Comparison of Intracanal EndoSequence Root Repair Material and ProRoot MTA to Induce pH Changes in Simulated Root Resorption Defects over 4 Weeks in Matched Pairs of Human Teeth

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Abstract

Introduction: Intracanal mineral trioxide aggregate (MTA) may provide an alternative to calcium hydroxide in the treatment of external inflammatory root resorption. This *in vitro* study using human matched pairs of teeth compared white ProRoot MTA (WMTA; (Dentsply Tulsa Dental Specialties, Tulsa, OK) and an alternative material with purportedly improved handling properties, EndoSequence Root Repair Material (ES; Brasseler USA, Savannah, GA), by measuring pH in simulated root surface resorptive defects after intracanal placement. The null hypothesis tested was that there is no difference between WMTA and ES. **Methods:** Bilaterally matched pairs (n = 24) of extracted, human, single-rooted teeth were instrumented to apical size 50/.06, and root surface cavities were prepared at 5 mm and 2 mm from the apex. Root canals of experimental matched pairs (n = 20) were filled with WMTA or ES; control pairs (n = 4) were filled with calcium hydroxide (positive control [POS]) or saline (negative control [NEG]). Teeth were sealed coronally and apically and immersed in saline. The pH in root surface cavities was measured at 20 minutes, 3 hours, 24 hours, 1 week, 2 weeks, 3 weeks, and 4 weeks. **Results:** The pH at 5 mm when compared with the 2-mm level was significantly higher for the WMTA, ES, and POS groups ($P < .05$, paired t tests); therefore, each level was analyzed separately. At both the 2-mm and 5-mm levels, significant pH changes occurred over time in the WMTA, ES (both $P < .0001$, repeated-measures analysis of variance), and POS ($P < .0001$, Friedman test) groups and not in the NEG group (mean pH = 7.32 $\pm$ 0.04, $P > .05$). There were no differences between WMTA and ES at 20 minutes and 3 hours at both levels or at 24 hours at 5mm. The pH of WMTA was higher than ES by 24 hours at the 2-mm level (8.79 vs 8.56, $P < .05$, paired t test) and after 1 week at the 5-mm level (8.91 vs 8.05, $P < .0001$) and was thereafter always significantly higher in WMTA compared with ES ($P < .0001$). The null hypothesis was rejected. **Conclusions:** In matched pairs of teeth, intracanal placement of WMTA compared with ES resulted in a higher pH in simulated root resorption defects that was time and root level dependent. *(J Endod 2011;37:502–506)*

Key Words

4 weeks, calcium hydroxide, dentin, diffusion, EndoSequence Root Repair Material, human, hydroxyl ion, *in vitro*, matched pairs, mineral trioxide aggregate, pH, pH changes, ProRoot 14 MTA, root canal, root resorption, root surface cavities, saline, simulated root resorption defects, teeth

Calcium hydroxide ($Ca[OH]_2$) has been advocated as an intracanal medicament in the treatment of external inflammatory root resorption (1–3). The treatment rationale for $Ca(OH)_2$ is its highly alkaline pH, which is bactericidal and induces limited necrosis of the resorptive cells on the root surface (4–6), and the inactivation of lipopolysaccharide, a potent inducer of inflammation (7). Although this treatment modality has wide acceptance and use, concerns regarding weakening of roots leading to increased susceptibility to fracture along with patient compliance have been raised (8, 9).

Mineral trioxide aggregate (MTA) has many endodontic applications (10). Among its desirable properties, MTA is biocompatible, exhibits good sealing ability, is bioactive inducing hydroxylapatite formation, and shows high alkalinity during and after its setting reaction (11–13). MTA has also been shown to release $Ca(OH)_2$ as a principal compound once hydrated (14). These properties of MTA have led to the consideration of its use as an obturation material (15). MTA use might mitigate the potential weakening of roots associated with long-term $Ca(OH)_2$ treatment and patient noncompliance with regard to multiple treatment visits (8, 9).

