Histology of NeoMTA Plus and Quick-Set2 in Contact with Pulp and Periradicular Tissues in a Canine Model

Ryan M. Walsh, DDS, MS, Karl F. Woodmansey, DDS, MA,‡ Jianing He, PhD, DDS,† Kathy K. Svoboda, PhD,* Carolyn M. Primus, PhD,§ and Lynne A. Opperman, PhD**

Abstract

Introduction: NeoMTA Plus (Avalon Biomed Inc, Bradenton, FL) is a tricalcium silicate material similar to the first mineral trioxide aggregate product, ProRoot MTA (Dentsply Sirona, York, PA), but with improvements such as decreased setting time, increased ion release, increased water sorption, and nonstaining radiopacifiers. Quick-Set2 (Avalon Biomed Inc) is a newly formulated calcium aluminosilicate material that has a faster setting time and increased acid resistance and is nonstaining. The purpose of this study was to compare the healing of pulpal and periapical tissues in dogs after exposure to NeoMTA Plus and Quick-Set2 after pulpotomy and root-end surgery procedures. **Methods:** Seventy-two teeth (36 for each procedure) in 6 beagle dogs received pulpotomy or root-end surgery using either NeoMTA Plus or Quick-Set2. The dogs were sacrificed at 90 days, and the teeth and surrounding tissues were prepared for histologic evaluation. Sixty teeth were evaluated and scored histologically (29 with pulpotomies and 31 with root-end resections). Specimens were scored for inflammation, quality and thickness of dentin bridging, pulp tissue response, cementum and periodontal ligament formation, and apical bone healing. **Results:** Both materials displayed favorable healing at 90 days. The only significant difference was the quality of dentin bridge formation in pulpotomies using NeoMTA Plus compared with Quick-Set2. **Conclusions:** Quick-Set2 and NeoMTA Plus had similar effects on inflammation, pulp response, periodontal ligament and cementum formation, and apical tissue healing in dogs. NeoMTA Plus had superior dentin bridge quality compared with Quick-Set2. *(J Endod 2018;44:1389–1395)*

Key Words

Bioceramic, calcium aluminate, NeoMTA Plus, pulpotomy, Quick-Set2, root-end surgery, tricalcium silicate

Significance

Currently, no *in vivo* animal studies have been performed on the calcium aluminate material Quick-Set2. This study histologically evaluates the pulpal and periapical healing of Quick-Set2, a calcium aluminate, and NeoMTA Plus, a tricalcium silicate, in pulpotomies and root-end fillings in a canine model. If determined suitable for use in a canine model, these materials may be investigated further in a human clinical trial.

For the past 2 decades, the original hydraulic tricalcium silicate cement used in dentistry has been ProRoot MTA (Dentsply Sirona, York, PA). Despite clinical and commercial success for the past 2 decades, ProRoot MTA has suffered from clinician criticism because of its poor handling, long setting time, tooth discoloration, and high cost. To overcome the shortcomings of ProRoot MTA, several newer hydraulic tricalcium silicate cements have been developed with easier handling, faster setting, improved washout resistance, and lower material costs.

When considering bioceramic cements for dental uses, 2 primary categories have been tested: tricalcium silicates (mineral trioxide aggregate [MTA]-like materials) and calcium aluminosilicates (Quick-Set & Quick-Set2 [Avalon Biomed Inc, Bradenton, FL]), Capasio [Primus Consulting, Bradenton FL], and Endobinder [Binderware, Sao Carlos, Brazil]). MTA Plus and NeoMTA Plus (Avalon Biomed Inc) are tricalcium silicate–based materials (1, 2). Both MTA Plus and NeoMTA Plus kits contain a cement powder and an identical gel that when mixed have easier handling and washout resistance (3–5). The powder of MTA Plus has a finer particle size than ProRoot MTA, which may contribute to its decreased setting time, increased ion release, increased water sorption, and decreased porosity compared with ProRoot MTA (6, 7). MTA Plus has shown an equivalent favorable biological response to ProRoot MTA (3, 8). MTA Plus and NeoMTA Plus are indistinguishable materials with the exception of the radiopacifying agent (1, 2). NeoMTA Plus contains tantalum oxide as a radiopacifier, rather than bismuth oxide, to prevent postprocedural tooth discoloration (8). NeoMTA Plus has shown biological properties similar to MTA Plus and has been marketed for clinical use since 2013 (9).

Much less scientific literature is available regarding the calcium aluminate–based biomaterials. The Endobinder calcium aluminate material has been successfully tested for the repair of bony defects (10). Subcutaneous implantation showed its biocompatibility in rats (11). The physical properties and sealing ability of Endobinder are similar to other tricalcium silicate materials (12).

