

Biodentine™

The dentine in a capsule
or more?



Josette Camilleri

B.Ch.D., M.Phil., Ph.D., FICD, FADM, FIMMM, FHEA (UK)
School of Dentistry,
Institute of Clinical Sciences
College of Medical and Dental Sciences
The University of Birmingham, Birmingham, U.K.



Introduction

Tooth structure is lost by dental caries, trauma and tooth wear and is often replaced by inert dental materials that replace the bulk. If the pulp health is jeopardised a series of interventions need to be undertaken. Initially the pulp vitality needs to be maintained. Later elimination of infection and filling of the pulp space is necessary. When pulpal involvement occurs the choice of material has to change and materials that interact with the pulp or the dentine are indicated. Interactive materials used for dental procedures include calcium hydroxide in its various presentations and more recently hydraulic calcium silicate cements. The main feature of the hydraulic calcium silicate cements is their hydraulic nature. These materials can be used in wet areas without deteriorating. Thus these materials are indicated for root-end filling and perforation repair. Another important feature of these materials includes the release

of calcium hydroxide as a by-production of the hydration reaction. These makes these materials appropriate for use as pulp capping materials, for apexification and apexogenesis and more recently also for regenerative endodontic procedures. The calcium hydroxide creates an environment where calcium ions are released and also antibacterial activity is high.

The choice of material is important for successful clinical outcome. There are a number of hydraulic calcium silicate cements available for the various procedures as indicated in Table 1. These materials vary greatly and it is important that the clinician appreciates the importance of choosing the right material for each clinical application. This article highlights Biodentine™ (Septodont, Saint-Maur-des-Fossés, France) and its suitability for various clinical applications.

| Material | Cement type | Radiopacifier | Additives | Presentation | Mixing |
|-------------|---------------------|------------------|--|---------------|------------|
| Biodentine | Tricalcium silicate | Zirconium oxide | Calcium carbonate, Calcium chloride, polymer | Powder/liquid | Mechanical |
| MTA Angelus | Portland cement | Bismuth oxide | Calcium oxide | Powder/liquid | Manual |
| Theracal | Portland cement | Barium zirconate | Strontium glass, resin | Syringe | Premixed |
| ProRoot MTA | Portland cement | Bismuth oxide | - | Powder/liquid | Manual |

Table 1: Hydraulic calcium silicate materials types available for various procedures



Fig. 1: Presentation of Biodentine™ in powder and liquid form.

Biodentine™ characteristics

Biodentine™ is presented as powder and liquid. The powder is placed in a capsule while the liquid is in an ampoule (Figure 1). The powder is composed of tricalcium silicate, zirconium oxide, calcium carbonate and some minor additives of iron oxide added to give the colour. The liquid is made up of water with some additions of calcium chloride and a water soluble polymer. Biodentine™ powder and its hydrated materials have been characterised well. The design of Biodentine™ ensures optimal properties and thus enhanced clinical performance.

The powder is finer than other cement types of this category (Table 2). The finer powder ensures a higher reaction rate. The powder is mostly composed of tricalcium silicate (Table 3) as opposed to the other hydraulic cements which are predominantly Portland cement based as shown in Table 1. The pure tricalcium silicate ensures no inclusions of aluminium (1, 2) and trace metals (3) that are present in Portland cement-based dental cements. The use of zirconium oxide ensures adequate radiopacity and stability with no risk of leaching and discolouration which is implicated with all materials using bismuth oxide radiopacifier (4-6). The main constituents are clearly shown in the X- ray diffraction analysis of the Biodentine™ powder (Figure 2).

| Material | BET surface area (m ² /g) |
|---------------------|--------------------------------------|
| Tricalcium silicate | 1.1187 |
| Biodentine | 2.8116 |
| MTA Angelus | 1.0335 |

Table 2: Specific surface area measurement of Biodentine™ powder to show its fine powder consistency when compared to other cements.

