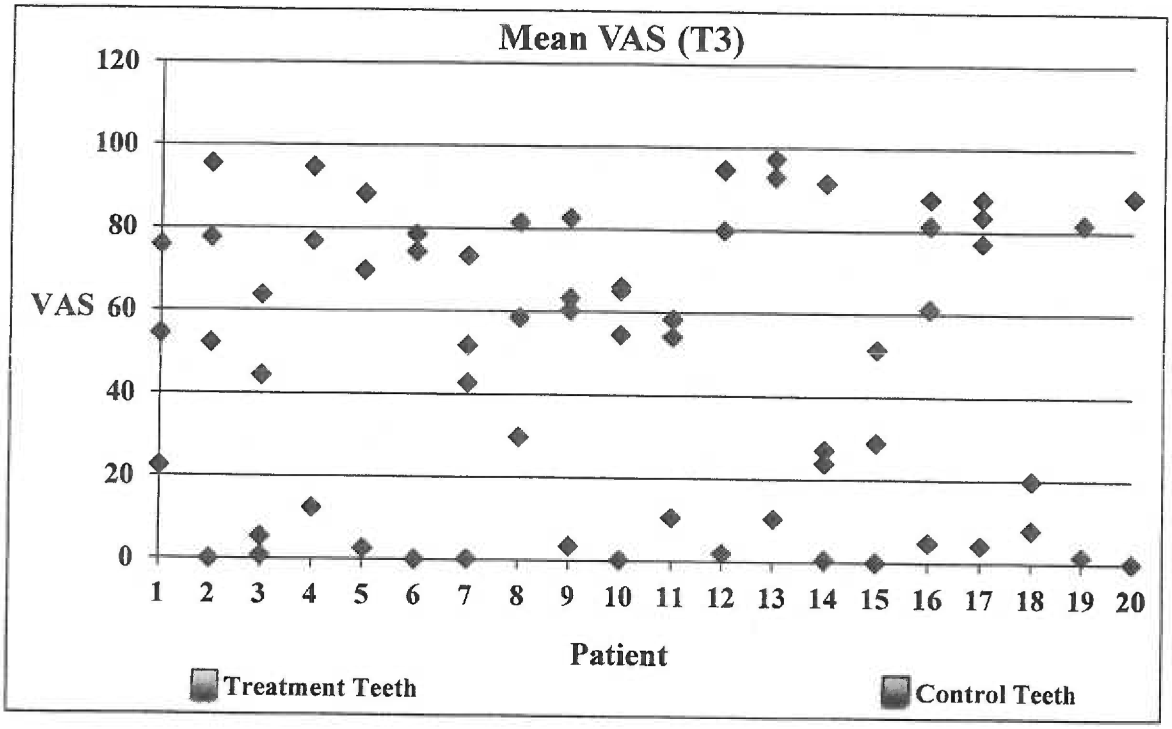









VAS Rating
100
90
80
70
60
VAS 50
40
30
20
10
0
Control
Treatment
T2
T3


Mean VAS (T3)
120
100
80
VAS 60
40
20
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Patient
Treatment Teeth
Control Teeth