From the Departments of *Biomedical Sciences and †Endodontics, Center for Craniofacial Research and Diagnosis, Texas A&M University College of Dentistry, Texas; ‡Center for Advanced Dental Education, St. Louis University, St. Louis, Missouri; and §Lake Erie College of Osteopathic Medicine, School of Dental Medicine, Bradenton, Florida.

Address requests for reprints to Dr Ryan M. Walsh, Departments of Biomedical Sciences and Endodontics, Center for Craniofacial Research and Diagnosis, Texas A&M University College of Dentistry, 3302 Gaston Avenue, Dallas, TX 75246. E-mail address: ryan.walsh.dds@gmail.com

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Like its predecessors, Quick-Set and Capasio, Quick-Set2 is reported to have a similar short setting time, final pH, tubule penetration, acid resistance, and washout resistance (13–15). Both Quick-Set and Quick-Set2 have been shown to be as biocompatible as ProRoot MTA *in vitro*, and Quick-Set has demonstrated favorable healing and osteogenic/dentinogenic properties in *in vivo* animal models (16–19). Also, Quick-Set has similar osteogenic/dentinogenic properties to ProRoot MTA *in vitro* (19).

Quick-Set2 is composed of a calcium aluminosilicate powder, a radiopacifier, and other proprietary components mixed with a unique water-based gel. Like NeoMTA Plus, Quick-Set2 also contains tantalum oxide as the radiopacifier to avoid tooth discoloration associated with the presence of bismuth oxide, which is present in ProRoot MTA and some other MTA-type materials (20). Additionally, Quick-Set2 contains fewer free alumina particles than the predecessor materials Quick-Set and Capasio. The free alumina particles in Quick-Set were hypothesized to cause histologic evidence of inflammation in the periapical region after endodontic procedures in canines (20–22). However, no *in vivo* animal studies have been performed on Quick-Set2. The purpose of this study was to histologically evaluate the pulpal and periapical healing of Quick-Set2 compared with NeoMTA Plus in pulpotomies and root-end fillings in a canine model.

Materials and Methods

The study was approved by the Institutional Animal Care and Use Committee, Texas A&M University College of Dentistry, Dallas, TX. Seventy-two teeth were treated in 6 beagle dogs to evaluate healing of pulpal tissues after endodontic procedures with either Quick-Set2 or NeoMTA Plus (Table 1). The material assigned to each tooth was randomized by a computerized random sequence generator. Both materials were mixed with their corresponding gel according to the manufacturer's recommendations. Thirty-six maxillary premolar teeth received pulpotomy procedures with a puttylike mixture of either material. The distal roots of mandibular premolars were instrumented and obturated with either material mixed to a putty consistency. Immediately after the orthograde treatment, an apicoectomy was performed on the distal root. This procedure simulated root canal treatment followed by root-end resection, which may be performed after root canal treatment failure, further minimizing the treatment time and the animal's trauma. For the pulpotomy and root-end filling procedures, the powder was mixed at approximately a 3:1 powder-to-gel ratio to achieve a puttylike consistency. Clinical procedures were similar to those reported previously (21, 22). Before every procedure, 11 mg/kg clindamycin was injected intramuscularly 1 hour preoperatively, and then 2.2 mg/kg ketamine and 0.22 mg/kg xylazine 100 were delivered intramuscularly to induce general anesthesia. The dogs were intubated and 1 L/min 1%–2% isoflurane in oxygen was used as an inhalational anesthetic throughout the procedure. Local anesthesia with 3.6 mL 2% lidocaine with 1:100,000 epinephrine (Novocol Pharmaceutical, Cambridge, Ontario, Canada) was achieved. For the surgical procedures, an additional 1.8–3.6 mL 2% lidocaine with 1:50,000 epinephrine (Novocol Pharmaceutical) was injected for hemostasis adjacent to the apices of teeth planned for resection. Preoperative digital radiographs of the teeth were obtained. Then, the teeth were cleaned of debris using an ultrasonic scaler (NSK Dental, Chicago, IL) and disinfected with 0.12% chlorhexidine (Patterson Dental, Southlake, TX).

