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The use of beta-tricalcium phosphate, white MTA, white Portland cement and calcium hydroxide for direct pulp capping of primary pig teeth

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Abstract – *Aim:* The purpose of this study was to evaluate and compare the response of the pulp of primary pig teeth after capping with beta-tricalcium phosphate (β-TCP), white mineral trioxide aggregate (WMTA), white Portland cement (WPC) and calcium hydroxide [$Ca(OH)_2$]. *Material and Methods:* Forty teeth of two 3-month old pigs were capped with these materials. Three weeks later, the animals were killed and the specimens were prepared for histological examination and evaluation of inflammatory cell response, tissue disorganization, hard tissue formation and bacteria presence was performed. The data collected from the histological examinations were statistically analyzed using Kruskal–Wallis and Dunn multiple comparison tests. *Results:* There was no significant difference between β-TCP, WMTA, WPC and CH in terms of primary pulp response, hard tissue formation and normal pulp tissue preservation. *Conclusion:* Beta-tricalcium phosphate, WMTA and WPC in primary pig teeth are as effective as $Ca(OH)_2$ in primary pig teeth capping.

Direct pulp capping of primary teeth is one of the most controversial treatments for deciduous teeth and consists of dressing exposed pulp to maintain pulp vitality throughout the life of the tooth. A definitive procedure for the treatment of primary pulp exposure has yet not been defined, though the degree of pain and the extent of the pulp exposure are two factors that are frequently considered in permanent teeth as well as in deciduous teeth (1). Direct pulp capping should be used only on a vital pulp that has been accidentally injured and shows no other symptoms. It should not be performed on pulp that has been exposed as a result of penetrating caries, as studies have shown that primary teeth react differently to traumatism and bacterial invasion. In fact, the abundant blood supply because of enlarged apical foramina allows a faster inflammatory response (2), and more reparative dentin is formed in permanent teeth. In primary teeth, however, the use of direct pulp capping is more limited than in permanent teeth. Pulp infection occurs earlier in primary teeth as a result of a faster progression of caries and thinner hard tissues.

Based on the work performed by Zander in 1937 (3), direct pulp capping is traditionally performed with various formulations of calcium hydroxide $Ca(OH)_2$, whose high pH has a bactericidal effect and which helps to produce dentinal bridges on the exposed pulpal area. Different studies have reported successful results for use in primary teeth (4–6), while others have focused on the increased risk of internal resorption and reserved this treatment for traumatic or iatrogenic exposures in asymptomatic teeth, either during radicular formation or when exfoliation is nearly complete (7). The major disadvantage of $Ca(OH)_2$ is its dissolution over time. As most dentin bridges form under the $Ca(OH)_2$, they may contain tunnels and allow pulp to become infected or necrotic due to microleakage (8). Clearly, bacterial microleakage occurs under unsealed pulp material and causes pulp pathosis.

In recent years, direct pulp capping – placing an adhesive resin on exposed pulp – was proposed for permanent teeth as a means to achieve a hermetic seal at the dentin-pulp interface (9, 10). The use of adhesive resin could thus prevent bacterial access, thus protecting pulp tissue against bacterial invasion. Histopathological studies using such direct methods on molars in animals (11, 12) and humans (13, 14) have had higher success rates with animal teeth than human teeth, in terms of hard tissue formation and the degree of pulp inflammation. In fact, studies of adhesive resin use in humans indicate that this material apparently does not stimulate hard tissue formation. As these materials are not really 'leak-proof' over time, pulp infection cannot be totally avoided after a period of time.

In light of the information presented above, it would appear that an effective capping material should be biocompatible, prevent microleakage and promote dentin formation. Pulp capping materials has developed in what is called the 'biological era' (15). This research has pointed to materials that encourage dentin and bone regeneration/formation. Several of these new materials may have promise for pediatric dentistry, for example**;** mineral trioxide aggregate (MTA), Portland cement (PC) and Tricalcium phosphate (TCP):