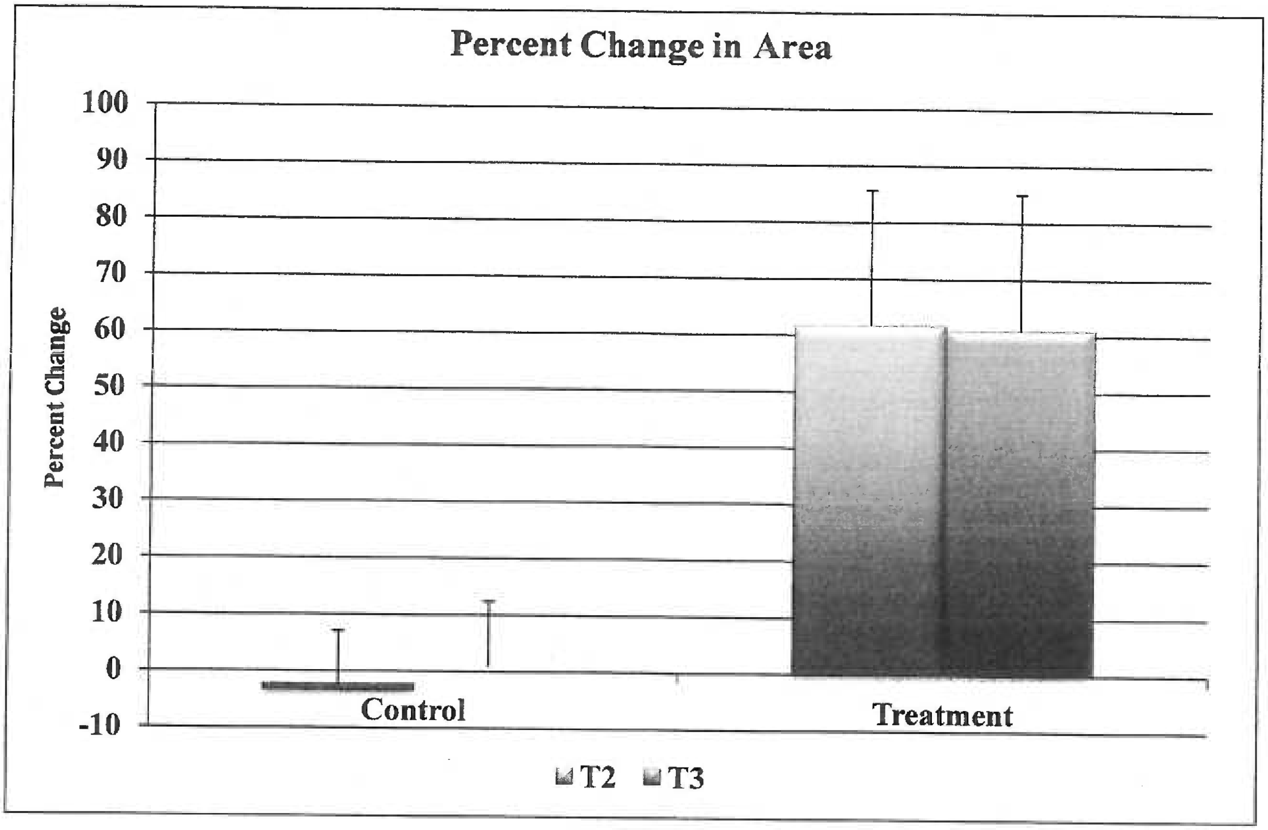

Percent Change in Area
Percent Change
100
90
80
70
60
50
40
30
20
10
0
-10
Control
Treatment
T2
T3

Table 1: Factors for VAS ratings and percent reduction in treatment teeth (T1-T2 only)

Factor	N	Mean	SD	Min	Max	P Value (VAS)	P Value (%reduction)
Age (years)	20	16.6	1.8	14	21	0.1936	0.3913
Gender	20	NA	NA	NA	NA	0.9055	0.4220
Time in Braces (months)	20	32.5	8.4	21	48	0.6386	0.5918
Time elapsed since removal (months)	20	12.3	11.1	3	48	0.1769	0.2562
Tooth type	46	NA	NA	NA	NA	0.1548	0.3055
Severity (% of tooth w/ WSL at T1)	46	25.0	16.16	1.6	79.1	0.2815	0.7124

LITERATURE REVIEW

SPECIFIC AIMS

Enamel demineralization is a common iatrogenic effect associated with orthodontic fixed appliance therapy (Goerlick 81, Ogaard 89, Ogaard 04). The esthetic goals of orthodontic treatment are directly compromised by white spot lesions (WSL), this can be extremely frustrating for both the clinician and the patient. It can be difficult if not impossible to completely remineralize WSL(Ogaard08). Furthermore, in a small percentage of orthodontic patients demineralization can progress to the point of frank cavitation requiring restoration (Goerlick82), resulting in a negative change in long term prognosis of these teeth.

Reported prevalence of WSL in orthodontic patients ranges considerably from 4.9% (Goerlick 82) to 97% (Boersma 05) depending on preventative measures, assessment methods, and variability of criteria utilized by investigators (Benham 09). Despite advances in other areas of orthodontics WSL's continue to be prevalent among post-orthodontic patients. A recent study by Richter *et al* showed 72.9% of post-orthodontic patients developed a new WSL during treatment while 2.3% had cavitated lesions. Richter asserted that " this widespread problem is alarming and warrants significant attention from both patients and providers"(Richter 11).

Considerable variation in effectiveness of preventative measures is evident in the literature. Despite the general agreement that fluoride can improve remineralization of early WSL there is little consensus on effectiveness, method of delivery, or dose (Benson 05). Benson concluded that there is a definite need for more high quality trials concerning WSL prevention protocols. The lack of effective prevention of WSL is multi-factorial and extremely complex involving prevention protocols, clinical factors, clinician factors, patient factors and their respective interactions.

Patients have multiple options for post-orthodontic WSL (PO WSL) treatment after fixed appliance removal ranging from reliance on natural remineralization to restoration. Unfortunately, salivary remineralization is highly variable ranging from continued demineralization resulting in cavitation (Mitchell 92)to complete regression of the WSL(Ogaard89). For the majority of patients complete remineralization of WSL does not occur (Dirks 66, Ogaard 89) Various remineralization products, primarily fluoride, casein phosphopeptide amorphous calcium phosphate (CPP-ACP), and a combination CPP-ACP and fluoride , have shown contradictory results in the remineralization treatment of PO WSL (Reynolds 97,03,08, Pulido 08, Ogaard 01, Steckson-Blicks07, Andersson 07) Some recent studies provide in vitro evidence that CPP-ACP with fluoride shows increased remineralization compared to CPP-ACP or fluoride alone (Reynolds 08,Kumar 08, Cochrane 08).

Restorative options for treatment of WSL include acid micro-abrasion, composite restoration, veneers, and full coverage crowns. Recently resin infiltration has been proposed as a treatment for post-orthodontic WSL. Resin infiltration is a micro-invasive procedure involving penetration of a resin composite into the body of the WSL with minimal removal of existing enamel (Kielbasa 09). In vitro studies have shown masking of WSL using resin infiltration techniques (Paris 09, Gray02, Torres11) Initial in vivo results have been promising, showing immediate and in some cases dramatic improvement of post-orthodontic WSL (Neuhaus 10,Kim 11) The results from a clinical trial by Kim *et al* showed complete masking of post-orthodontic WSL in 61% of patients while 33% had partial masking (Kim 11) Although resin infiltration has been utilized for restoration of interproximal incipient caries for some time, there is a lack of research regarding resin infiltration of post-orthodontic WSL .