Pulpotomy

The teeth were isolated with a dental dam for the pulpotomy procedures. The pulpotomy procedures followed the protocol of Dominguez et al (23). The access preparations and coronal pulp removal were made using 3 to 3.5× magnification and high-speed #4 carbide round burs. The pulp chambers were irrigated with 10 mL 6% sodium hypochlorite until hemostasis was achieved. Each material was mixed according to the manufacturer's directions, and then the material was gently placed over the pulp tissues and the chamber floor to a depth of approximately 3 mm. The access cavities were restored with Ketac Nano Light-Curing Glass Ionomer (3M ESPE, St Paul, MN), and the occlusion was adjusted to ensure no occlusal trauma. Posttreatment radiographs were obtained after all the other procedures.

Root-end Surgery

The surgical phase was performed immediately after the nonsurgical root canal treatment of mandibular premolars. An additional 1.8–3.6 mL 2% lidocaine with 1:50,000 epinephrine (Novocol Pharmaceutical) was injected for hemostasis adjacent to the apices of teeth planned for resection. A buccal, full-thickness, mucoperiosteal flap was reflected. Osteotomies approximately 5 mm in diameter were made using a Lindemann bone bur (Hu-Friedy, Chicago, IL) at the apex of each distal root. Approximately 3 mm was resected from the distal roots to expose the root filling materials to the periapical tissues. Saline irrigation was used continuously during the osteotomy and root-end resection. Flaps were reapproximated and closed with 4-0 Vicryl sutures (Ethicon, Somerville, NJ).

The dogs were restricted to a soft diet for 90 days postoperatively. Postoperative care included an intramuscular injection of 2.0 mg/kg ketoprofen immediately after the procedures to control inflammation. After surgery, 2 mg/kg nalbuphine was administered subcutaneously immediately and every 12 hours for 1 week postoperatively for pain control. The dogs were sacrificed 90 days after surgery with methods in accordance with the recommendations of the Panel on Euthanasia of the American Veterinary Medical Association using 2.2 mg/kg ketamine intramuscularly, 0.22 mg/kg xylazine 100 intramuscularly, and 2 mL Beuthanasia-D (Merck Animal Health, Millsboro, MI) (24). One liter of normal saline was used to flush the blood from the head followed by perfusion with 1 L 70% ethanol. Block sections of

TABLE 1. Procedures and Teeth for Testing

Teeth	Procedure	No. of teeth/roots treated			No. of teeth/roots scored/analyzed		
		Experimental (QS2)	Control (NMTA)	Total treated	Experimental (QS2)	Control (NMTA)	Total teeth analyzed
Maxillary premolars	Pulpotomy	6 × 4 = 24	6 × 2 = 12	36	19	10	29
Mandibular premolars	Obturation and root-end resection	6 × 4 = 24	6 × 2 = 12	36	21	10	31
				72	40	20	60

NMTA, NeoMTA Plus; QS2, Quick-Set2.

TABLE 2. Grading Scale for Pulpotomy Histologic Samples

Inflammation	Pulp tissue organization
0 = none or a few scattered inflammatory cells	0 = normal tissue
1 = slight inflammatory cell infiltrate with polymorphonuclear or mononuclear leukocytes	1 = odontoblastic layer disorganization but central pulp normal
2 = moderate inflammatory cell infiltrate involving the coronal pulp	2 = total disorganization of the pulp tissue morphology
3 = severe inflammatory cell infiltrate involving the coronal pulp or abscess present	3 = pulp necrosis
Reactional dentin formation	**Quality of dentinogenesis**
0 = intense hard tissue deposition beneath the exposed area appearing as 75%–100% complete	0 = highly organized dentinogenesis, greater than 75% up to 100% normal tubular dentin formation
1 = moderate hard tissue deposition beneath the exposed area, bridge up to 50% complete	1 = mixture of organized (tubular) and irregular, dystrophic dentinogenesis 25%–50%
2 = modest hard tissue deposition beneath the exposed area, bridge up to 25% complete	2 = minimal cells and matrix, up to 25% organized
3 = no bridge	3 = none

bones containing the treated teeth were dissected at sacrifice and stored in a container of 70% ethanol waiting fixation.

Histology

The resected blocks were gradually demineralized in 0.5 mol/L EDTA. When demineralized, the blocks were embedded in paraffin, and 5-μm serial sections were cut and stained with hematoxylin-eosin. Histologic samples were prepared from all teeth treated, with 2 to 8 sections per tooth. Sections that were damaged, distorted, or did not contain the necessary anatomy for scoring were excluded.