- Mineral trioxide aggregate has recently attracted attention in the field of pediatric dentistry for pulpotomy treatment because of its excellent sealing ability (16), its biocompatibility (17) and its ability to stimulate hard tissue formation (18). It also has a higher (though not statistically significant) long-term clinical and radiographic success rate than a pulp dressing material like formocresol (19). Because gray MTA (GMTA) could potentially stain the tooth structure, especially in front teeth where esthetics is an issue, White MTA (WMTA) was introduced on the market. Several studies have shown that there are no significant differences between GMTA and WMTA in terms of biocompatibility and cell response (20–22).
- Portland cement has also been judged by certain authors to have the same physical and chemical properties as MTA, as they have a similar composition (23, 24). Several studies have reported no difference in the biological effect of MTA and PC (25, 26). Still, the two substances are not exactly the same: MTA contains a smaller quantity of gypsum than PC, is composed of smaller particles, and incorporates bismuth oxide to improve radiopacity (27). This product has yet to be tested for use in dentistry. The PC comes in numerous varieties depending on geographical source; some contains arsenic and possibly other dangerous contaminants. This material still needs to be tested extensively before it can be used in dentistry, and therefore no recommendation can be made for human use.
- Tricalcium phosphate is a porous bioceramic material whose biological properties include non-reactivity and resorbability. It can serve as scaffolding for bone ingrowths, as it progressively degrades and is replaced by bone. Both the alpha and beta types of tricalcium phosphate have been shown to play important roles in bone grafting procedures, though physical investigations using density functional calculations suggest that beta-TCP is more stable than alpha-TCP (28). Because of its osteoconductivity and bone replacement capability, TPC is highly promising for use in numerous dental and craniofacial procedures, including the reconstruction of frontal sinus cavities (29), augmentation of craniofacial skeletal defects (30) and the repair of periodontal tooth and bone defects (31). It is also proving useful in endodontic (32). Theoretically, the biocompatibility of TCP combined with calcium release may allow TCP to stimulate odontoblasts, thus promoting the formation of dentin bridges. TCP also seems to promote bone regeneration (33), and it provides a better barrier than $Ca(OH)_2$ in the obturation of open apexes, providing equivalent repair (34).

Among the studies cited above, there are only a few published studies of animal teeth that investigate the interaction of direct pulp capping agents with the pulp of primary teeth. The study described in this paper was designed to evaluate the response of the pulp of primary pig teeth after capping with $Ca(OH)_2$, white mineral trioxide aggregate (WMTA), industrially manufactured white Portland cement (WPC) and beta-tricalcium phosphate (β-TCP).

Materials and methods

Forty deciduous teeth of two 3-month old pigs were used in this study: including eight incisors and 12 molars per pig. After injection of 10 mg kg^{-1} Ketamine HCl (Ketamine 1000 CEVA, Ceva santé animale, Libourne, France) and 25–35 mg kg^{-1} sodium pentobarbital (NEMBUTAL, Abbott laboratories-Sanofi santé animale Benelux, Brussels, Belgium), all teeth (except for the canines, which were reserved as a control) were subjected to a class V preparation on their buccal surface under general anesthesia. An infiltration of Lidocaine 2% (Xylonor 2%; Septodont, Saint-Maur France) was used as a local anesthesia. Because of difficulties in applying rubber dam to pigs' teeth, such dam was not used in this experiment. The teeth were kept dry using gauze swabs and then wiped with chlorhexidin digluconate 0.2% solution (Corsodyl®, GlaxoSmithKline, Genval, Belgium) for 1 min. A small pulp exposure was made using a high speed bur (ISO 806 314). Bleeding was controlled with saline and cotton pellets.

The teeth of each hemi-maxillary segment (four incisors and six molars) were used for one comparison. The right maxillary and mandibular teeth of the first pig were assigned to the calcium hydroxide (CH) group and the left maxillary and mandibular teeth were assigned to the WMTA group. The right maxillary and mandibular teeth of the second pig were assigned to the β-TCP and the left maxillary and mandibular teeth were assigned to the WPC group (Table 1).

The relatively high costs of *in vivo* studies using animals, such as non-human primates, have led to the use of pigs for this study. This animal model is relatively inexpensive, easier to work on and the tissue response, genetic map and anatomy are similar to human. The pigs are used increasingly in biomedical research for studies of a spectrum of human diseases including obesity, arthritis, cardiovascular disease, and skin and eye

Table 1. Distribution of treated teeth

Pig no. 1		Pig no. 2	
Calcium hydroxide	Mineral trioxide aggregate	Beta-tricalcium phosphate	Portland cement
Calcium hydroxide	Mineral trioxide aggregate	Beta-tricalcium phosphate	Portland cement

conditions (35, 36). During the experimental period, our two female pigs, all from the same litter, were kept in individual cages in the medical research animal care unit of the Free University of Brussels.