To my knowledge there have not been any *in vivo* clinical trials evaluating the efficacy of resin infiltration. We propose a randomized clinical trial at the Oregon Health & and Science University Department of Orthodontics evaluating the effectiveness of resin infiltration (Icon™ Resin Infiltration System) in the treatment of post-orthodontic WSL. A split mouth study design will be used with each patient having one tooth with a WSL selected as a control (no treatment) and the remaining teeth with WSL being treated with resin infiltration.

Specific Aim: Our objective is to compare outcomes between the treatment group and control group.

This trial will provide evidence for the effectiveness of a promising treatment modality for post-orthodontic WSL. This will contribute to the development of evidence based best practices for treatment of WSL in orthodontic patients.

WHITE SPOT LESIONS

White spot lesions are defined as subsurface enamel porosities caused by an imbalance between demineralization and remineralization (Beerens 10) The opaque white appearance is due to subsurface demineralization and subsequent optical changes within the body of the lesion (Chang 97, Benson 08) Light that would normally pass through intact enamel is scattered at the demineralized area resulting in a white appearance (Benson 08) The surface of the WSL may be chalky or have surface erosion that may be able to be detected tactilely (Chang 97) This characteristic along with distribution pattern, shape, stability over time, and association with fixed appliances facilitate discernment between developmental opacities and WSL (Chang 97) As stated by Lovrov et al, despite improvements in materials and preventative efforts, orthodontic treatment continues to carry considerable risk of enamel demineralization (Lovrov 07).

WHITE SPOT LESION ETIOLOGY

Demineralization associated with orthodontic treatment is essentially a bacterial disease very similar to interproximal smooth surface caries (Chang97) By bonding fixed appliances on the facial surfaces of teeth we create a niche not unlike that found interproximally. This niche is more difficult to mechanically clean, increases surface area (habitat), and provides an area where carbohydrates can be retained. This provides a favorable environment for mutans streptococci and lactobacilli, a group of species significantly associated with caries prevalence and caries increment (Emilson 85, Bjarnason 93, Chang 97) Studies have shown an increase in proliferation of the mutans streptococci and lactobacilli species in patients with fixed orthodontic appliances (Lundstrom 87, Rosenbloom 91) These species are both acidogenic and aciduric meaning they produce acid and thrive in an acidic environment, in addition they synthesize extracellular glucans from sucrose which shield the bacteria from the buffering effect of saliva. Without regular mechanical removal of the biofilm the tooth surface is exposed to an acidic environment for an extended period of time and demineralization of enamel predominates resulting in cavitation (Chang 97) At pH 5.5 remineralization and demineralization are in equilibrium; below pH 5.5 saliva is undersaturated relative to enamel, net diffusion of calcium and phosphate is from enamel to the oral environment resulting in demineralization(Mitchell 92, Cross 04, Garcia Godoy 08) With removal of the cariogenic challenge, i.e. hygiene or appliance removal, the surface of these lesions are preferentially remineralized in the presence of calcium and phosphate in the pellicle and saliva(Garcia-Godoy 08) Unfortunately, surface remineralization can decrease or eliminate sufficient access for ions to remineralize the subsurface lesion resulting in an arrested WSL(Garcia-Godoy08)

Development of WSL is multifactorial and complex involving patient behavior, patient physiology, preventative measures, clinician behavior, clinical factors, and many other factors. WSL have been shown to be associated with treatment time, salivary flow bacterial load, specific bacteria species, preventative measures, hygiene, and diet(Chang 97).

WHITE SPOT LESION PREVALENCE/INCIDENCE

There is tremendous variation in the literature regarding prevalence and incidence of WSL. Reported prevalence ranges from 2% to 96%; this considerable range is due to study variation in WSL assessment, presence of pre-existing lesions, prevention methods, and other factors(Benham09) In 1982 a study compared a control group of 50 children with 121 orthodontic patients finding the percentage of WSL to be 25% and 49.6% respectively(Gorelick 82). Ogaard found the prevalence to be 88% at the time of fixed appliance removal(Ogaard 01). A more recent finding reported a 25% prevalence of WSL post-orthodontics, however it must be noted that the study included rigorous OHI and fluoride applications (Lovrov 07) Another contemporary retrospective study looking at 350 orthodontically treated patients showed 72.9% of patients developed at least one new WSL (Richter11)

Post-orthodontic WSL most commonly occur between the gingiva and the fixed appliance on the facial surface of the tooth(Goerlick82) As with prevalence there is some variation reported distribution of WSL. Goerlick reported 7% of both maxillary central and lateral incisors had WSL(Goerlick82) while Ogaard showed 9.8% of maxillary central incisors to 25.5% of maxillary lateral incisors were effected(Ogaard89) In contrast Lovrov reported that maxillary central incisors developed WSL more frequently than maxillary laterals(Lovrov07) It is generally agreed that maxillary lateral incisors and canines along with mandibular canines and premolars experience a relatively high WSL incidence compared to other teeth, excluding first molars (Gorelick82,Mizrahi83,Artun86,Ogaard 89)