Reproduced with permission from Camilleri et al. 2013.

| Phase identified | Material type in mass % | | |
|----------------------|-------------------------|------------|-------------|
| | TCS | Biodentine | MTA Angelus |
| Tricalcium silicate | 100 | 80.1 | 66.1 |
| Dicalcium silicate | - | - | 8.4 |
| Tricalcium aluminate | - | - | 2.0 |
| Calcium carbonate | - | 14.9 | - |
| Calcium oxide | - | - | 8.0 |
| Bismuth oxide | - | - | 14.0 |
| Zirconium oxide | - | 5.0 | - |
| Silicon dioxide | - | - | 0.5 |
| Aluminium oxide | - | - | 1.0 |

Table 3: Powder assessment by Rietveld X-ray diffraction analysis to show the main constituents of Biodentine™.

Reproduced with permission from Camilleri et al. 2013.

Biodentine™ includes additives to enhance the material properties. These include calcium carbonate which is present in the powder, calcium chloride and water soluble polymer in the liquid. The calcium carbonate is a source of free calcium ions that are present in solution as soon as the powder is mixed to the liquid. Their

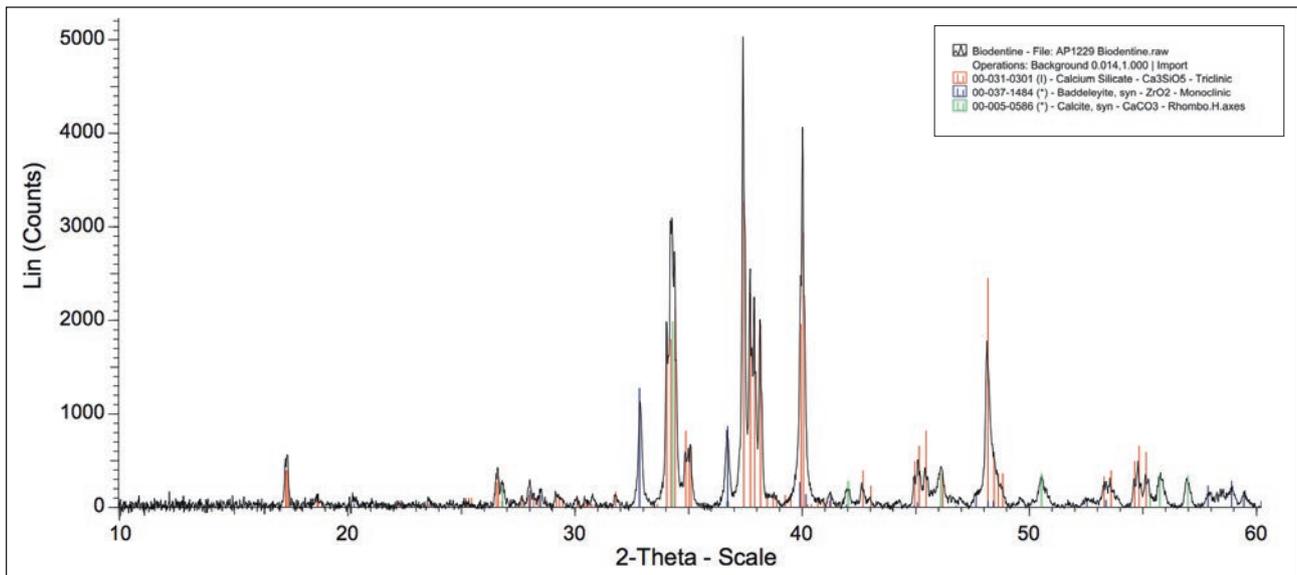


Figure 2: X-ray diffraction analysis of Biodentine™ powder to show the main constituent phases namely tricalcium silicate, zirconium oxide and calcium carbonate.

Reproduced with permission from Camilleri et al. 2013.

presence results in a higher heat flux earlier in the reaction thus enhancing the reaction rate (2) as shown in Figure 3. The calcium chloride reduces the setting time of the Biodentine™ considerably when compared to other similar material types (7, 8). The water soluble polymer enables the reduction of the water to cement ratio thus enhancing the Biodentine's physical properties. In fact the compressive strength and micro-hardness of Biodentine™ are much higher than those reported for other similar material types (7). The microstructure of Biodentine™ (Figure 4) shows how hydration proceeds with the tricalcium silicate reacting and being deposited around the calcium carbonate particles (9). The

calcium hydroxide is produced in high amounts as indicated in the X-ray diffraction scan of the hydrated materials (10) where the calcium hydroxide peak is clearly evident at 18 degrees (Figure 5). The specific material chemistry, the fine particle sizes, the low water to cement ratio and the presence of calcium carbonate all contribute to optimal materials properties aimed for clinical performance. Furthermore the material also exhibits low porosity (Table 4) when compared to similar material types (11) and this is also beneficial clinically. Since the material is hydraulic it is very important that it is not allowed to dry out as this will lead to cracks at the interface (Figure 6) and in the material bulk (11).