- In the β-tricalcium phosphate group: RTR® (Septodont) was mixed with sterile saline to create a putty-like mixture, which was applied over the exposure.
- In the white MTA group**:** ProRoot® powder (Dentsply DeTrey GmbH, Konstanz, Germany) was mixed with sterile water according to the manufacturer's instructions and applied over the exposure.
- In the WPC group**:** PC powder (Cantillana, BE) was mixed with sterile saline at the same ratio as with WMTA and applied over the exposure.
- In the CH group**:** Dycal® (Dentsply DeTrey GmbH) was mixed according to the manufacturer's instructions and applied over the exposure.

Beta-TCP, WMTA and WPC powder were placed over the pulp exposure by three separated amalgam carriers.

Following these different procedures, the coronal cavities of each tooth were filled with IRM (Dentsply DeTrey GmbH). Three weeks later, the animals were killed by administering Embutramide 4–6 ml 50 kg^{-1} (T61®; Intervet Int. GmbH-D, Unterschleißheim, Germany). This protocol was approved by the Animal Ethics Commission of the Medical Sciences Division at the Free University of Brussels *(Université Libre de Bruxelles)* under the case number 241N.

Histological procedure

After killing, both jaws were removed from each pig, were fixed in a 10% neutral-buffered formalin solution, and were decalcified in Surgipath Decalcifier I (Surgipath, Grayslake, IL, USA). The jaw segments were then prepared for histological examination: they were embedded in paraffin and sectioned to a thickness of 6 μm. Every tooth was prepared using the following two procedures: first, a serial section was stained with hematoxylin and eosin; then, a second serial section was prepared for bacterial recognition using the Brown and Brenn technique. All sections were viewed under a light microscope and were evaluated according to the criteria listed in Table 2 A–D. All 8 control canines were used to provide a histological comparison between capped and non-capped teeth.

The data collected from the histological examinations (Table 3) were statistically analyzed using Kruskal-Wallis and Dunn multiple comparison tests. The statistical analyses were performed using the software, Prism (version 3.0; Graph Pad Software, San Diego, CA), with a level of significance set at $P < 0.05$.

Results

There was no significant difference between the various materials in terms of pulp response, hard tissue formation and normal pulp tissue preservation and between incisors and molars in each group in terms of criteria mentioned above ($P > 0.05$).

Beta-tricalcium phosphate

All specimens showed a complete calcified bridge. Nine specimens presented a normal histological pulp pattern and odontoblast layer (Fig. 1). One specimen showed a mild inflammation beneath the pulp exposure because of a blood clot, with calcified tissue observed under the necrotic zone and inside the coronal pulp tissue. One specimen showed a calcification zone within coronal pulp tissue (Fig. 2). No stained bacteria were observed in any specimens.

White mineral trioxide aggregate

In all specimens, the pulp exposures were closed by a complete thin calcified bridge and the pulp tissue was normal and free of inflammation (Fig. 3), except for one specimen which presented a few scattered inflammatory

Table 2. Scores used during the histological exams

(A) Inflammatory cell response
0 None or a few scattered inflammatory cells beneath the site of pulp exposure
1 Mild inflammatory cells as mono- or poly-morphonuclear leukocytes
2 Moderate inflammatory cell infiltration involving the third coronal radicular pulp
3 Severe inflammatory cell infiltration involving the third coronal or more radicular pulp
(B) Tissue disorganization
0 Normal tissue beneath the site of pulp exposure
1 Odontoblast like cells, odontoblasts and pulp tissue pattern disorganization or odontoblasts hyperactivity, but normal central pulp tissue pattern
2 General disorganization of the pulp tissue pattern
3 Pulp necrosis
(C) Hard tissue formation
0 No hard tissue formation
1 Slight incomplete hard tissue formation beneath the site of pulp exposure
2 Moderate hard tissue formation beneath the site of pulp exposure
3 Thick hard tissue formation beneath the site of pulp exposure, characterizing a complete dentin bridge
(D) Stained bacteria
0 Absence
1 Presence of stained bacteria along the cavity lateral walls
2 Presence of stained bacteria along the cavity lateral and axial walls
3 Presence of stained bacteria along the cavity walls within the cut dentin tubules or over the pulp tissue

Table 3. Grading of histological features for each material from scores listed in Table 2

	Inflammatory cell response				Pulp tissue disorganization				Hard tissue formation				Stained bacteria			
Materials	0	1	2	3	0	1	2	3	0	1	2	3	0	1	2	3
β-TCP	9	1	0	0	8	2	0	0	0	0	0	10	10	0	0	0
WMTA	10	0	0	0	8	2	0	0	0	0	0	10	10	0	0	0
WPC	10	0	0	0	9	1	0	0	0	0	0	10	10	0	0	0
$Ca(OH)_2$	9	1	0	0	8	2	0	0	1	0	1	8	10	0	0	0

β-TCP, Beta-tricalcium phosphate; WMTA, white mineral trioxide aggregate; WPC, white Portland cement.