WHITE SPOT LESION PREVENTION

It has been shown that best predictor for development of WSL is the presence of a visible mutans streptococci plaque around fixed appliances(Ogaard01) Oral hygiene is made difficult by the presence of fixed appliances predisposing the teeth to increased biofilm accumulation(Chang97) The regular mechanical removal of this biofilm has been shown to reduce WSL in orthodontic patients It is generally agreed upon that fluoride treatment is the most effective agent in preventing WSL in orthodontic patients (Ogaard08, Lovrov07,Chang 97, Benson 05) A reduction in development of WSL was shown in orthodontic patients rinsing daily with acidulated fluoride or sodium fluoride (O'reilly87, Ogaard88) Fluoride varnish has also been shown to be effective in preventing WSL(Chadwick05) Todd et al reported a 50% reduction in WSL in patients with fluoride varnish compared to a control(Todd99)Some evidence has also been given for the efficacy fluoride containing bonding material, however, that evidence is weak and more studies are needed(Benson05) Patient compliance is a major factor in prevention, one study reported that only 42% of patients complied with fluoride rinse protocol; notably, the poor compliance group developed more WSL(Geiger92) A systematic review on the subject concluded more well designed clinical trials are needed, recommending daily 0.05% sodium fluoride rinse as the best practices for WSL prevention(Benson05) Another study recommends risk assessment, regular OHI, dietary education, and daily fluoride rinse(Chang97)

WHITE SPOT LESION TREATMENT

A number of studies have followed the changes in WSL after the removal of fixed appliances. The evidence suggests that demineralization ceases and WSL naturally regress to some extent after appliances are removed(Artun86,Ogaard89,Chang97, Ogaard01) Both remineralization and tooth brush abrasion have been shown to contribute to the amelioration of PO WSL(Artun 86,Ogaard94). The majority of regression in WSL is most probably due to natural and toothbrush surface wear rather than remineralization (Artun86, Chang97) Despite this regression of WSL after appliance removal many were present years after removal of fixed appliances, especially in advanced WSL(Artun86,Ogaard89) Al-Khateeb et al followed patients with PO WSL and found that remineralization does contribute to WSL regression, most prominently in the first three months, but that the rate of remineralization decreases with time(Al-Khateeb98)

FLOURIDE

The use of fluoride to treat PO WSL is currently somewhat controversial. It is generally agreed that fluoride can promote remineralization of enamel. There is, however, little consensus on effectiveness, method of delivery, timing, or dose. One study showed no difference in WSL regression between those treated with fluoride toothpaste (50ppm) and with non-fluoride toothpaste suggesting this level of fluoride does not improve WSL.(Willmot04) Some studies have reported high concentrations of fluoride remineralized the subsurface zone of incipient carious lesions(Mellberg 85, Castellano84) Fluoride varnish has also been shown to improve remineralization of incipient lesions(Trairatvorakul08, Hazelrigg03) Importantly, it was also reported that mineralization of the outer enamel layer increased while demineralization decreased in the inner enamel indicating preferential mineralization of the outer layer of enamel. Some evidence suggests greater mineralization in the outer layer of enamel also occurs with higher concentration fluoride rinses(Linton96,Ogaard99) Willmot stated that high doses of fluoride completely arrest the carious process, and that arrest is undesirable for PO WSL. He goes further, saying that these arrested WSL regress very little and frequently become stained and unsightly(Willmot04) This statement parallels Ogaard et al assertion that concentrated fluoride solutions arrest and prevent complete repair of WSL(Ogaard). In contrast to these findings a recent study showed that an higher concentration fluoride (5000 ppm) showed greater remineralization of incipient caries than a lower concentration fluoride (1500 ppm)(ten cate08) However, the study did not show distribution of mineralization within the lesion. It may be that higher concentrations of fluoride establish a larger gradient enabling a higher concentration of fluoride at deeper areas of the lesion(Clarkson 81)

CPP-ACP

Casein phosphopeptide amorphous calcium phosphate (CPP-ACP) is another, more recently developed, remineralizing agent. CPP is essentially a ligand which can ionically bind 25 calcium ions, 15 phosphate ions, and 5 fluoride ions (Hicks04) Cross summarized the proposed mechanism of CPP-ACP "they [CPP-ACP molecules] localize ACP at the tooth surface, where ACP buffers the free calcium and phosphate ion activities, thereby helping to maintain a state of supersaturation with respect to tooth enamel depressing demineralization and enhancing remineralization. In effect the CPP-ACP complex behaves as delivery vehicle for calcium and phosphate ions"(Cross04) Multiple studies have shown evidence of remineralization in incipient caries treated with CPP-ACP based remineralization technologies (Manton08,Iijima04,Reynolds03,Andersson07,Bailey09) Significant improvement of PO WSL have also been reported in the literature showing more regression in CPP-ACP treated lesions(Bailey09) Andersson compared 0.05% sodium fluoride, fluoridated toothpaste, and CPP-ACP treatment regimens and concluded that although all groups showed lesion regression but the CPP-ACP had more aesthetically favorable outcomes(Andersson07) Contradictory evidence in small number of studies has shown no differences in remineralization between CPP-ACP and control groups(Pulido08,Beerens10) Additionally there is some question as to the ideal concentration of calcium and phosphate; it may be that excessively high concentrations lead to surface mineralization and WSL arrest by similar mechanisms proposed for high fluoride concentrations(Garcia-Godoy08)

