Effectiveness of a newly developed fluoride-releasing O-ring for prevention of white spot lesions

2022 Research Aid Awards (RAA)

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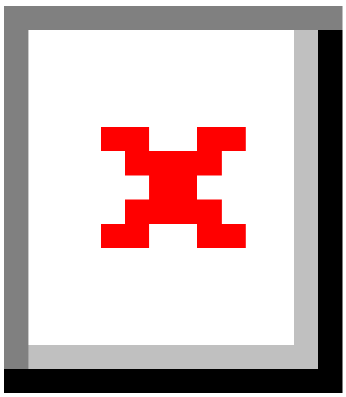
FollowUp Form

Award Information



In an attempt to make things a little easier for the reviewer who will read this report, please consider these two questions before this is sent for review:

- *Is this an example of your very best work, in that it provides sufficient explanation and justification, and is something otherwise worthy of publication? (We do publish the Final Report on our website, so this does need to be complete and polished.)*
- *Does this Final Report provide the level of detail, etc. that you would expect, if you were the reviewer?*

Title of Project:*

Effectiveness of a newly developed fluoride-releasing O-ring for prevention of white spot lesions

Award Type

Research Aid Award (RAA)

Period of AAOF Support
July 1, 2022 through June 30, 2023

Institution
Texas A&M College of Dentistry Department of Orthodontics

Names of principal advisor(s) / mentor(s), co-investigator(s) and consultant(s)
Dr. Yan Jing, Dr. Peter Buschang, Dr. Amal Noureldin

Amount of Funding
$5,000.00

Abstract
(add specific directions for each type here)

White spot lesions (WSLs) occur on the smooth enamel surfaces of teeth surrounding fixed orthodontic appliances and, as such, pose substantial esthetic problems for orthodontic patients. Approximately 50% of orthodontic patients develop WSLs on at least one tooth. In response to this prevalent problem, various fluoride releasing products have been developed. However, the current approaches require patient compliance in order to maintain a therapeutic effect because they exhibit a "burst effect", which severely limits the time that the fluoride-releasing materials are effective. To avoid the "burst effect", fluoride needs to be released slowly. It has been demonstrated that calcium fluoride (Ca- F) can act as a sustained fluoride-releasing reservoir system due to its low solubility and effectiveness at low pH and therefore can be an ideal candidate for WSL prevention.

Our long-term goal is to develop efficient strategies to prevent orthodontic-associated WSLs. To achieve this goal, we have designed a series of projects. In the previous study (supported by AAOF-BRA award to Jing, 07/2020-12/2021), we have established an efficient and reliable method to incorporate Ca-F particles to Polycaprolactone (PCL, a commonly used biomaterial in health care), which was subsequently coated onto the surface of an ordinary O-ring (American Orthodontics, Wisconsin) to modify it as a Ca-F O-ring. SEM was used to demonstrate the successful coating of Ca-F particles onto the O-rings. More importantly, the Ca-F O-rings can release a continuous therapeutic level of fluoride for up to 7 weeks. In addition, the modification strategy had limited impact on the mechanical performance of the O-ring based on the evaluation of elastic property with Instron. These exciting data indicate Ca-F O-ring is likely to be a promising product for the prevention of WSLs during orthodontic treatment.

In this proposal, we will determine the effects of Ca-F O-ring in the prevention of WSLs in vitro. Our central hypothesis is that the Ca-F O-rings can efficiently protect the enamel from the demineralization during pH cycling and significantly decrease the risk of WSLs.

Our study is significant because there is currently no ideal strategy to prevent WSLs during orthodontic treatment. Our previous study has demonstrated the long-term therapeutic release of fluoride from the novel Ca-F O-ring. Successful completion of this proposal will further determine the effectiveness of the Ca-F O-ring for the prevention of WSLs in vitro, and provide valuable evidence for the future clinical application.

I plan to attain this goal by evaluating the effectiveness of the Ca-F-O-ring for the enamel remineralization in vitro. Extracted human teeth with sound enamel will be put in a 9-day pH cycling, to mimic the daily alteration of demineralization and remineralization in the human mouth. In particular, I will evaluate the enamel color changes, mineral density, and the evidence of Ca-F deposits by using spectrophotometer, FluoreCam, Micro-CT, and SEM, respectively.