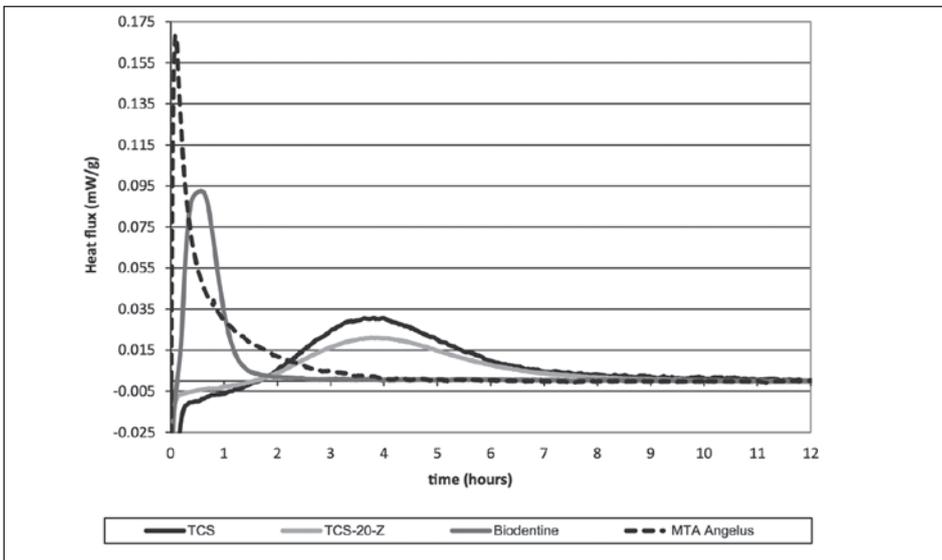


Figure 3: Heat flux assessment of Biodentine™ to show high rate of action early in the hydration. (TCS: Tricalcium silicate cement; TCS-20-Z is a tricalcium silicate cement with 20% replacement of zirconium oxide).
Reproduced with permission from Camilleri et al. 2013.

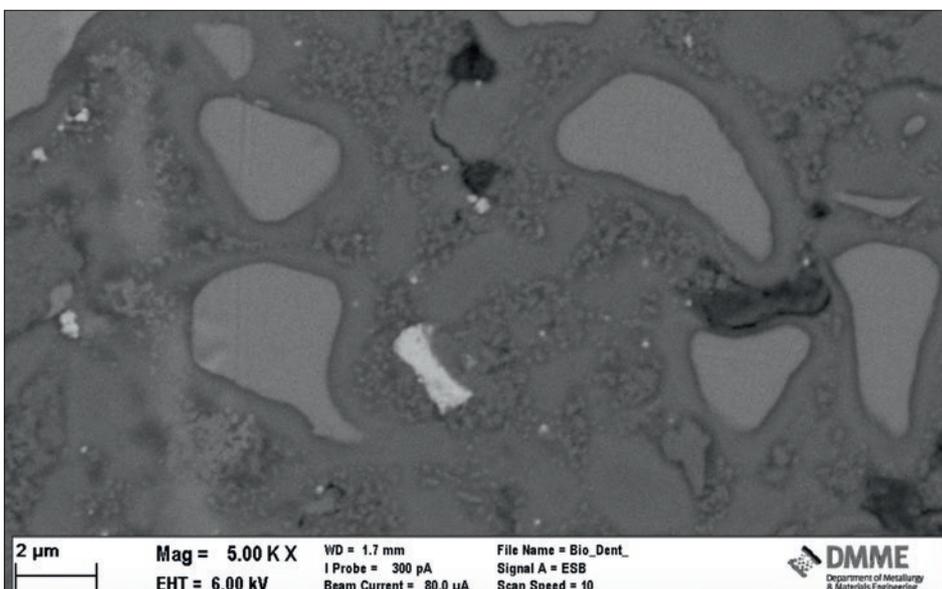


Figure 4: Scanning electron micrograph of set biodentine™ to show the material microstructure.
Reproduced with permission from Camilleri et al. 2013.