CPP-ACP + Fluoride

The combination of CPP-ACP with fluoride has been the focus of some recent research. As previously stated the CPP molecule has the ability to ionically bond to fluoride in addition to calcium and phosphate. Binding of fluoride results in minimal change in the structure of CPP compared to when it is bound to calcium and phosphate ions only making it an effective delivery vehicle for fluoride, calcium and phosphate ions(Cross04) Early data have supported this theoretical synergy of fluoride and CPP-ACP. Reynolds et al showed a dentifrice containing CPP-ACP with 1100 ppm fluoride was superior to other formulations in remineralization of WSL. Interestingly CPP-ACP alone showed similar remineralization to 2800 ppm fluoride alone. Another significant finding was that the fluoride only groups had predominantly surface remineralization while CPP-ACP alone and in combination with fluoride showed "more homogenous remineralization throughout the body of the lesion" Another study showed that CPP-ACP applied as a topical after use of fluoride toothpaste resulted in greater remineralization potential(Kumar07) In the trials by Pulido et al and Beerens et al they found no evidence of increased remineralization from CPP-ACP alone or in combination with fluoride(Pulido08, Beerens10)

Although early studies on CPP-ACP are promising there is relatively little research on the topic to date. In a systematic literature review of the subject one author concluded that "the quantity and quality of clinical trial evidence are insufficient to make conclusions regarding the long-term effectiveness of casein derivatives, specifically CPP-ACP…"(Azarpazhoo08)

Restoration

Traditional restorative options for WSL include composite fillings, composite veneers, ceramic veneers, and full coverage crowns. While these options can provide an esthetic improvement they require removal of sound tooth structure. Resin infiltration provides a minimally invasive alternative to these traditional restorations. Resin infiltration is defined as the act or process of infiltrating pores or cavities of subsurface enamel lesions using a resin mixture with high a penetration coefficient(Kielbasa09). The technique was developed for the treatment of incipient carious lesions and has been shown to be effective in the treatment of incipient lesions. More recently resin infiltration has been proposed as a treatment for post-orthodontic WSL.

Resin Infiltration

As early as 1975 the potential of infiltrating incipient lesions with low viscosity resin was recognized; Davila et. al. concluded that "…plastification offers potential use in preventing, arresting, and restoratively infiltrating incipient proximal lesions" (Davila1975). Further studies demonstrated that in vitro artificial carious lesions could be partially penetrated by a number of commercially available sealants and adhesives(Gray02,Schmidlin04,Meyer-leuckel08) This treatment was also shown to reduce lesion progression compared to untreated groups when teeth were exposed to a cariogenic environment en vitro.(Davila75,Robinson76,01,Donly92, Paris06. More recently Martignon et. al. showed reduction in lesion progression in lesions infiltrated with a commercially available resin in vitro(Martignon06) Resin infiltration was shown to be superficial (approximately 25μm) using commercially available adhesives and sealants and etching with phosphoric acid, subsequently deeper portions of the lesions were not infiltrated.(Paris07) The incomplete infiltration can be explained by the preferential remineralization of surface layers of incipient carious lesions(Garcia-Godoy08)

More recent investigations have shown that a major factor contributing to the incomplete infiltration is inadequate removal of the mineralized surface layer of incipient lesions. Sufficient removal of this layer is necessary to allow the resin infiltrant access to the deeper portions of the lesion(Gray02). Meyer-Leuckel et. al. showed surface depth can vary considerably ranging from 10 to 197μm in natural enamel lesions. However the majority of lesions have a surface layer thickness between 20 and 50μm, with 29% having a surface layer thickness greater than 50μm(Meyer-L0708). In addition the remineralized surface layer of WSL has been shown to be more resistant to phosphoric acid etching than adjacent sound enamel (Lee 95). Two studies comparing etching of natural WSL showed an etching protocol using 15% HCl gel etchant to remove the surface layer completely without causing cavitation while 37% phosphoric acid gel was shown to result insufficient removal of the surface layer(Meyer-L07,08Paris07)

Subsequently, HCl etched lesions showed significantly greater resin penetration depth; within the HCl group, those lesions with complete surface layer removal showed the greatest penetration depth(Paris07). It should be noted that the surface layers were not completely removed in all cases, most probably due to variation in surface layer depth(Meyer-L07)

Use of HCl etchant protocol coupled with improvements in the resin infiltrant material itself have lead to overall greater resin penetration depths(Meyer-L 07,08) . Once sufficient access to the body of the lesion has been established through etching, and the lesion is dried the infiltrant can progress into the lesion via capillary action. The ability of resin infiltrants to penetrate into a porous solid is described by the Washburn equation. The penetration coefficient (PC) is a part of this equation and is dependent on viscosity, surface tension, and contact angle(Meyer-L08) A comparison of a commercially available adhesive with experimental resin infiltrants with variable PC's provided evidence that a greater penetration coefficient is strongly correlated to greater penetration speed and depth(Meyer_L08, Kielbassa09) The use of alcohol based agents as an adjunct to desiccation with forced air has also been used to more completely remove water in the porous structure increasing the capillary potential of the infiltrant. These advances in methods and materials used for resin infiltration have made it possible to predictably infiltrate incipient lesions. Data on early resin infiltration studies showed penetration depths in the range of 25μm, whereas more recent studies have reported penetration depths of 300μm and greater(Paris07). While more complete penetration of a lesion may improve resistance to lesion progression it also can result in esthetic improvement of the lesion. Obturation of the voids in demineralized enamel results in optical properties similar to that of natural enamel, in effect masking the WSL(Paris09). Several preliminary studies showed resin infiltration to be effective in the restoration of WSL (Grey02,Paris09,Kim11) In light of recent evidence and advances in resin infiltration technology researchers have advocated for resin infiltration as a possible alternative to traditional treatment modalities for WSL(Grey02,Kielbassa09,Paris09,Kim11) In an extensive review Kielbassa recommended resin infiltration for "Improved esthetic outcome when used as a masking resin on demineralized labial surfaces (white spot lesion, i.e., with orthodontic patients)" (Kielbassa09) In a recent study the effectiveness of masking white spot enamel lesions with the resin infiltration technique was investigated(Kim11) A total of 18 teeth with PO WSL were treated en vivo with a commercially available resin infiltration system (ICON®). Kim et al showed 11 teeth categorized as "completely masked", 6 teeth as "partially masked", and 1 tooth with no change(Kim 11). Despite the small sample size of this group these results are encouraging with 94% of the teeth showing marked esthetic improvement using a minimally invasive resin infiltration technique.