As a first-year orthodontic resident, I am truly interested in orthodontic related research, especially treatment and prevention of WSLs. I will take this study as my research project for my master's degree. To ensure the successful completion, I have developed a strong committee including Drs. Jing, Buschang and Noureldin, who have broad knowledge and expertise in orthodontics and white spot lesions. In this project, I will put 20% of my efforts to focus on the research plan, including managing, designing and executing the proposed research project, and to be responsible for data collection and interpretation. I will have four formal meetings with my committee for progress report, data discussion and trouble shooting.

Respond to the following questions:

Detailed results and inferences:*

If the work has been published, please attach a pdf of manuscript below by clicking "Upload a file".
OR
Use the text box below to describe in detail the results of your study. The intent is to share the knowledge you have generated with the AAOF and orthodontic community specifically and other who may benefit from your study. Table, Figures, Statistical Analysis, and interpretation of results should also be attached by clicking "Upload a file".

Lemoine final report charts 2022 RAA.pdf
Nomenclature:

Ca-F	Calcium fluoride
L*	Lightness
ΔL*	Change in lightness
NaF	Sodium fluoride
O-CaF	Group containing the Ca-F O-rings
O-F	Group containing regular O-rings with topical fluoride
O-R	Group containing regular O-rings
R-DE	Micro-CT region containing deep enamel control
R-SE	Micro-CT region containing surface enamel control
R-TW	Micro-CT region containing treatment window
SEM	Scanning electron microscopy
T0	Baseline data timepoint, before pH cycling
T1	Data timepoint after pH cycling
WSL(s)	White spot lesion(s)

Results and Discussion:

When looking at the lightness (L*) of the treatment windows, no differences were found between groups at baseline (T0) (Figure 1). The mean L* increased after pH cycling (T1) for all groups, which is indicative of demineralization (Figure 2). Compared to the control groups with regular O-rings with (O-F) and without topical fluoride application (O-R), the group containing the Ca-F O-rings (O-CaF) exhibited treatment windows with a smaller change in lightness (ΔL*) after pH cycling, signifying that potentially more remineralization of the enamel surface had occurred within this group (Figure 3). After Bonferroni corrections, however, there were no statistically significant between-group differences in ΔL* for the O-CaF group compared to that of the O-F ($p = 1.00$) and O-R ($p = 0.602$) groups (Figure 4). Among all the groups, O-R exhibited the most prominent treatment windows in terms of whiteness, although this finding did not reach significance (Figures 3, 4). This observation aligns with the absence of fluoride in O-R, which could have contributed to its limited remineralization potential. While there was a trend of decreasing ΔL* from O-R to O-F to O-CaF, the present study failed to achieve statistical significance in the comparison of ΔL* after pH cycling (Figure 3). Some explanations include variation in the spectrophotometer reading positions and insufficient pH cycling time to induce significant fluoride release from the Ca-F O-rings.

Micro-CT analysis revealed a significant decrease in mineral densities of the treatment windows (R-TW) in O-CaF compared to those in O-F ($p < 0.00$) and O-R ($p < 0.00$) (Figures 5, 6). One explanation for this could be that unlike NaF, Ca-F does not migrate into the lesion to attach to hydroxyapatite crystals and increase the mineral content; it will instead precipitate on the surface as fluorapatite when demineralization occurs. However, since Ca-F has a lower critical pH at which demineralization occurs than fluorapatite, it can withstand lower pH levels before it dissolves to redeposit as fluorapatite on the surface. Therefore, the O-CaF group potentially exhibited lower mineral densities due to a lowering of the critical pH by Ca-F and therefore less deposition of fluorapatite. Another explanation for the lower mineral densities in the O-CaF group is less of a hypermineralized surface enamel layer in the treatment windows that is characteristic of WSLs than O-F group. SEM-EDX measurements showed no significant differences in the Ca% of the surface layer of R-TW between groups, although the O-F and O-CaF groups were in similar level and the O-R group was the lowest (Figure 7). This is consistent with Micro-CT analysis.