The histologic sections were evaluated using transmission light microscopy by 2 calibrated examiners (R.W. and L.O.). The examiners were blinded to the type of material used in each sample. The scoring criteria were adapted from Stanley (25), Dominguez et al (23), and Kohout et al (22). The criteria are described in Table 2 for pulpotomy histology and Table 3 for apical histology. The pulpotomy sections were scored for inflammation, pulp tissue organization, reactionary dentin formation, and dentinogenesis. The root-end surgery sections were scored for inflammation, cementum deposition on the root canal aperture, apical periodontal ligament (PDL) formation, and bone quality. Lower scores represent desirable healing responses for all categories. If a discrepancy in scoring a section occurred, the examiners conferred to reach a consensus for the scores. Each tooth and each procedure within the same tooth were scored independently. When multiple sections were available for each tooth, the scores were averaged. Statistical analysis was performed using the Mann-Whitney *U* test with a significance level of $P = .05$.

Results

Pulpotomy

Presacrifice radiographs show the material was confined to the pulp chamber region with minimal extension into the root canal space. At sacrifice, the glass ionomer restoration had remained intact, providing a sufficient coronal seal. No evidence of periapical pathosis was noted (Fig. 1*A* and *B*) for any specimens.

Twenty-nine of the 36 teeth could be scored. Seven teeth were unable to be accurately scored because of damage during histologic processing. Dentin with well-defined tubules was visible in the dentin bridge adjacent to the experimental and control materials (Fig. 2*A–D*). Thick layers of dentin were routinely visible separating the materials from the underlying pulp tissue. The dentin was more organized in the presence of NeoMTA Plus, with some dystrophic dentin present in sections with Quick-Set2. Odontoblasts were adjacent to the secondary dentin along the canal walls. The pulp tissue was normal with organized cells. Occasionally, pulp tissue tags were contained completely within the dentin bridge.

No significant differences were noted for inflammation, pulp tissue organization, or dentin bridge formation between the experimental and control materials (Fig. 3). Significant differences between materials were only noted for the quality of dentin formation ($P = .002$), with NeoMTA Plus showing better results.

Moderate inflammation was noted in 2 teeth, and mild inflammation was observed in 2 other teeth, the latter both in the Quick-Set2 group. Two of the sections with inflammation were from the same animal (dog F). No inflammation was observed in the NeoMTA Plus group in this animal. The differences in pulp tissue organization and

TABLE 3. Grading Scale for Apical Histologic Samples

Inflammation	Bone quality, apical resorption
0 = none	0 = normal bone formation, no resorption
1 = mild	1 = lack of bone formation, no resorption
2 = moderate	2 = normal bone formation, concomitant resorption
3 = severe	3 = lack of bone formation, resorption
Cementum deposition on root canal aperture	**Apical periodontal ligament formation***
0 = Cementum observed on >75%	0 = FOCF >75%
1 = Cementum covering >50% <75%	1 = FOCF >50% <75%
2 = Cementum covering >25% <50%	2 = FOCF >25% <50%
3 = Cementum covering <25%	3 = FOCF <25%

FOCF, functionally oriented collagen fibers.

*Percent functionally oriented collagen fiber insertion in the new cementum and bone.

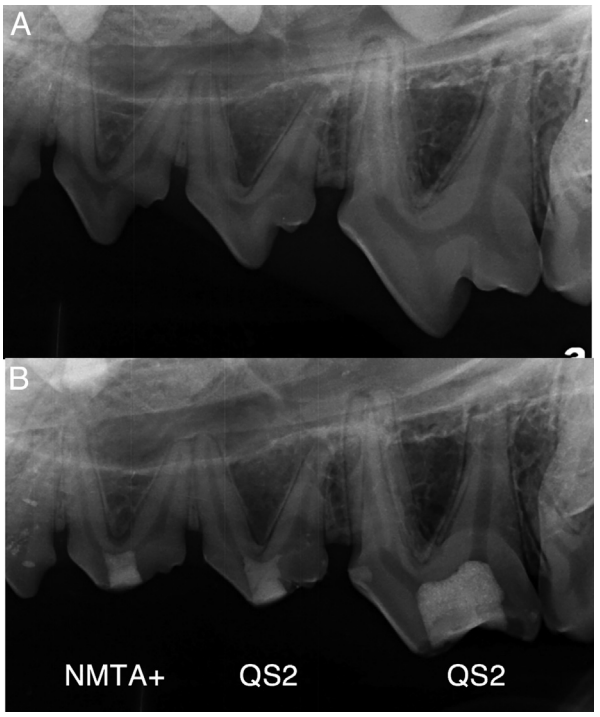

Figure 1. (*A*) Preoperative and (*B*) presacrifice radiographs depicting 90-day healing after pulpotomy procedures.

dentin bridge formation trended toward a better outcome associated with NeoMTA Plus; however, the difference was not statistically significant ($P > .05$).