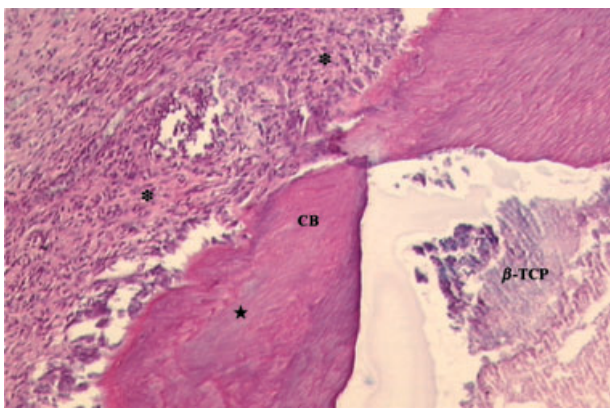


Fig. 1. Direct pulp capping with β-TCP, maxillary central incisor (H&E × 10). Fiberblasts activity (★) with a few scattered inflammatory cells under calcified bridge (CB). Notice calcium deposition (*).

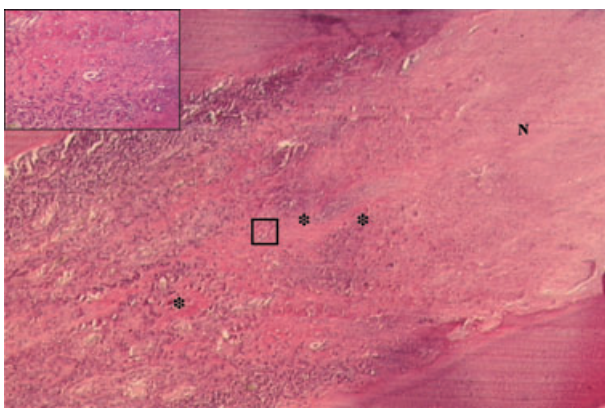


Fig. 2. Direct pulp capping with β-tricalcium phosphate, mandibular third molar (H&E × 5). Notice necrotic layer (N) because of clot formation and the calcification zone (*) under the necrotic layer and within coronal pulp tissue. Inset: calcification in coronal pulp (H&E × 10).

cells under the calcified bridge. Stained bacteria were not observed in any specimens.

White Portland cement

In all specimens, a complete calcified bridge was observed, and the pulp tissue presented a normal histological architecture and was free of inflammation (Fig. 4). No stained bacteria were observed.

Calcium hydroxide

Eight specimens presented a complete calcified bridge without an inflammatory reaction (Fig 5a and 5b). One specimen showed the moderate incomplete formation of a calcified bridge, and one presented no dentin bridge formation but showed a mild inflammatory reaction. Stained bacteria were not observed in any specimens.

Discussion

When primary tooth pulp is exposed accidentally during caries removal or because of trauma, dentists, even pediatric dentists, often opt for a pulpotomy treatment because there is a real lack of information from animal and clinical human studies about direct pulp capping in primary teeth. As Ranly has reported, this leads to the needless pulpotomy of many primary teeth because of a generalization (37).

To our knowledge, this is the first experimental animal study of direct capping agents designed to compare the pulpal response of primary teeth to bioactive materials (e.g. white mineral aggregate, WPC and β-tricalcium phosphate) with the response solicited by $Ca(OH)_2$. Our results show that vital primary pulp tissue is capable of healing after traumatic injury by perforation.

During bone regeneration after injury, the inflammatory phase is followed by a reparative phase, characterized by the formation of a hard callus that occurs when the matrix mineralizes. Within 3–6 weeks, the new bone acquires a trabecular pattern, which may be observed in bone histology (38). As the processes of bone and tooth mineralization are similar, the authors set the experimental period at 3 weeks to determine the potential for a reparative phase following the inflammatory phase for each material.