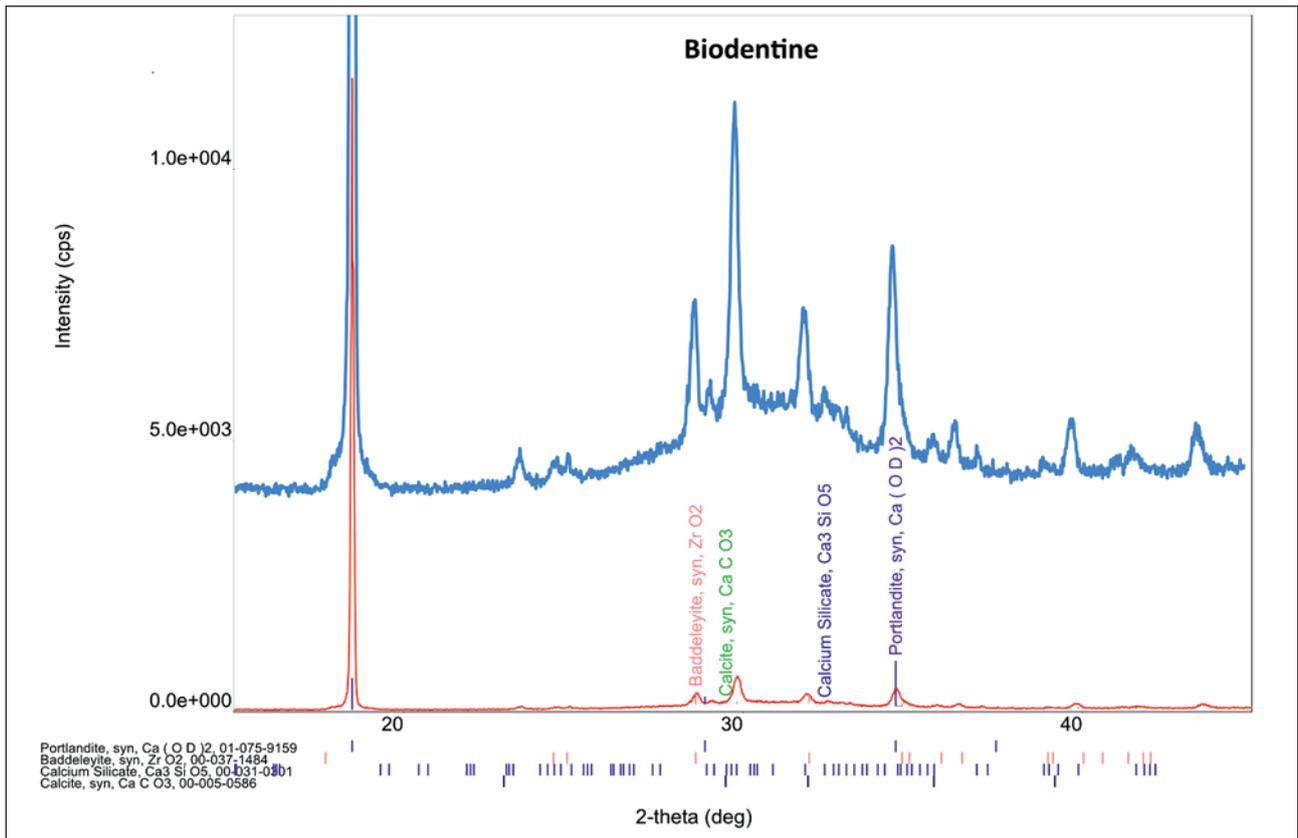


Figure 5: X-ray diffraction plot of set Biodentine™ to show the main phases present after setting. The calcium hydroxide predominates the plot. Reproduced with permission from Camilleri 2014.