The search for bioceramic materials exhibiting properties similar to MTA but with improved handling characteristics and shorter setting times has led to the development of EndoSequence Root Repair Material (ES) (Brasseler USA, Savannah, GA). According to the manufacturer, this material is composed of calcium silicates, zirconium oxide, tantalum oxide, calcium phosphate monobasic, and filler agents. ES is manufactured in a premixed state (moldable putty form and in a preloaded syringe with delivery tips appropriate for intracanal delivery of the material) with a working time of 30+ minutes and a setting reaction initiated by moisture with a final set achieved approximately 4 hours thereafter.

The manufacturer describes ES as having antibacterial properties during its setting reaction because of a high alkaline pH. These properties would support its use as an alternative to $Ca(OH)_2$ or MTA in the treatment of external inflammatory root resorption. Because the extent and duration of the elevated pH on the external root surface are not known, the aim of this study was to compare intracanal ES and white ProRoot MTA (WMTA) (Dentsply Tulsa Dental Specialties, Tulsa, OK) in the diffusion of hydroxyl ions through dentin. The null hypothesis tested was that there is no difference.

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Materials and Methods

Tooth Selection

The study was approved by the Research Integrity Office at Oregon Health and Science University, Portland, OR. The protocol used was based on previous studies (16–18). Twenty-four matched pairs of freshly extracted, human teeth were collected and stored in 0.9% unbuffered sterile saline (saline) at room temperature (total $n = 48$ teeth). Teeth included single-rooted, mature, maxillary incisors and canines and mandibular premolars and canines all with intact crowns. Radiographs (buccolingual and mesiodistal angulations) were used to verify the presence of a single canal and to ensure similar root dimensions and canal morphology within each matched pair. Teeth were gently debrided of any exterior soft tissue, taking care to avoid damage to cementum.

Tooth Preparation

To simulate root resorption defects, buccal root surface cavity preparations measuring 0.7-mm deep and 1.4 mm in diameter were made at 2 mm and 5 mm from the apex using a high-speed 1.4-mm carbide round bur (Brasseler) with water coolant. The cavities were filled with 17% neutral-buffered EDTA (Pulpdent Corp, Watertown, MA) for 3 minutes and then flushed with sterile distilled water. Teeth were then decoronated to a standard length of 10 mm.

The root canal working length (WL) was determined by inserting a #10 C-File (Dentsply Tulsa Dental Specialties) until just visible at the apical foramen under 10 × magnification and then subtracting 0.5 mm. Root canals were prepared using a crown-down technique with EndoSequence Rotary Files (Brasseler) to a master apical file size of 50/.06 with irrigation of 0.5 mL of 6.0% sodium hypochlorite (NaOCl) (Clorox Regular-Bleach; The Clorox Company, Oakland, CA) between each instrument using a 30-G ProRinse irrigation needle (Dentsply). At the completion of instrumentation, canals were irrigated with 3 mL EDTA over 3 minutes followed by 3 mL NaOCl to remove the smear layer (19) and then 2 mL 5% sodium thiosulphate solution to inactivate the NaOCl followed by 10 mL saline; the canals were then dried with paper points.

The 24 matched pairs of roots were randomly assigned to experimental ($n = 20$ matched pairs) or control ($n = 4$ matched pairs) groups (http://www.random.org/). The experimental groups were as follows: (1) ES for the placement of intracanal EndoSequence and (2) WMTA for the placement of intracanal WMTA. The control groups were as follows: (1) POS for the placement of intracanal calcium hydroxide (the positive control) and (2) NEG for the placement of intracanal saline (the negative control).

Placement of Intracanal Materials and Determination of pH

Experimental materials were prepared and handled according to the manufacturers' instructions. The pH of the experimental and control materials was measured immediately before placement in each of the respective canals using a calibrated microelectrode (model MI 415/2; Microelectrodes, Inc, Londonderry, NH) and pH meter (Accumet Basic AB15 pH Meter; Thermo Fisher Scientific Inc, Waltham, MA) at room temperature.