Over long periods, pulp inflammation is usually caused by the toxicity of capping material or by bacterial invasion due to microleakage through the restorative material. In the short period studied here, bacteria were detected dentin tubuli of some specimens. These bacteria did not appear to cause any pulpal inflammatory reaction. Though it is true that a histological process like decalcification could eliminate bacteria or reduce the effectiveness of bacterial staining procedures, given the absence of moderate or severe pulp inflammation, the intact pulpal and odontoblastic layers indicate the biocompatibility and regenerative ability of these capping materials.

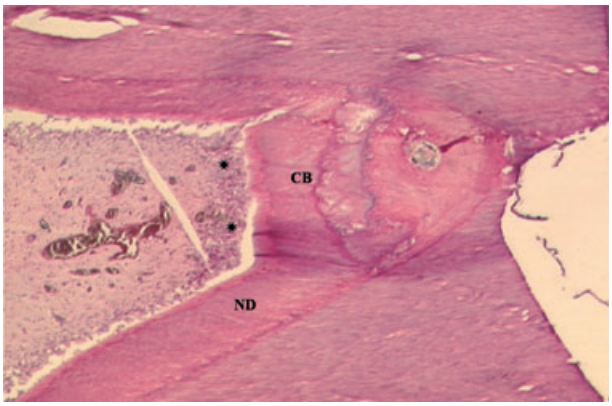


Fig. 3. Direct pulp capping with white mineral trioxide aggregate, mandibular second molar (H&E × 5). Important odontoblast activity (✳), normal pulp tissue with enlarged blood vessels (☞) under the calcified bridge (CB). ND: new-dentin.

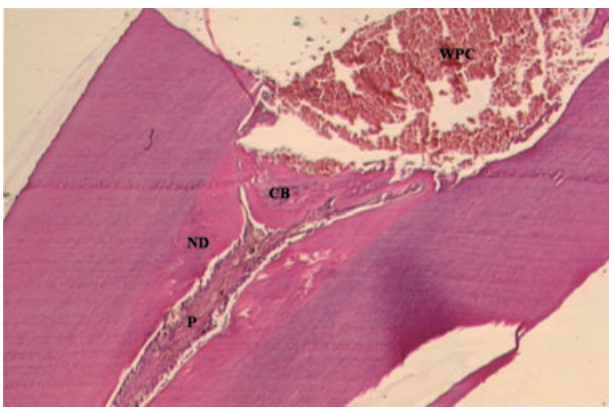
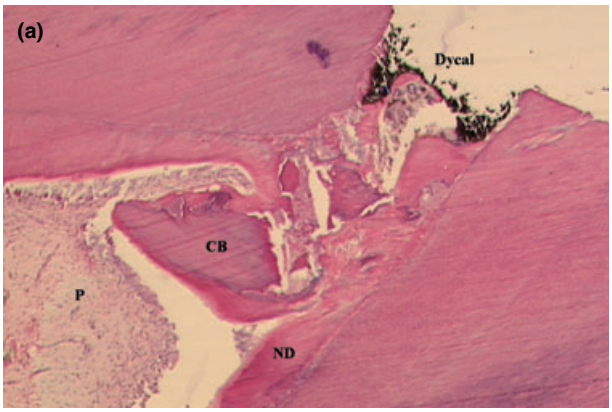


Fig. 4. Direct pulp capping with white Portland cement, maxillary first molar (H&E × 2.5). Normal pulp and intact odontoblastic layer under the calcified bridge (CB). ND: new-dentin.



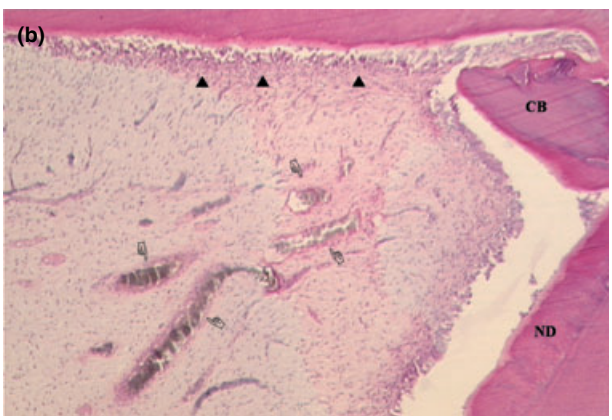


Fig. 5. (a) Direct pulp capping with calcium hydroxide (Dycal), mandibular lateral incisor (H&E × 5). Notice a normal appearing pulp tissue pattern. ND: new-dentin, P: pulp, CB: calcified bridge. (b) Coronal pulp view (H&E × 5). Notice the enlarged blood vessels (☞) under calcifed bridge (CB) and intact odontoblastic layer (▲). ND: new-dentin.