Lastly, there were no significant between-group differences in mineral densities of the surface enamel (R-SE) regions adjacent to the treatment windows (Table 1). This indicates that coating the adjacent regions with nail polish protected the control enamel surfaces from demineralization and remineralization during the pH cycling and that R-TW can be adequately compared between groups since there was no statistical difference in the enamel mineral content between groups. There were also no significant between-group differences in deep enamel (R-DE) regions between groups, except O-F had significantly lower mineral densities in R-DE than O-CaF ($p = 0.049$) (Table 2). This significant finding could be explained by the higher variation present within the R-DE data for the O-F group (Figure 8). In general, this finding indicates that the demineralization caused by the pH cycling caused a subsurface enamel lesion, which is also characteristic of WSLs, rather than a deep enamel lesion associated with caries.

In conclusion, the use of 5% PCL-coated Ca-F O-rings for prevention of white spot lesions (WSLs) in orthodontic patients is promising, but future studies with longer pH cycling times, decreased variation in data collection, and SEM analysis are needed to confirm their efficacy.

Were the original, specific aims of the proposal realized?*

The original specific aims of the proposal were realized. Micro-CT and light spectrophotometer were used to compare the effectiveness of the Ca-F O-ring to regular O-rings in the prevention of WSLs in premolar teeth subjected to in vitro pH cycling. SEM was used to analyze the level of mineral contents in the treatment window in all groups.

Were the results published?*

No

Have the results of this proposal been presented?*

Yes

To what extent have you used, or how do you intend to use, AAOF funding to further your career?*

AAOF funding was used to support the research project, which allowed for specimen and solution preparation, pH cycling, and analysis by micro-CT and spectrophotometer. Under the support of AAOF funding, the author also won the Distinguished Research Award. Since the author will be in private practice in the early career stage, there are no intentions to use the AAOF funding to further the author's career.

Accounting: Were there any leftover funds?

$0.00

Not Published

Are there plans to publish? If not, why not?*

There are plans in the upcoming years to publish the results of the project within a peer-reviewed orthodontic research journal.

Presented

Please list titles, author or co-authors of these presentation/s, year and locations:*

1) Masters Thesis Defense (2024, Texas A&M School of Dentistry)
    a. Title: Fluoridated O-Rings for WSL Prevention
    b. Author: N. Lemoine

2) 15th Annual Dr. Tom Matthews Lectureship (2024, Texas A&M School of Dentistry)
    a. Title: Fluoridated O-Rings for WSL Prevention
    b. Author: N. Lemoine

3) 2024 IADR/AADOCR/CADR meeting (New Orleans, poster)
    a. Title: Effectiveness of Novel CaF O-rings in White Spot Lesion Prevention
    b. Author: N. Lemoine, C. Chang, J. Lowe, Y. Liu, C. Ma, Y. Jing

Was AAOF support acknowledged?

If so, please describe:

AAOF support was acknowledged by the author(s).

