

Simultaneous Non-Invasive Diagnosis and Therapeutic Treatment of Dental Caries

Layra Valdes¹, Juaana Xie¹, Ellen Yaacoub², Masahiko Maeno³, Yoshiki Ishida³, Hiroshi Ishikawa³, Hiroe Ohyama¹, Jirun Sun⁴, Shigemi Nagai¹

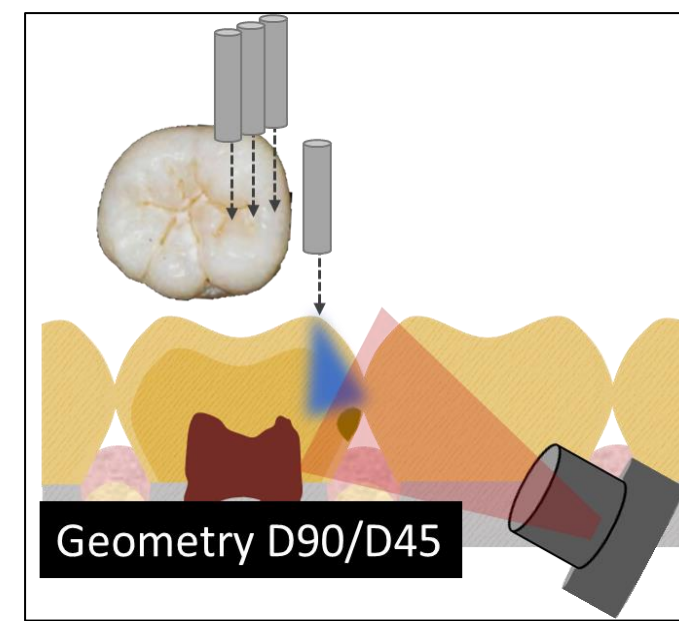
1: Harvard School of Dental Medicine, 2: International University Of Catalonia-Barcelona, 3: The Nippon Dental University, 4: ADA Forsyth Institute.

Introduction and Goal

Early diagnosis and treatment are vital for managing dental caries, a widespread chronic disease. Previous studies using OsteoSense (OS750) and etidronate showed promise in diagnosing and treating caries by promoting remineralization. Challenges like tooth autofluorescence and dye agglomeration arose. Our research aims to combine the benefits of OS750 and etidronate using Eti-BPP-QDs, utilizing surface-functionalized Ag2S quantum dots dispersed in etidronate solutions. BPP-QDs offer adjustable emission wavelengths, minimizing tooth autofluorescence with long-wavelength emission (> 900 nm) and enabling detection of advanced and incipient caries missed by radiographs. Moreover, BPP-QDs exhibit higher quantum yield and longer fluorescence life compared to OS750, enhancing sensitivity in caries diagnosis. The goal is to develop a novel dental varnish that detects and inhibits caries progression through a combination of bisphosphonate and quantum dots, enabling non-invasive optical diagnostic imaging with NIR fluorescence QDs emitting beyond the tooth autofluorescence region.

Aims and Methods

Aim 1: To detect dental caries using NIR fluorescence imaging with Eti-BPP-QDs created at Forsyth. Our diagnosis method involves ex vivo assessment using NIR Camera (Digital VIS-SWIR Camera, Ninox 1280). Human teeth were assembled in a typodont, created artificial caries lesion on occlusal and interproximal I surfaces. The D90/D45 optical geometry was used to capture fluorescence signal from lesions. Specificity and sensitivity were determined by comparing FL signals to bitewing radiography, considered the gold standard.



Aim 2: To assess the therapeutic efficacy of Eti-BPP-QDs to enamel and dentin caries. The therapeutic performance of the Eti-BPP-QDs on inhibiting caries progression of enamel and dentin caries was determined and compared to commercial fluoride varnish. The white-spot lesions were created on enamel and dentin specimens. Each specimen was treated by Eti-BPP-QDs, fluoride varnish or distilled water. The micro CT was taken before and after 2 cycles of demineralization challenges. The volume of each sample was measured and percentage of volume remained after 2 cycles of demineralization challenges was calculated.

Aim 3: To assess the impact of BPP treatment on tooth aesthetic and tooth structure.