Canals of each matched pair of experimental teeth were filled with either ES or WMTA to a level 8 mm from the WL. In the ES group, canals were filled using the manufacturer-provided preloaded syringe with the delivery tip inserted to just short of its binding point in the canal (approximately 1 mm short of the WL) followed by backfill. In the WMTA group, canals were filled by placing the mixed WMTA in the canals with an amalgam carrier and condensing to the WL using Buchanan pluggers (SybronEndo Corp, Orange, CA) and paper points. Canals in the POS group were filled with $Ca(OH)_2$ paste (UltraCal XS [a 0.35 w/w aqueous calcium hydroxide paste]; UltraDent Products Inc, South Jordan, UT) using 30-G NaviTips (UltraDent) inserted to 1 mm from the WL; the canals were filled to a level 8 mm from the WL. Canals in the NEG group were filled with saline using a 30-G ProRinse irrigation needle inserted to the WL.

After root filling, the specimens were radiographed (Suni CCD sensor size 2; Suni Medical Imaging Inc, San Jose, CA) from a mesiodistal dimension; if voids in the material were detected, they were rinsed out with distilled water and replaced until seen to be free of radiographic voids from the WL to a distance 2 mm short of the coronal access. The images were imported into Emago Advanced Diagnostic Radiography System (Oral Diagnostic Systems, Amsterdam, The Netherlands), and the calibrated Emago measurement tool was used to measure the remaining dentin thickness from the base of the defects to the wall of the canal at both levels in each root specimen.

Sticky wax (Kerr Corporation, Orange, CA) was used to seal the coronal access and apex and to mount the coronal aspect of the root on the internal surface of a 20-mL scintillation vial polypropylene lid (Sigma-Aldrich Corp, St Louis, MO). Each root was then completely immersed in saline in a scintillation vial and stored at 37°C.

The pH at the base of each root surface cavity was measured after 20 minutes, 3 hours, 24 hours, 1 week, 2 weeks, 3 weeks, and 4 weeks as follows. Each tooth was removed from its vial, rinsed with distilled water, and lightly blotted dry using sterile 2 × 2-inch gauze. Distilled water was placed in the root surface cavities and allowed to stand for 10 minutes before measuring pH. The microelectrode was recalibrated after every five samples.

At the completion of the 4-week evaluation, each root was sectioned perpendicular to its long axis through the center of the cavities at the 2-mm and 5-mm levels and examined at approximately ×5 magnification for extent of obturation and consistency of intracanal material using the tip of an endodontic explorer.

Statistical Analysis

Paired *t* tests were used to compare pH values at the 2-mm and 5-mm levels of the same tooth and to compare matched pairs of teeth. Changes in pH over time were analyzed using repeated-measures analysis of variance for the ES and WMTA groups and the Friedman test for the POS and NEG groups. Prism 4.0a for Macintosh software (GraphPad Software, Inc, La Jolla, CA) was used for statistical analyses. Significance was set at $P < .05$.

Results

The pH measurements of the materials immediately before their placement in the canal were 12.40 (ES), 12.57 (WMTA), 12.36 ($Ca[OH]_2$), and 6.52 (saline). After root surface cavity preparation, the remaining dentin thickness at the 2-mm and 5-mm levels ranged from 0.2 to 0.5 mm (mean 0.4 mm) and 0.7 to 1.2 mm (mean 0.9 mm), respectively. The mean pH values at the 2-mm and 5-mm levels at each time point are shown in Table 1.