After 3 weeks, all the materials used in this study allowed the formation of a complete thick layer of hard tissue under the exposure site; the only exception to this was two specimens in the CH group. Cell inclusions were common in the reparative hard tissue for all tested materials. Calcium hydroxide and its compounds are well-documented. Its ability to stimulate hard tissue formation and its antibacterial effect lead to over-induction and over-regulation of odontoblast-like cell differentiation in new matrix deposition, especially growth factors from the dentin matrix (39). MTA and PC were shown to be equally effective as pulp protection for primary teeth by encouraging hard tissue formation, thus confirming the results of other studies about permanent teeth (40, 41). Some authors have reported that MTA and PC release calcium ions when they are in contact with tissue fluid, thus promoting an alkaline PH. This hydration produces calcium silicate hydrate gel and calcium hydrate, which would explain why MTA, PC and $Ca(OH)_2$ provoke the same tissue reaction (20).

Our study also showed that beta-TCP promoted hard tissue formation in the zone of pulp exposure of primary pig teeth, which could be related to the release of Ca ions after the bio-degradation of material in contact with tissue fluids. This biodegradation implies cell-mediated degradation *in vitro* or *in vivo*. Cellular activity during biodegradation occurs in acid media, and the enrichment of the microenvironment because of the release of calcium and phosphate ions from the dissolving Ca-P materials affects both cell proliferation and cell activity. The increased concentrations of the calcium and phosphate ions promote the formation of carbonate apatite, which is similar to the bone apatite. In this study, three specimens in the β-TCP group showed signs of hard tissue formation in the radicular pulp.

Controlling bleeding could improve the success rate of pulp capping because a blood clot could form a barrier between the pulp tissue and the capping material, with the blood clot acting as a substrate for microorganisms. Despite clot formation in two β-TCP group specimens, calcified tissue was present under the blood clot and in pulp tissue. In orthopedic or maxillofacial surgery, β-TCP is mixed with the patient's blood or with physiological solution and the surgical site in contact with it must be well vascularized. Thus, much like MTA, β-TCP as a root-end filling material shows biological activity in bloody environments.

Our study showed that WMTA, WPC and beta-TCP are biocompatible and represent an excellent substrate on which odontoblast-like cells can attach themselves to produce a hard tissue, thus preserving normal histological pulp patterns and pulp vitality in primary pig teeth.

These three agents, however, have certain disadvantages. For example, both beta-TCP and MTA are expensive. Portland cement, on the other hand, is much cheaper and has similar properties compared to MTA and beta-TCP, making it a reasonable choice for use in pulp therapy. Such an inexpensive and easily available material could allow very successful pulp treatments in primary teeth. Nevertheless, further studies and considerations of limitations and the potential unknown risks involved in the use of PC as a medical device are necessary to ensure its safety. For the moment, however, industrially manufactured PC is not currently approved for use in dentistry, and therefore no clinical recommendation can be made for its use in the human body.

It is time to admit that the pulp of primary teeth has a greater regenerative power than has previously been expected, and direct pulp capping of primary teeth should be reconsidered. As Ranly reported (37), biological compounds and new materials that may completely transform our whole philosophy of pulp treatment are on the horizon; therefore the axiom 'exposed pulp is the sign of a doomed organ' may soon need to be rejected, replaced by a new axiom: 'an exposed pulp under the right circumstances may survive'.

Conclusion

The results of the present histological study showed that, in the short term and in non-carious pig teeth, there appears to be no difference between beta-TCP, WMTA and PC in terms of primary pulp response, hard tissue formation and normal pulp tissue preservation. Nevertheless, these results were obtained in healthy pulp tissue and the correlation with the response in inflamed pulp should be made with caution. Clearly, the presence of bacteria or their metabolites could provoke pulp degeneration and expressive molecular alterations. Therefore, additional studies are needed to investigate the response of these agents in pulp tissue that has previously been injured during the caries process. In addition, further research with larger samples and a more extended study time is necessary. Clinical studies should also be encouraged.

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