The majority of studies to date have focused on resin infiltration of incipient carious proximal lesions. Specifically, the studies focused on the inhibition of lesion progression and not necessarily the cosmetic effect of resin infiltration. Although there is very little research on resin infiltration of PO WSL specifically these lesions are, in essence, incipient carious lesions differing only in etiology, location, and progression. Accordingly, the current evidence on resin infiltration of incipient proximal carious lesions is applicable to PO WSL. The two key differences between PO WSL and incipient carious lesions are that PO WSL are located in the esthetic zone and that they tend to regress naturally. Because PO WSL regress due to abrasion and remineralization it is unknown how these processes will be augmented by restoration with resin infiltration. For both patient and practitioner, the goal for resin infiltration of PO WSL is primarily esthetic. To date very few studies have evaluated the esthetic outcomes for resin infiltration, to my knowledge there have been no studies comparing remineralization with CPP-ACP and fluoride with resin infiltration.

REFERENCES

Al-Khateeb, S., C. M. Forsberg, et al. (1998). "A longitudinal laser fluorescence study of white spot lesions in orthodontic patients." Am J Orthod Dentofacial Orthop 113(6): 595-602.

Alexander, S. A. and L. W. Ripa (2000). "Effects of self-applied topical fluoride preparations in orthodontic patients." Angle Orthod 70(6): 424-30.

Andersson, A., K. Skold-Larsson, et al. (2007). "Effect of a dental cream containing amorphous cream phosphate complexes on white spot lesion regression assessed by laser fluorescence." Oral Health Prev Dent 5(3): 229-33.

Artun, J. and B. O. Brobakken (1986). "Prevalence of carious white spots after orthodontic treatment with multibonded appliances." Eur J Orthod 8(4): 229-34.

Azarpazhooh, A. and H. Limeback (2008). "Clinical efficacy of casein derivatives: a systematic review of the literature." J Am Dent Assoc 139(7): 915-24; quiz 994-5.

Bailey DL, Adams GG, et al. (2009). "Regression of post-orthodontic lesions by a remineralizing cream." J Dent Res. 2009 Dec;88(12):1148-53.

Beerens MW, van der Veen MH, et al. (2010). "Effects of casein phosphopeptide amorphous calcium fluoride phosphate paste on white spot lesions and dental plaque after orthodontic treatment: a 3-month follow-up." Eur J Oral Sci. 2010 Dec;118(6):610-7. doi: 10.1111/j.1600-0722.2010.00780.x.

Benham AW, Campbell PM, Buschang PH. (2009) "Effectiveness of pit and fissure sealants in reducing white spot lesions during orthodontic treatment. A pilot study." Angle Orthod. 2009 Mar;79(2):338-45.

Benson, P. E., A. Ali Shah, et al. (2008). "Polarized versus nonpolarized digital images for the measurement of demineralization surrounding orthodontic brackets." Angle Orthod 78(2): 288-93.

Benson, P. E., A. A. Shah, et al. (2005). "Fluorides, orthodontics and demineralization: a systematic review." J Orthod 32(2): 102-14.

Bishara, S. and A. Ostby (2008). "White spot lesions: formation, prevention, and treatment." Seminars in Orthodontics 14(3): 174-182.

Castellano, J. B. and K. J. Donly (2004). "Potential remineralization of demineralized enamel after application of fluoride varnish." Am J Dent 17(6): 462-4.

Chadwick BL, Roy J, et al. (2005). "The effect of topical fluorides on decalcification in patients with fixed orthodontic appliances: a systematic review."Am J Orthod Dentofacial Orthop. 2005 Nov;128(5):601-6; quiz 670. Review.

Chang, H. S., L. J. Walsh, et al. (1997). "Enamel demineralization during orthodontic treatment. Aetiology and prevention." Aust Dent J 42(5): 322-7.

Clarkson, B. H., J. S. Wefel, et al. (1981). "Redistribution of enamel fluoride during white spot lesion formation: an in vitro study on human dental enamel." Caries Res 15(2): 158-65.

Cochrane, N. J., S. Saranathan, et al. (2008). "Enamel subsurface lesion remineralisation with casein phosphopeptide stabilised solutions of calcium, phosphate and fluoride." Caries Res 42(2): 88-97.

Cross, K. J., N. L. Huq, et al. (2004). "NMR studies of a novel calcium, phosphate and fluoride delivery vehicle-alpha(S1)-casein(59-79) by stabilized amorphous calcium fluoride phosphate nanocomplexes." Biomaterials 25(20): 5061-9.