Internal Review

Reviewer comments

Reviewer Status*

Approved

File Attachment Summary

Applicant File Uploads

- Lemoine final report charts 2022 RAA.pdf

Tables and Figures

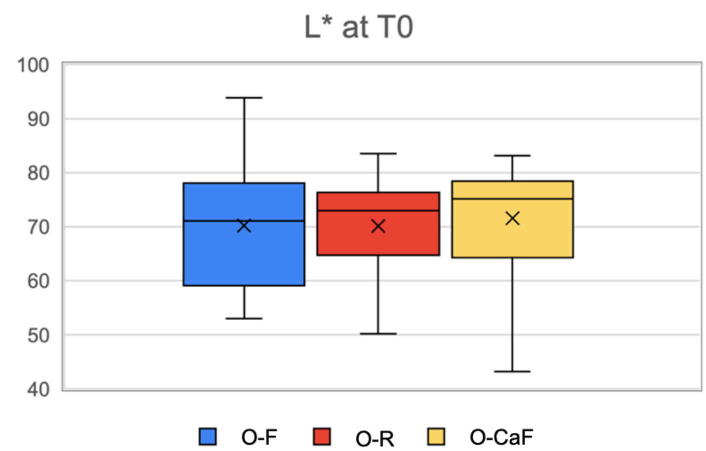


Figure 1. Average L* at T0

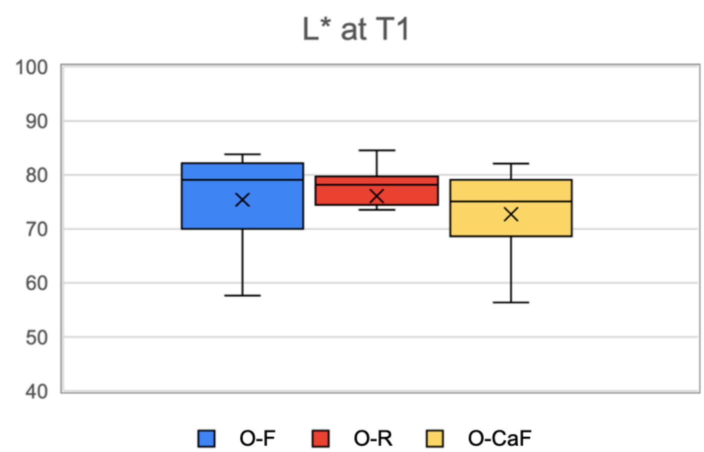


Figure 2. Average L* at T1

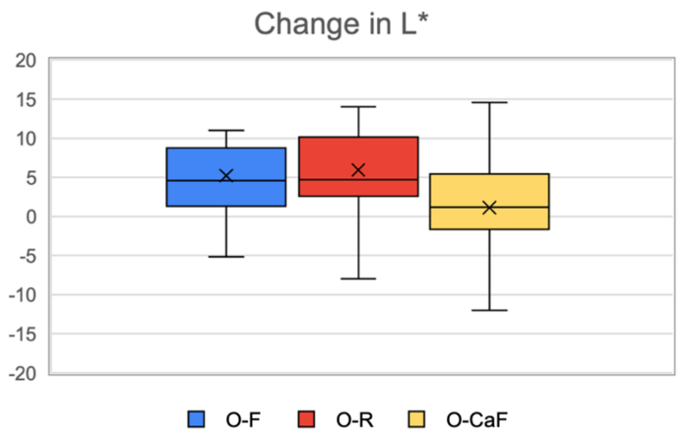


Figure 3. Average ΔL* between groups from T0 to T1

Dependent Variable	(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Before	1.00	2.00	.0916666658	3.258807215	1.000	-7.94679072	8.130124048
		3.00	-1.38500000	3.258807215	1.000	-9.42345738	6.653457383
	2.00	1.00	-.091666666	3.258807215	1.000	-8.13012405	7.946790716
		3.00	-1.47666667	3.258807215	1.000	-9.51512405	6.561790717
	3.00	1.00	1.384999999	3.258807215	1.000	-6.65345738	9.423457382
		2.00	1.476666665	3.258807215	1.000	-6.56179072	9.515124047
After	1.00	2.00	-.646666667	2.597894953	1.000	-7.05486037	5.761527034
		3.00	2.716666666	2.597894953	.900	-3.69152703	9.124860367
	2.00	1.00	.6466666667	2.597894953	1.000	-5.76152703	7.054860367
		3.00	3.363333333	2.597894953	.602	-3.04486037	9.771527033
	3.00	1.00	-2.71666667	2.597894953	.900	-9.12486037	3.691527034
		2.00	-3.36333333	2.597894953	.602	-9.77152703	3.044860367

Figure 4. ANCOVA results after Bonferroni corrections comparing mean differences in ΔL* between O-F (Group 1.00), O-R (Group 2.00), and O-CaF (Group 3.00)