Aim 3-1: We assessed the tooth color changes on enamel and dentin surface (n=4, human extracted teeth) treated by Eti-BPP-QDs and SDF using dental spectrophotometer (Crystaleye).

Aim 3-2: The adhesives' bonding strength of composite block on the Eti-BPP-QDs treated enamel surface (2 minuts) and non-treated enamel surface (control) were compared. A vertical cut was made horizontally to the tooth axis to divide it into mesio-distal areas, and the mesial area was used as the experimental tooth surface and the distal area was used as the control tooth surface. The specimens were etched (40 seconds), washed, dried and Eti-BPP-QDs was applied for 2 minutes. Both experimental and control tooth surfaces were bonded with resin composite block (Clearfil AP-X) with Clearfil SE bond 2(adhesive). Specimens were stored in distilled water at 37°C for 24 hours. The micro tensile adhesive strength was measured using the Instron machine (n=6).

Results

Aim 1. Accuracy of caries detection

Using geometry-D90/D45, fluorescence signal on the interproximal demineralized lesion was clearly detected (Figure 1). Diagnostic accuracy by 3 experienced restorative dentists indicated high specificity and sensitivity (Table 1).



Figure 1: NIR images on caries

Table 1: Diagnostic accuracy.

DMD	Sensitivity	Specificity	True Positive	False Positive	True Negative	False Negative
1	0.93	1	1	0	0.9	0.1
2	0.93	1	1	0	0.9	0.1
3	0.9	1	1	0	0.857	0.143

Aim 2. Therapeutic efficacy

The caries progression was seen after each of 2 treatment. Figure 2 shows micro CT images and reconstructed 3D images before and after 2 demineralization challenges. The lesion depth increased significantly. Average of percentage of volume remained after 2 challenge cycles on specimens treated by both NaF and Eti-BPP-QD was higher than control for enamel and dentin, but there was no significant difference (Figure 3, One way ANOVA)

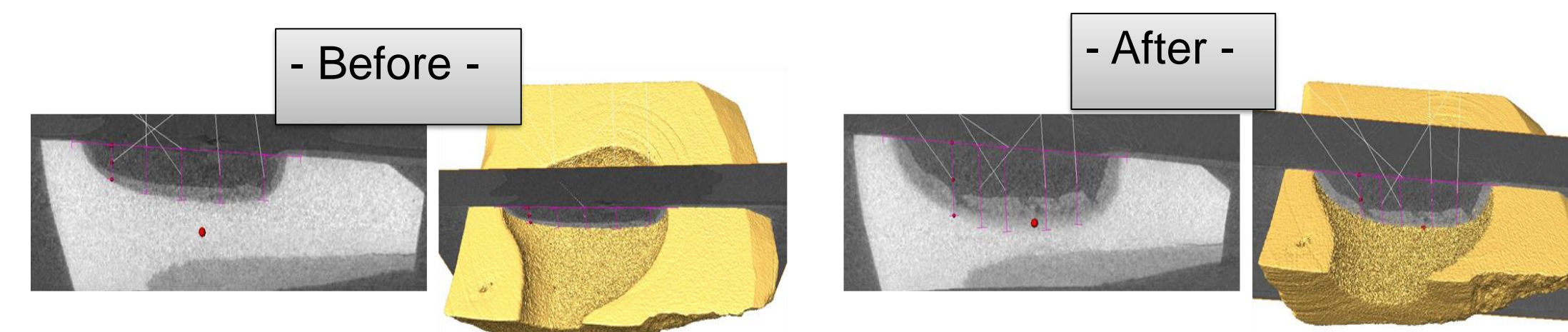


Figure 2: Micro CT and reconstructed 3D images before and after 2 demineralization cycles.