Jorge M. Dayila, Michael G. Buonocore, et al. (1975). "Adhesive Penetration in Human Artificial and Natural White Spots DOI: *J DENT RES* 1975 54: 999

Dirks, O. B. (1966). "Posteruptive Changes in Dental Enamel." J. Dent. Res. 45(3): 503-511.

Emilson CG, Krasse B (1985). "Support for and implications of the specific plaque hypothesis." Scand J Dent Res. 1985 Apr;93(2):96-104.

Garcia-Godoy, F. and M. J. Hicks (2008). "Maintaining the integrity of the enamel surface: the role of dental biofilm, saliva and preventive agents in enamel demineralization and remineralization." J Am Dent Assoc 139 Suppl: 25S-34S.

Geiger AM, Gorelick L, et al. (1992). "Reducing white spot lesions in orthodontic populations with fluoride rinsing." Am J Orthod Dentofacial Orthop. 1992 May;101(5):403-7.

Gorelick, L., A. M. Geiger, et al. (1982). Incidence of white spot formation after bonding and banding. Am J Orthod 81(2): 93-8.

Gray GB, Shellis P (2002). "Infiltration of resin into white spot caries-like lesions of enamel: an in vitro study. Eur J Prosthodont Restor Dent. 2002 Mar;10(1):27-32.

Hazelrigg, C. O., J. A. Dean, et al. (2003). "Fluoride varnish concentration gradient and its effect on enamel demineralization." Pediatr Dent 25(2): 119-26.

Hicks, J., F. Garcia-Godoy, et al. (2004). "Biological factors in dental caries: role of remineralization and fluoride in the dynamic process of demineralization and remineralization (part 3)." J Clin Pediatr Dent 28(3): 203-14.

Iijima, Y., F. Cai, et al. (2004). "Acid resistance of enamel subsurface lesions remineralized by a sugar-free chewing gum containing casein phosphopeptide-amorphous calcium phosphate." Caries Res 38(6): 551-6.

Kielbassa AM, Muller J, Gernhardt CR (2009). "Closing the gap between oral hygiene and minimally invasive dentistry: a review on the resin infiltration technique of incipient (proximal) enamel lesions." Quintessence Int. 2009 Sep;40(8):663-81.

Kim S, Kim EY, et al. (2011). "The evaluation of resin infiltration for masking labial enamel white spot lesions." Int J Paediatr Dent. 2011 Jul;21(4):241-8.

Kumar, V. L., A. Itthagarun, et al. (2008). "The effect of casein phosphopeptide-amorphous calcium phosphate on remineralization of artificial caries-like lesions: an in vitro study." Aust Dent J 53(1): 34-40.

Lee CQ, Shey Z, Cobb CM, (1995). "Microscopic appearance of enamel white-spot lesions after acid etching." Quintessence Int. 1995 Apr;26(4):279-84.

Linton, J. L. (1996). "Quantitative measurements of remineralization of incipient caries." Am J Orthod Dentofacial Orthop 110(6): 590-7.

Lovrov, S., K. Hertrich, et al. (2007). "Enamel Demineralization during Fixed Orthodontic Treatment - Incidence and Correlation to Various Oral-hygiene Parameters." J Orofac Orthop 68(5): 353-63.

Lundström F, Krasse B (1987). "Caries incidence in orthodontic patients with high levels of Streptococcus mutans." Eur J Orthod. 1987 May;9(2):117-21.

Manton, D. J., G. D. Walker, et al. (2008). "Remineralization of enamel subsurface lesions in situ by the use of three commercially available sugar-free gums." Int J Paediatr Dent 18(4): 284-90.

Martignon S, Ekstrand KR, Ellwood R (2006). "Efficacy of sealing proximal early active lesions: an 18-month clinical study evaluated by conventional and subtraction radiography." Caries Res. 2006;40(5):382-8.

Mellberg, J. R., W. G. Chomicki, et al. (1985). "Remineralization in vivo of artificial caries lesions by a monofluorophosphate dentifrice." Caries Res 19(2): 126-35.

Meyer-Lueckel H, Paris S, et al. (2006). "Influence of the application time on the penetration of different dental adhesives and a fissure sealant into artificial subsurface lesions in bovine enamel." Dent Mater. 2006 Jan;22(1):22-8. Epub 2005 Jul 25.

Meyer-Lueckel H, Paris S. (2008). "Improved resin infiltration of natural caries lesions." J Dent Res. 2008 Dec;87(12):1112-6.

Mitchell, L. (1992). "An investigation into the effect of a fluoride releasing adhesive on the prevalence of enamel surface changes associated with directly bonded orthodontic attachments." Br J Orthod 19(3): 207-14.

Mitchell, L. (1992). "Decalcification during orthodontic treatment with fixed appliances--an overview." Br J Orthod 19(3): 199-205.

Murphy, T. C., D. R. Willmot, et al. (2007). "Management of postorthodontic demineralized white lesions with microabrasion: a quantitative assessment." Am J Orthod Dentofacial Orthop 131(1): 27-33.

Neuhaus KW, Graf M, Lussi A, Katsaros C. "Late infiltration of post-orthodontic white spot lesions." J Orofac Orthop. 2010 Nov;71(6):442-7. Epub 2010 Nov 17.

O'Reilly, M. M. and J. D. Featherstone (1987). "Demineralization and remineralization around orthodontic appliances: an in vivo study." Am J Orthod Dentofacial Orthop 92(1): 33-40.