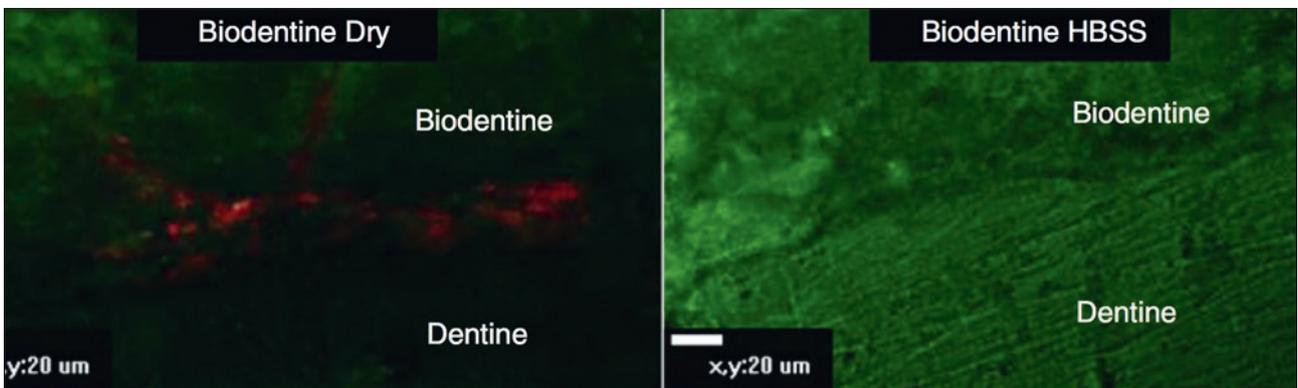


Figure 6: Confocal laser microscopy of Biodentine™ stored dry and wet in HBSS and wet to highlight the need to keep it moist at all times. Reproduced with permission from Camilleri et al. 2014.

| Parameter measured | Units | Material | | | |
|-----------------------|-------------------|----------|--------------|------------|--------|
| | | TCS-20-Z | Bioaggregate | Biodentine | IRM |
| Average pore diameter | μm | 0.0508 | 0.0337 | 0.0121 | 0.0205 |
| Total pore area | m ² /g | 13.101 | 24.321 | 21.752 | 10.545 |
| Bulk Density | g/ml | 1.8637 | 1.8007 | 2.0444 | 2.3455 |
| Porosity | % | 30.98 | 36.86 | 13.44 | 12.66 |

Table 4: Percentage porosity of Biodentine™ compared to similar material types. Reproduced with permission from Camilleri et al. 2014.

Clinical applications

Pulp capping and dentine replacement

Biodentine™ is calcium ion releasing (10, 12) with the initial rate of release higher than other similar material types (12, 13), thus it is ideal for use as a pulp capping material. The Biodentine™ surface exhibits the thickest surface calcium concentration compared to ProRoot MTA, Dycal and Theracal (14). Dentine bridge formation is evident clinically when Biodentine™ is used for direct pulp capping (15, 16, 17). Clinical cases showing evidence of irreversible pulpitis that were treated with Biodentine™ exhibited reduction in the sizes of the apical areas when evaluated with cone beam computed tomography (18). The pulpal reaction to Biodentine™ is similar to other similar material types like mineral trioxide aggregate (19) with favourable cell proliferation and alkaline phosphatase activity of human dental pulp cells (20). This same reaction was observed when testing leachates of Biodentine™ (13). The calcium releasing ability contributes also for the antimicrobial properties of Biodentine™. This property is important since dental caries is a bacterial induced disease. Biodentine™ exhibits adequate antimicrobial properties (13) and which were lower than calcium hydroxide pulp capping materials. However, the increase in the antimicrobial properties of calcium hydroxide was accompanied by higher cytotoxicity (21).

Furthermore its physical properties allow the material to be used in bulk thus avoiding unnecessary layering and interfaces that can allow micro-leakage and restoration failure. In fact Biodentine™ shows less micro-leakage than resin-based dentine replacement materials (22). Placing a final restoration over Biodentine™ can be challenging as it is water-based. The final restoration should be delayed for at least 2 weeks and both total etch and self etch adhesives can be used (23). Total etching can lead to material micro-structural changes (24) and although in vitro composite restorations were all lost on thermocycling the total etch proved to be more effective than self etching (25). The microstructure at the interface of the Biodentine™ and composite resin using total-etch and self-etch adhesive is shown in Figure 7. Biodentine™ was shown to be able to restore teeth for up to six months and when overlaid with a composite resin it provided an effective dentine replacement material (26).