Intragroup Effects

For the WMTA, ES, and POS groups, the pH was significantly higher at the 5-mm level compared with the 2-mm level ($P < .0001$, paired *t* tests), and therefore the data for each level were analyzed separately. At each of the 2-mm and 5-mm levels, significant pH changes occurred over time in the WMTA, ES (both $P < .0001$, repeated-measures analysis of variance), and POS ($P < .0001$, Friedman test) groups and not in the NEG group ($P > .05$, Friedman test); pH values declined

TABLE 1. pH Readings in Simulated Root Resorption Defects over 4 Weeks in Matched Pairs of Human Teeth

		Experimental (n = 20 matched pairs)																				
		Time																				
		20 min			3 h			24 h			1 wk			2 wk			3 wk			4wk		
Group	Apical Level	Mean	SD	SEM	Mean	SD	SEM	Mean	SD	SEM	Mean	SD	SEM	Mean	SD	SEM	Mean	SD	SEM	Mean	SD	SEM
ES	2 mm	8.39	0.67	0.15	8.56	0.69	0.15	8.56	0.48	0.11	7.91	0.48	0.11	7.47	0.22	0.05	7.30	0.12	0.03	7.36	0.06	0.01
	5 mm	8.77	0.43	0.10	8.99	0.49	0.11	8.81	0.44	0.10	8.05	0.51	0.11	7.59	0.25	0.06	7.41	0.17	0.04	7.44	0.12	0.03
WMTA	2 mm	8.73	0.64	0.14	8.74	0.51	0.12	8.79	0.41	0.09	8.77	0.39	0.09	8.27	0.28	0.06	7.74	0.35	0.08	7.57	0.20	0.04
	5 mm	9.02	0.64	0.14	9.10	0.64	0.14	8.94	0.39	0.09	8.91	0.37	0.08	8.42	0.38	0.08	7.91	0.28	0.06	7.76	0.25	0.05
		Controls (n = 4 matched pairs)																				
		Time																				
		20 min			3 h			24 h			1 wk			2 wk			3 wk			4wk		
Group	Apical Level	Mean	SD	SEM	Mean	SD	SEM	Mean	SD	SEM	Mean	SD	SEM	Mean	SD	SEM	Mean	SD	SEM	Mean	SD	SEM
POS	2 mm	9.18	0.40	0.20	9.31	0.32	0.16	9.31	0.27	0.13	9.26	0.15	0.07	9.14	0.18	0.09	8.40	0.27	0.14	8.04	0.23	0.11
	5 mm	9.43	0.35	0.17	9.49	0.34	0.17	9.48	0.31	0.15	9.51	0.36	0.18	9.18	0.18	0.09	8.52	0.25	0.12	8.11	0.32	0.16
NEG	2 mm	7.35	0.07	0.04	7.39	0.08	0.04	7.35	0.05	0.02	7.30	0.04	0.02	7.26	0.04	0.02	7.29	0.07	0.04	7.27	0.06	0.03
	5 mm	7.35	0.12	0.06	7.38	0.10	0.05	7.34	0.02	0.01	7.37	0.03	0.02	7.25	0.04	0.02	7.29	0.02	0.01	7.34	0.04	0.02

SD, standard deviation; SEM, standard error of the mean.

during the 24-hour and 1-week evaluations in the ES group and between the 1-week and 2-week evaluations in the WMTA group. By 4 weeks, pH levels for both the WMTA and ES groups were similar to the NEG group.

Intergroup Effects

There were no differences between the WMTA and ES groups at 20 minutes and 3 hours at either of the 2-mm and 5-mm levels and between WMTA and ES at 24 hours at the 5-mm level. At all other time points, the pH was significantly higher in the WMTA group compared with the ES group ($P < .05$ at 24 hours at the 2-mm level, all others $P < .0001$, paired t tests) (Fig. 1).

Sectioned teeth viewed at approximately × 5 magnification at 4 weeks showed complete obturation of the canal space at both the 2-mm and 5-mm levels, with both the WMTA and ES showing a hard set on probing with the tip of an explorer. The positive control samples contained unset white $Ca(OH)_2$ paste at both levels examined.

Discussion

This *in vitro study* showed that there were time- and root level–dependent differences between intracanal ES and WMTA with regard to diffusion of hydroxyl ions through root dentin. Although both materials showed diffusion of ions through dentin, this effect was less pronounced closer to the apex and was sustained for a longer duration in the WMTA group. The null hypothesis was rejected.