Ogaard, B. (1989). "Prevalence of white spot lesions in 19-year-olds: a study on untreated and orthodontically treated persons 5 years after treatment." Am J Orthod Dentofacial Orthop 96(5): 423-7.

Ogaard, B. (1999). "The cariostatic mechanism of fluoride." Compend Contin Educ Dent 20(1 Suppl): 10-7; quiz 34.

Ogaard, B. (2008). "White spot lesions during orthodontic treatment: mechanisms and fluoride preventatvie aspects." Seminars in Orthodontics 14(3): 183-193.

Ogaard, B., E. Larsson, et al. (2001). "Effects of combined application of antimicrobial and fluoride varnishes in orthodontic patients." Am J Orthod Dentofacial Orthop 120(1): 28-35.

Ogaard, B., G. Rolla, et al. (1988). "Orthodontic appliances and enamel demineralization. Part 2. Prevention and treatment of lesions." Am J Orthod Dentofacial Orthop 94(2): 123-8.

Ogaard, B. and J. J. Ten Bosch (1994). "Regression of white spot enamel lesions. A new optical method for quantitative longitudinal evaluation in vivo." Am J Orthod Dentofacial Orthop 106(3): 238-42.

Paris S, Meyer-Lueckel H et al. (2006). "Penetration coefficients of commercially available and experimental composites intended to infiltrate enamel carious lesions." Dent Mater. 2007 Jun;23(6):742-8. Epub 2006 Sep 5.

Paris S, Meyer-Lueckel H et al. (2007). "Resin infiltration of artificial enamel caries lesions with experimental light curing resins." Dent Mater J. 2007 Jul;26(4):582-8.

Paris S, Meyer-Lueckel H, Kielbassa AM (2007). "Resin infiltration of natural caries lesions." J Dent Res. 2007 Jul;86(7):662-6.

Paris S, Meyer-Lueckel H et al. (2007). "Penetration coefficients of commercially available and experimental composites intended to infiltrate enamel carious lesions." Dent Mater. 2007 Jun;23(6):742-8. Epub 2006 Sep 5.

Paris S, Meyer-Lueckel H. "Masking of labial enamel white spot lesions by resin infiltration--a clinical report." Quintessence Int. 2009 Oct;40(9):713-8.

Pulido, M. T., J. S. Wefel, et al. (2008). "The inhibitory effect of MI paste, fluoride and a combination of both on the progression of artificial caries-like lesions in enamel." Oper Dent 33(5): 550-5.

Reynolds, E. C. (1997). "Remineralization of enamel subsurface lesions by casein phosphopeptide-stabilized calcium phosphate solutions." J Dent Res 76(9): 1587-95.

Reynolds, E. C., F. Cai, et al. (2003). "Retention in plaque and remineralization of enamel lesions by various forms of calcium in a mouthrinse or sugar-free chewing gum." J Dent Res 82(3): 206-11.

Reynolds, E. C. (2008). "Calcium phosphate-based remineralization systems: scientific evidence?" Aust Dent J 53(3): 268-73.

Reynolds, E. C., F. Cai, et al. (2008). "Fluoride and casein phosphopeptide-amorphous calcium phosphate." J Dent Res 87(4): 344-8.

Richter AE, Arruda AO et al. (2011). "Incidence of caries lesions among patients treated with comprehensive orthodontics." Am J Orthod Dentofacial Orthop. 2011 May;139(5):657-64.

Robinson C, Hallsworth AS, et al. (1976). "Arrest and control of carious lesions: a study based on preliminary experiments with resorcinol-formaldehyde resin." J Dent Res. 1976 Sep-Oct;55(5):812-8.

Robinson C, Brookes SJ, et al. (2001). "In vitro studies of the penetration of adhesive resins into artificial caries-like lesions." Caries Res. 2001 Mar-Apr;35(2):136-41.

Schmidlin PR, Zehnder M, et al. (2004). "Penetration of a bonding agent into De- and remineralized enamel in vitro." J Adhes Dent. 2004

Stecksen-Blicks, C., G. Renfors, et al. (2007). "Caries-preventive effectiveness of a fluoride varnish: a randomized controlled trial in adolescents with fixed orthodontic appliances." Caries Res 41(6): 455-9.

Ten Cate JM, (2009). "International Conference on Novel Anti-caries and Remineralizing Agents." Vina del Mar, Chile, January 10-12, 2008. Preface. Adv Dent Res. 2009;21(1):3.

Todd MA, Staley RN et al. (1999). "Effect of a fluoride varnish on demineralization adjacent to orthodontic brackets." Am J Orthod Dentofacial Orthop. 1999 Aug;116(2):159-67.

Rocha Gomes Torres C, Borges AB, Torres LM, Gomes IS, de Oliveira RS. "Effect of caries infiltration technique and fluoride therapy on the colour masking of white spot lesions." J Dent. 2011 Mar;39(3):202-7. Epub 2010 Dec 21.

Trairatvorakul, C., S. Kladkaew, et al. (2008). "Active management of incipient caries and choice of materials." J Dent Res 87(3): 228-32.

Willmot, D. (2008). "White spot lesions after orthodontic treatment." Seminars in Orthodontics 14(3): 209-219.

Willmot, D. R. (2004). "White lesions after orthodontic treatment: does low fluoride make a difference?" Journal of Orthodontics 31: 235-242.