Other tricalcium silicate-based pulp capping materials which are resin-based, thus have an advantage as they can be layered easily with a composite resin providing a strong bond (25). However, the effects on the pulp are adverse (27). The calcium ion release from such materials has been shown to be low and no crystalline calcium hydroxide is formed (10). The resin-based pulp

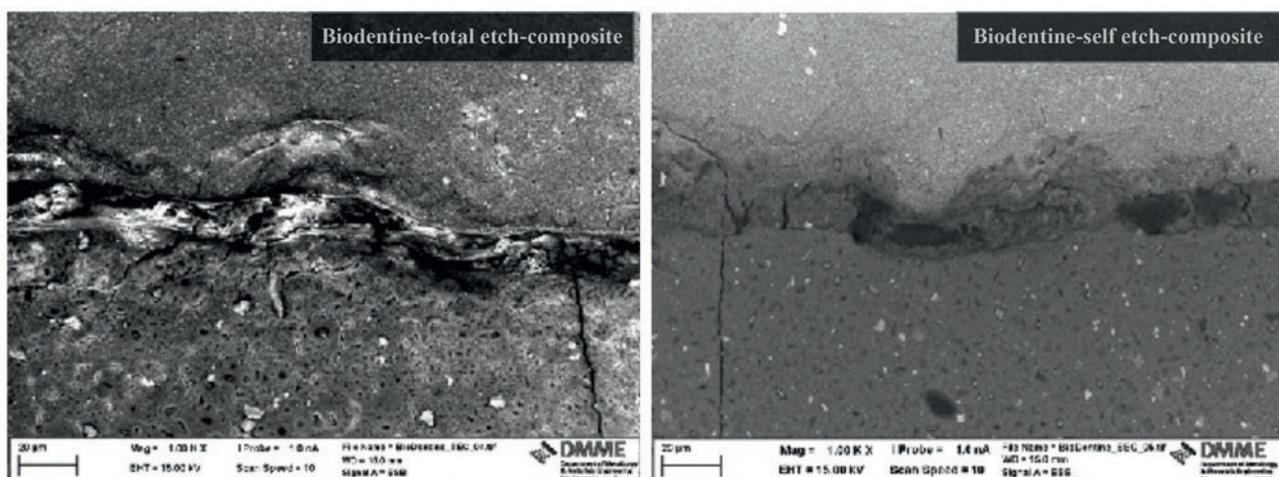


Figure 7: Interfacial characteristics of Biodentine™ and composite resin after total-etch and self-etch adhesive application.

Reproduced with permission from Meraji and Camilleri 2017.

capping materials such as Theracal depend on the environmental moisture to penetrate and allow hydration of the tricalcium silicate which is the active component of the material. The fluid penetration is not enough and a model using extracted teeth kept in media for 15 days showed limited hydration of the tricalcium silicate in Theracal (28). Also, in agreement with previous published work, in-vitro (29) and in-vivo (30) studies show that Theracal-conditioned media significantly decreased pulp fibroblast proliferation, and induced proinflammatory interleukin 8 release from cultured pulp fibroblasts and entire teeth cultures (29).

Using the whole tooth culture model (31) and in a recent clinical study (30), it is clear that Biodentine™ exhibits better biological and clinical outcomes than resin-based dentine replacement materials. Biodentine™ has been shown to promote pulp healing using both the whole tooth culture model (29) and also in clinical trials where it presented the best clinical outcome when compared to resin-based pulp capping materials (30).

Pulpotomy procedures

More advanced pulp involvement particularly in primary teeth will necessitate pulpotomy procedures to be undertaken. Biodentine™ exhibited better cytocompatibility and bioactivity than MTA Angelus, Theracal and IRM in contact with stem cells isolated from human exfoliated primary teeth (32). In an animal model the use of Biodentine™ as a pulpotomy agent resulted in thicker mineralised tissue bridges which are more easily detected radiographically when compared to MTA (33).