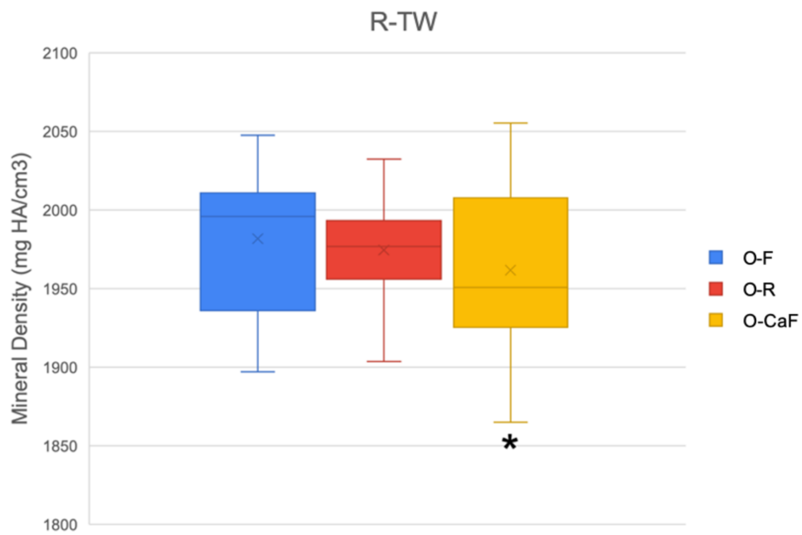


Figure 5. Mean mineral density in R-TW of groups at T1

Dependent Variable			Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
of BV (Material)	O-F	O-R	15.5868400	15.4081740	0.948	-22.420302	53.593982
		O-CaF	174.5529500*	15.4081740	**0.000**	136.545808	212.560092
	O-R	O-F	-15.5868400	15.4081740	0.948	-53.593982	22.420302
		O-CaF	158.9661100*	15.4081740	**0.000**	120.958968	196.973252
	O-CaF	O-F	-174.5529500*	15.4081740	**0.000**	-212.560092	-136.545808
		O-R	-158.9661100*	15.4081740	**0.000**	-196.973252	-120.958968

* The mean difference is significant at the 0.05 level.

Figure 6. ANOVA results with Bonferroni correction for multiple comparisons of mineral density in R-TW of groups O-F, O-R, and O-CaF

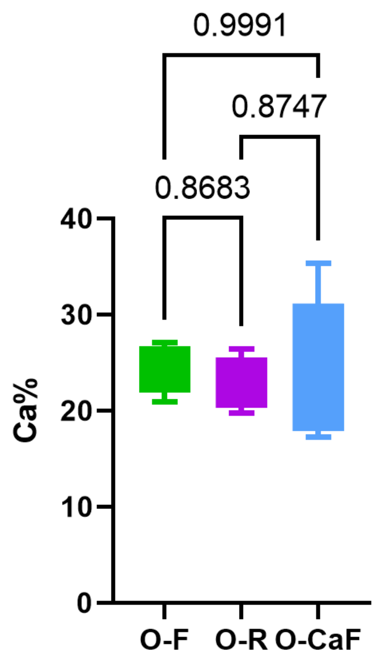


Figure 7. Mean Ca% in R-TW of groups at T1

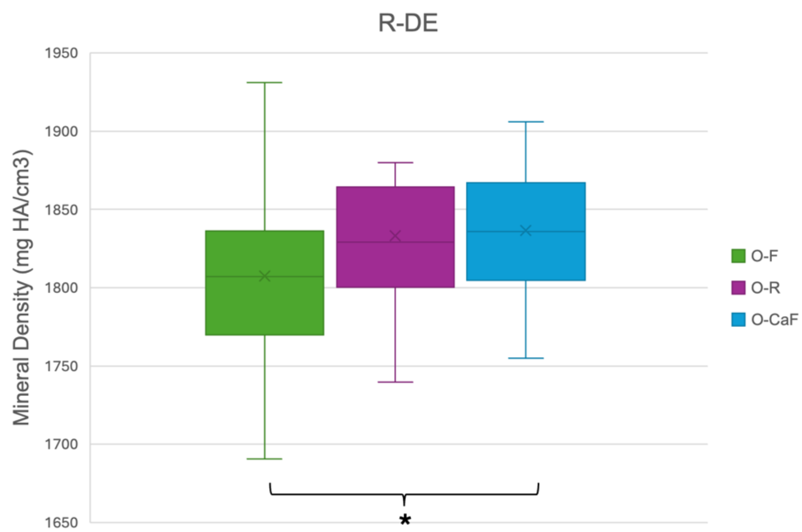


Figure 8. Mean mineral density in R-DE of groups at T1

Table 1. Mann-Whitney U test results comparing mean mineral density in R-SE at T1

	O-F to O-R	O-F to O-CaF
p-value	0.989	0.461

Table 2. Mann-Whitney U test results comparing mean mineral density in R-DE at T1

	O-F to O-R	O-F to O-CaF
p-value	0.142	0.049