Root-end Resection

Postoperative and presacrifice radiographs show the distal root obturations were of adequate length, density, and taper (Fig. 4*A–C*). The osteotomies at the root apices of the distal roots are visible radiographically in the postoperative radiograph. At 90 days postoperatively, the glass ionomer restorations remained intact, providing a sufficient coronal seal. Presacrifice radiographs (90 day) showed the osteotomy sites with bone healing and PDL formation (Fig. 4). For all specimens, no evidence of periapical pathosis is noted.

Thirty-one of the 36 teeth could be evaluated histologically and scored. Five teeth were unable to be accurately scored because of damage during histologic processing. The majority of specimens had some calcified cementum immediately adjacent to the materials (Fig. 5*A–D*). The calcified cementum extended from the lateral resected surface toward the center of the canal space. In some specimens, the cementum spanned the resected root surface. Functionally oriented PDL fibers were noted at the periphery of the root-end resection and continued across the resected surface. The fibers nearest the center of the resected surface were often not completely functionally oriented but were clearly ligamentous fibers. Dense and highly mineralized bone was present throughout the apical crypt. Some specimens displayed experimental material particles contained within the newly formed bone (*asterisks* in Fig. 5*C* and *D*). However, the majority of the material was clearly contained within the root canal space.

Inflammation was noted in 1 of the NeoMTA Plus specimens and in 3 of the Quick-Set2–treated roots (Fig. 6). Both groups had a low score (desirable healing) for inflammation and reparative bone formation and generally displayed cementum and PDL reformation. No significant differences were found in inflammation, cementum deposition, bone formation, or PDL formation between the 2 materials ($P > .09$).

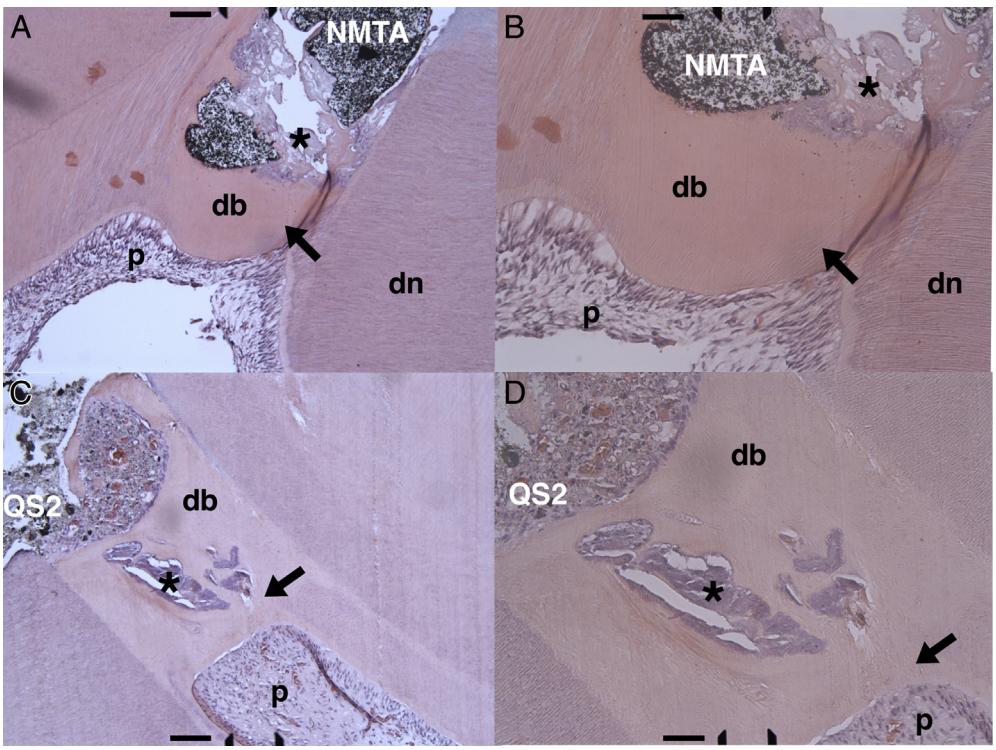

Figure 2. Micrographs showing hematoxylin-eosin–stained histologic sections of pulp tissue exposed to (*A* and *B*) NeoMTA Plus and (*C* and *D*) Quick-Set2. The *asterisks* indicate pulp tissue inclusion, and the *solid arrows* indicate dentin bridging. Scale bar: *A* and *C* = 62.5 μm, *B* and *D* = 31.25 μm. db, dentin bridge; dn, dentin; p, pulp; QS2, Quick-Set2; NMTA, NeoMTA Plus.