The experimental methodology was based on previous studies (16–18). Simulated resorptive defects were standardized in terms of the depth of defect (0.7 mm). The influence of variations between teeth in the distance between the base of the defect and the approximating canal wall was minimized by using a matched-pairs study design. The diffusion of hydroxyl ions through simulated root defects over 4 weeks in matched pairs of teeth obturated with either WMTA or ES was measured in root surface cavities positioned at 2 mm and 5 mm from the apex. There were significantly lower pH values in the WMTA, ES, and POS groups observed at the 2-mm level. These observations are consistent with those of Nerwich et al (17) and might be attributed to the orientation and diminishing number and diameter of dentinal tubules in the apical portion of roots (20–22).

ES represents a new bioceramic endodontic material available in preloaded syringeable and moldable putty forms. Cell cytotoxicity tests [MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assays] using L929 cells showed no difference between either set or freshly mixed states of ES and white or gray MTA (23), but the form of ES tested was not described. In this study, WMTA had a more prolonged release of hydroxyl ions compared with the preloaded syringeable form of ES; the putty form was not tested.

The time intervals selected for testing were based on the setting times of the experimental materials and previous studies (16–18, 21, 24, 25). The diffusion of hydroxyl ions during the first 24 hours for each of the experimental materials was similar; however, this was followed by a steeper decline in pH for ES compared with WMTA for the remainder of the 4-week experiment. This might be explained by differences between the materials in their initial and final setting time and their time required to fully cure. According to the manufacturer, ProRoot MTA sets over a period of 4 hours and requires approximately 4 weeks to fully cure. These reported times might vary because white MTA has been reported to have an initial setting time of 40 ± 2.94 minutes and a final setting time of 140 ± 2.58 minutes (26). The final setting time for ES has been reported as 4 hours (27), and no account could be found on the final curing time. However, the observed decrease in the pH of ES between 24 hours and 1 week might be attributable to the material reaching a full cure at that time, whereas