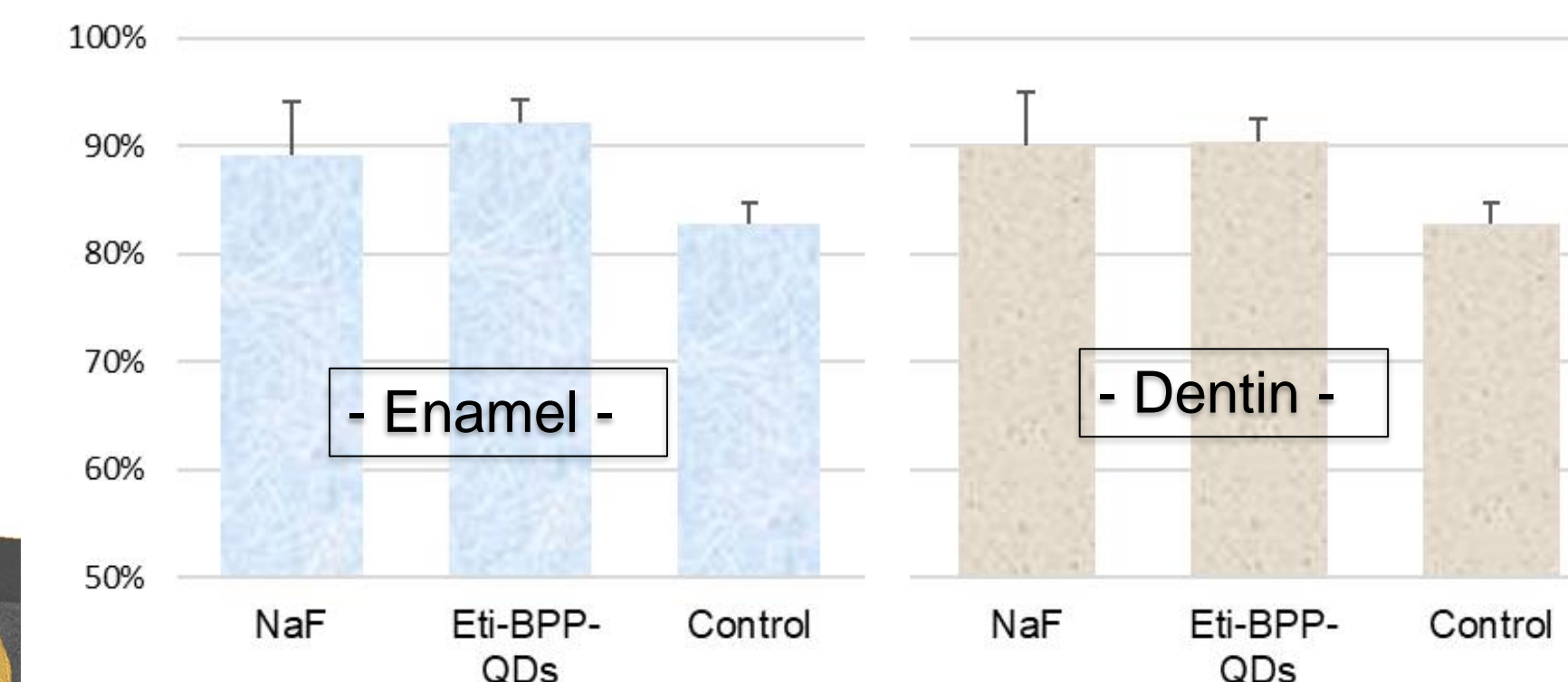


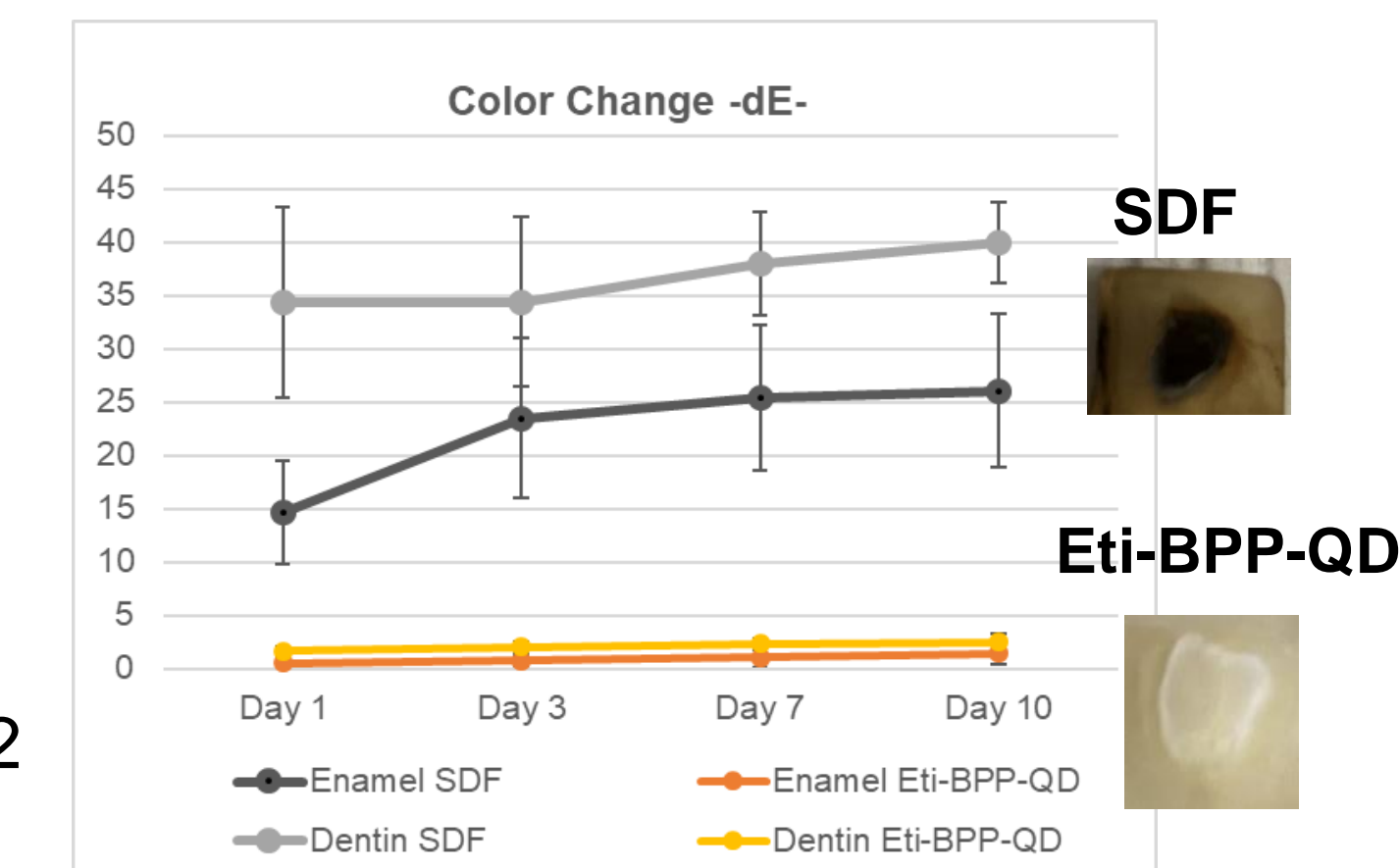
Figure 3: Average of percentage of volume remained after 2 challenge cycles in enamel and dentin group.

Aim 3-1. Color stability

The average CIE color difference dE values are shown in figure 4. $.2 \pm 1.4$ for control group. At 10 days, SDF groups indicated significantly larger dE than Eti-BPP-QD groups that dE values are clinically indistinguishable.

Aim 3-2. Bonding strength

The average bonding strength of Eti-BPP-QD group was 21.6 ± 3.3 and 22.2 ± 1.4 for control group. There was no statistical difference (Student t-test).



Conclusion

This study indicates a potential on clinical application for diagnostic and therapeutic treatment using Eti-BPP-QDs. There is a need of further investigations for therapeutic efficacy in mimicking in vivo condition.

References

- Sun, J.; Gil, M.; Khorashadi, S.; Chen, G.; Lee, C.; Ishida, Y.; Nagai, M.; Wada, S.; Ishikawa-Nagai, S.; Da Silva, J. D., Efficacy of bisphosphonates in detection of early enamel caries using NIR fluorescence imaging and inhibition of caries progression. *International Journal of Medical Sciences* 2021, 18 (13), 2971-2980.
- Gonzalez-Bonet, A.; Kaufman, G.; Yang, Y.; Wong, C.; Jackson, A.; Huyang, G.; Bowen, R.; Sun, J., Preparation of dental resins resistant to enzymatic and hydrolytic degradation in oral environments. *Biomacromolecules* 2015, 16, 3381-88.