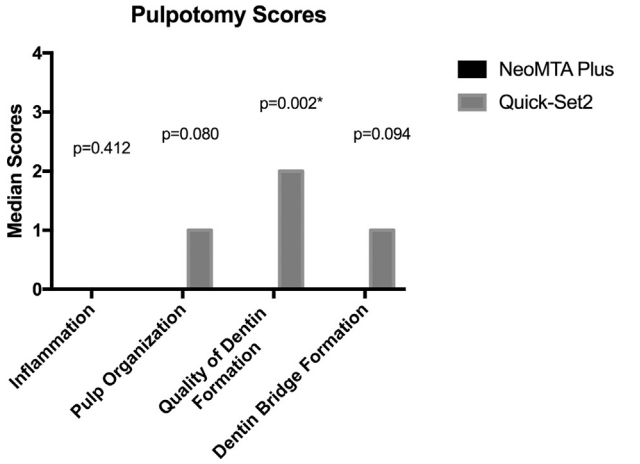

Figure 3. The median histologic scores. *Significant difference in quality of dentin formation between NeoMTA Plus and Quick-Set2. NeoMTA Plus: $n = 10$, Quick-Set2: $n = 19$.

Discussion

The current study evaluated the pulpal and periapical tissue healing response after exposure to Quick-Set2 and NeoMTA Plus. This is the first *in vivo* report on Quick-Set2 or NeoMTA Plus for procedures related to pulpotomy, root-end resection, and sealing *in vivo*. Both materials induced healing in the pulp and periapical tissues in this canine model after 90 days.

Previous studies have shown MTA Plus and ProRoot MTA to have similar bioactivity (7). Additionally, similar biologically favorable findings have been observed between MTA Plus and NeoMTA Plus (9). Given the very similar composition of MTA Plus and NeoMTA Plus, differing only in the radiopacifier used, and the previously reported similar biological responses, these materials were considered biologically equivalent for the purposes of this study (1, 2). In order to minimize the number of canine samples necessary for investigation, NeoMTA Plus was used as an established equivalent and the control group to compare with Quick-Set2.

Numerous researchers have shown the success of MTA for various endodontic applications (26). Tricalcium silicate cements have been used primarily for pulpotomy, perforation repair, or root-end fillings. Tricalcium silicate cements like NeoMTA Plus and calcium aluminosilicates like Quick-Set2 use their unique water-based gels to allow for variations in viscosity. By varying the powder–to–liquid gel ratio, the clinician can achieve a puttylike consistency or a more sealerlike texture. As previously demonstrated with MTA and Quick-Set, the biocompatibility of these materials remained unchanged when mixed in thin or thick consistencies (21, 22, 27). Additionally, Quick-Set has been shown to have comparable pulpal and periapical tissue healing with white ProRoot MTA (21, 22). The histologic results of this study showed equivalent healing with Quick-Set2 or NeoMTA Plus compared with earlier studies using experimental MTA or ProRoot MTA (26, 28, 29).

The only significant difference between the 2 materials in the current study was the quality of the dentin bridge after pulpotomy. The dentin bridge formed in response to NeoMTA Plus was more organized with less cell or matrix inclusion compared with Quick-Set2. An ideal dentin bridge has organized tubules produced by underlying odontoblasts (21, 30). These organized dentinal tubules may provide a superior barrier compared with amorphous calcified "dentinlike" tissue observed in pulp tissue underlying rapidly progressing caries lesions (21, 30). However, the clinical implications of the quality of dentin bridging are currently unknown because it can only be assessed histologically.