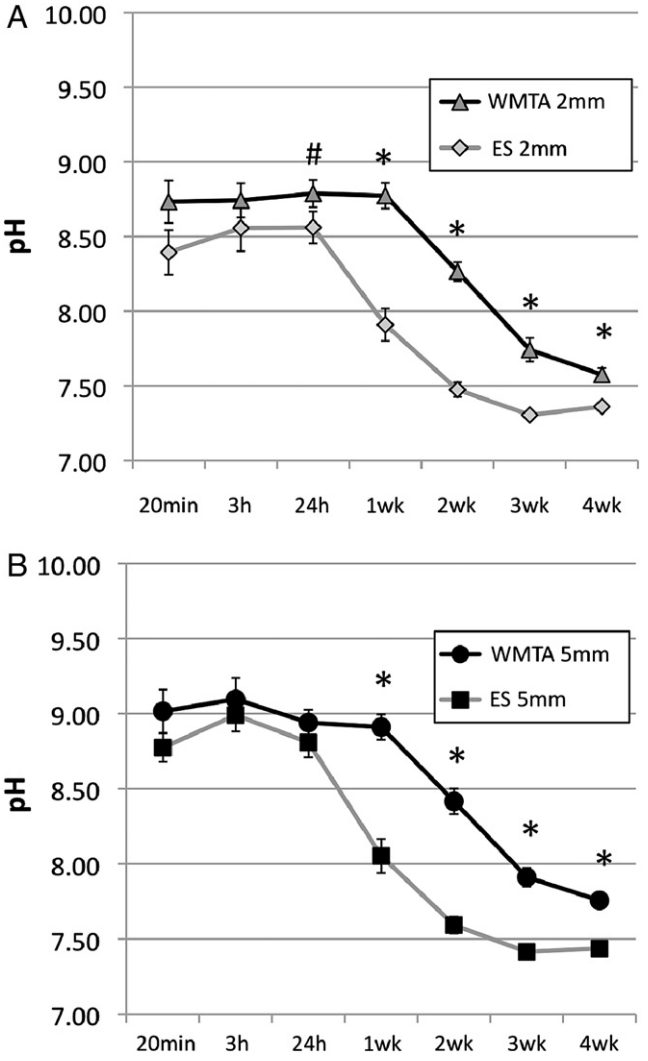

Figure 1. Mean pH values in root surface cavities prepared at (*A*) 2 mm and (*B*) 5 mm after root canals were filled with WMTA or ES. The symbols represent significant differences between WMTA and ES at each time point (#$P <$ .05, *$P <$ .0001). Data points represent mean ± standard error of the mean from 20 matched pair samples.

MTA continues to cure over a period of several weeks with continual leaching of ionic components (14, 21). Future studies could include additional evaluations between 24 hours and 1 week and 1 week and 2 weeks to further investigate these observations.

In this study, although both materials exhibited an elevated pH, this was higher in the WMTA group and was sustained for a longer period. Fridland and Rosado (28) described hydroxyl ion release from WMTA samples immersed in water that was sustained for up to 78 days. In contrast to this and other studies confirming significant pH increases on the surface of roots filled with MTA and $Ca(OH)_2$ (17, 18), Özdemir et al (21) found no rise in pH subsequent to intracanal MTA placement. The differences between these and other diffusion studies might be attributable to experimental variables that include whether the diffusion of hydroxyl ions through root dentin is measured in immersion media (21, 25) or in root surface cavities placed at various levels (16–18, 29) and whether immersion solutions are changed (17) or retained (16, 18) throughout the duration of the experiment.

No statistical comparisons were made between experimental and control groups in view of their unmatched status and group size

discrepancies. The saline negative controls maintained a constant pH throughout the study period as expected; however, the overall mean pH value of 7.32 reported here is lower than other reports of 7.6 to 8.3 (17) and ~8.3 (18); this difference might be attributed to methodological differences, including the use of sodium thiosulfate to inactivate the effects of NaOCl. The pH values of the $Ca(OH)_2$ positive control group are in agreement with previous observations using the same $Ca(OH)_2$ product with an overall average pH of 9.3 through 2 weeks and a steady decline thereafter (18). These findings contrast with reports of extended release of hydroxyl ions from roots filled with $Ca(OH)_2$ over 28 days (17) and 120 days (29). These difference might be explained in part by variations between different formulations because ionic dissociation of $Ca(OH)_2$ is dependent on the specific formulation used (29–31).

Within 20 minutes of the placement of the ES, WMTA, and $Ca(OH)_2$ material, an increase in the pH could be detected. Others have reported a more gradual increase in pH over a period of days to weeks (17, 18). Reasons for this disparity might be deeper cavity preparations with a subsequent decrease in dentin thickness with a potential lessening of buffering capacity (32). Smear layer removal from both intracanal dentin and in the root surface cavities might also allow for more rapid pH changes (33).

At the 24-hour observation period, it was noted that some of the WMTA root samples had discolored. By 1 week, all of the WMTA root samples had become discolored, whereas all of the ES samples maintained their original color throughout the study period. These findings are consistent with previous reports (34, 35) and could have clinical significance with regards to esthetics, especially in anterior teeth.

In the absence of long-term clinical studies, support for different protocols and materials to arrest external inflammatory root resorption relies on information from *in vitro* studies such as the evaluation of diffusion of hydroxyl ions through root dentin defects (17, 18, 21, 25, 33). In this study, intracanal placement of both WMTA and ES resulted in the diffusion of hydroxyl ions across dentin that was sustained for a longer period in the WMTA group. In the ES group, pH values declined during the 24-hour and 1-week evaluations compared with 1 week and 2 weeks in the WMTA group. By 4 weeks, pH levels for both WMTA and ES were similar to the negative control.

Acknowledgments

The authors deny any conflicts of interest related to this study.

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