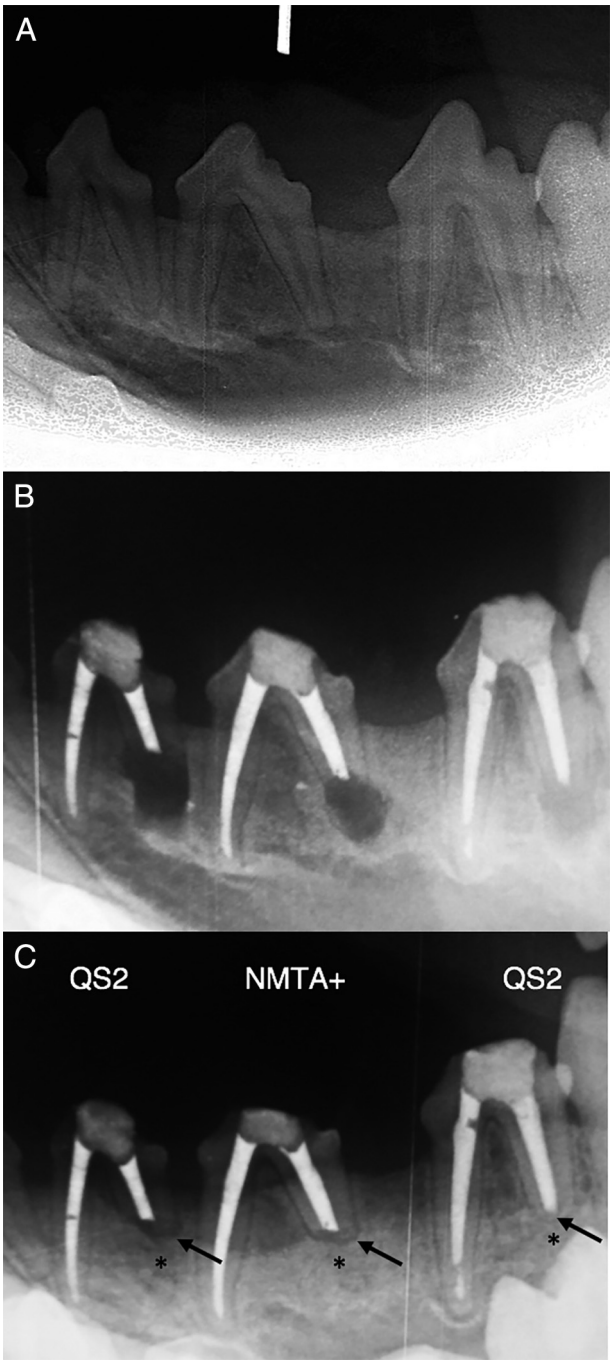

Figure 4. (*A*) Preoperative, (*B*) postoperative, and (*C*) presacrifice radiographs showing complete bone healing (*) with PDL reformation (*solid arrows*) at 90 days.

The difference in the quality of bridge formation may be attributed to the chemical differences between the materials. The free alumina particles present in Quick-Set, not present in Quick-Set2, may have increased inflammation. Although inflammation was still present in some sections in the current study, the degree of inflammation and the number of teeth with inflammation were significantly reduced with the modified formulation of Quick-Set2 (21, 22) compared to previous studies. The maximum pH of NeoMTA Plus and Quick-Set2

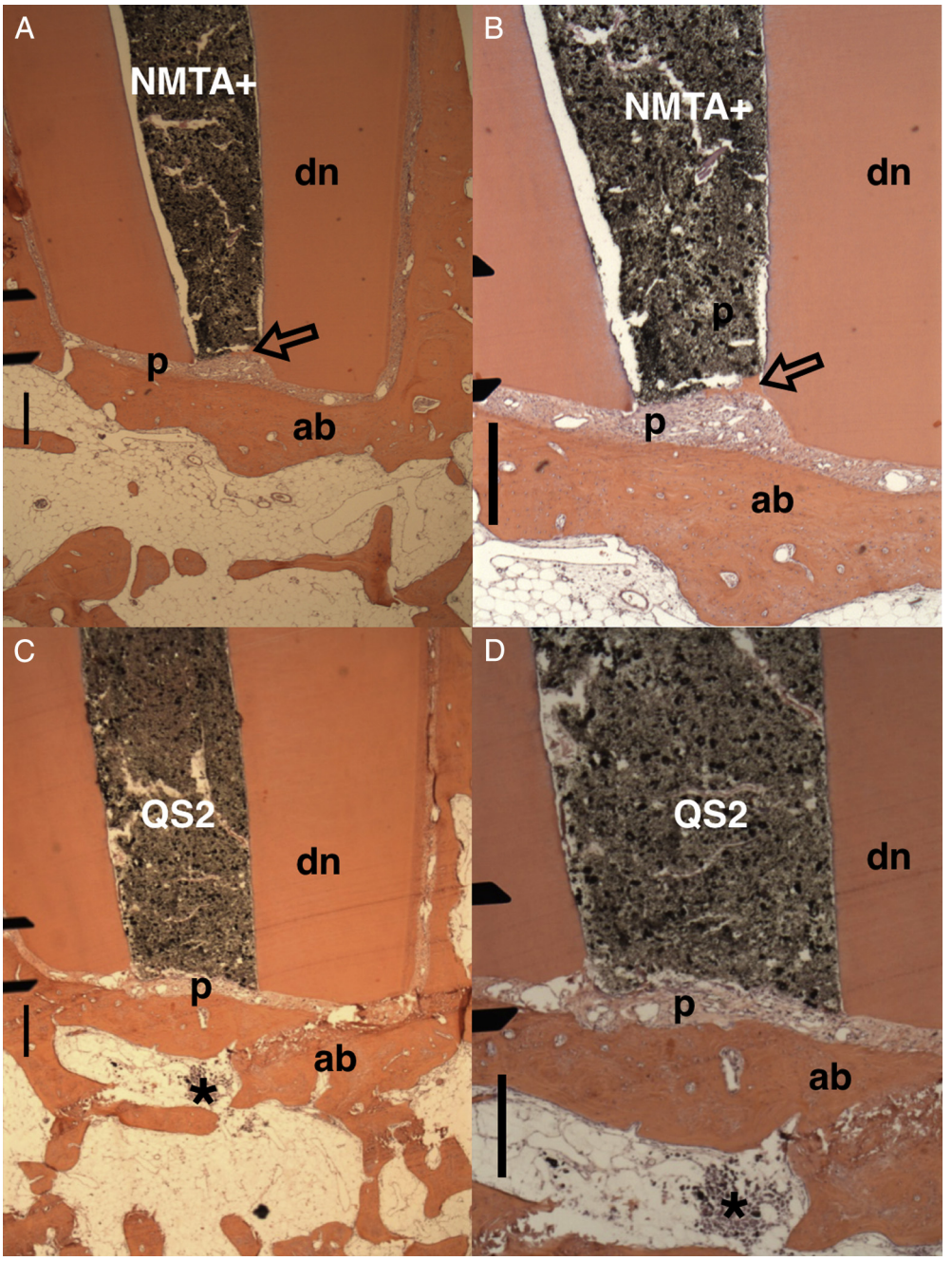

Figure 5. Micrographs showing hematoxylin-eosin–stained histologic sections of root-end resections exposed to (*A* and *B*) NeoMTA Plus and (*C* and *D*) Quick-Set2. Dense newly formed bone present in all samples. *Open arrows* indicate new cementum formation. The *asterisk* indicates experimental material particles contained within the newly formed bone in the Quick-Set2 sample. Scale bar: *A* and *C* = 250 μm, *B* and *D* = 125 μm. ab, alveolar bone; dn, dentin; p, PDL; NMTA+, NeoMTA Plus; QS2, Quick-Set2.

is approximately 12 and 10, respectively. For calcium aluminates, fewer calcium and hydroxyl ions will be present compared with the tricalcium silicates at the material-tissue interface, which may lead to poorer bridge quality during the healing process (21).

Both Quick-Set2 and NeoMTA Plus are mixed with a gel to form a puttylike consistency for pulpotomies. Because both materials were mixed to a similar consistency, the handling properties, placement, and material adaptation against dentin and pulp surfaces were nearly identical. Therefore, any differences in the regeneration of pulpal tissues may be attributed to differences in the material's individual chemistries.

Of the total inflammation observed across all procedures, the level of inflammation was disproportionately high in 1 animal having one third of all incidences. This single outlier had increased inflammation for unknown reasons.

When evaluating only the clinically relevant factors (ie, inflammation, pulp tissue organization, and the presence of dentin bridge formation), both materials performed similarly. However, this study may be underpowered to discern a statistical difference. Within the limits of this study, both materials appeared adequate for use in pulpotomy and root-end filling procedures in canines and suitable for further clinical investigations.

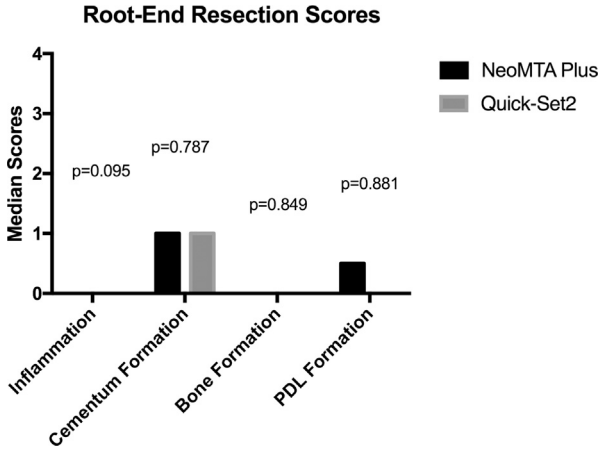

Figure 6. The median histologic scores. No significant difference between groups. NeoMTA Plus: $n = 10$, Quick-Set2: $n = 21$.

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