Clinically, high success rates were shown in pulpotomy procedures performed with Biodentine™ in primary molars showing more favourable results than formocresol, which is the standard treatment methodology (34, 35). When compared to calcium hydroxide in vital pulpotomies in primary molars the group treated with Biodentine™ revealed favourable regenerative potential along with clinical success sharing both indications and mode of action with calcium hydroxide, but without its drawbacks of physical and clinical

properties (36). Pulpotomy with Biodentine™ resulted in a predictable clinical outcome similar to that of MTA (37-41). Biodentine™ was superior to less standard treatment methodologies like laser (41) and propolis (39). Biodentine™ used for pulpotomy procedures does not cause tooth discolouration (42).

Treatment of the immature apex

Once the pulp tissue is lost, it is necessary to fill the root canal space. Immature teeth present a problem due to their anatomy as the roots are short and thin and routine canal obturation is difficult due to the root canal configuration. The thin dentine walls are also at risk of fracture.

Apexification procedures allow the formation of a calcific barrier at the root apex thus closing off the root-end from the periapical space. A calcific bridge is created by providing an environment where calcium ions from the dentine form a calcific bridge. Such conditions are created by materials releasing calcium hydroxide. Historically non-setting calcium hydroxide pastes were used. The calcium hydroxide releases calcium ions to create an ideal environment for the formation of a calcific bridge (43). Another advantage of the calcium hydroxide paste is its antibacterial properties as pulpless root canals usually result from non vital teeth which are prone to bacterial colonisation (44). The use of non setting calcium hydroxide involves several visits over a number of months and the calcified bridge formed following apexification was a porous structure (45).

Apexification with hydraulic calcium silicate cements as apical plugs permits apexification procedures to be performed in two visits. The two visits were necessary since MTA has a long setting time and needs to set prior to the placement of the final restoration. More recently it was shown that apexification with an apical plug of Biodentine™ a single visit is enough since wetting the surface of the material did not effect the material properties (46).

This treatment methodology can be considered as predictable, and may also be an alternative to the use of calcium hydroxide (47). The hydraulic nature of these material types and the formation of

calcium hydroxide make these materials ideal for such procedures. Biodentine™ has been shown to release more calcium ions in solution than MTA (2). Its success when used as apical plug in apexification cases has been reported (48-53). Its hydration is optimised by the addition of calcium carbonate as a nucleating agent spiking up the reaction rate in the early stages. The addition of calcium chloride accelerator and the water soluble polymer allow low water/powder ratios (2). There are no additives of pozzolanic materials and other cementitious substances as indicated in Table 1. The addition of such materials has been shown to restrict the formation of calcium hydroxide which is necessary when treating apexification cases (54, 55). The fracture resistance of immature teeth with an apical plug of Biodentine™ was similar to that of MTA and higher than the control (52). Biodentine™ has also been used successfully in cases of regenerative endodontics (56-58). The fracture resistance in the cases was also reported to be similar to that of MTA (59). Biodentine™ showed the least discolouration potential when used in these clinical cases (60), thus it is the material of choice for regenerative endodontics, especially for cases where aesthetics is a concern.

Root end filling and perforation repair

Materials used for root-end filling need to exhibit specific properties since they have to perform and attain clinical success under very adverse conditions. The hydraulic nature of all tricalcium silicate cements is thus a desirable property. In fact these material types were invented for

this purpose. The main issue with the hydraulic cements is that they react with the environment they are placed in. At the root-end the materials are placed in contact with blood as soon as they are placed. They are also in contact with the root dentine and remnants of gutta-percha and sealer used to obturate the root canal. The physical properties of Biodentine™ are not adversely affected by contact with tissue fluids and blood (61). The bond strength of Biodentine™ was better than that of MTA when used as a root-end filling material. Both materials were adversely affected by blood contamination (62). Less bacteria in apical root dentine were found when cases were treated with Biodentine™ and compared to MTA (63) indicating that the antimicrobial properties of Biodentine™ are superior too those of MTA. The biocompatibility of Biodentine™ was considered to be marginally better than that of MTA with better cell adhesion to the materials when it was used as a root-end filling material (64).

Biodentine™ was also found to be adequate to repair root perforations (65) producing a positive tissue response and mineral deposition at the perforation site. This response is related to the release of calcium hydroxide in solution. It also seals well the area (66, 67) since perforations are inadvertently highly infected thus an adequate seal is necessary.

Root perforation repair materials are also subject to dislodgement during tooth restoration. Biodentine™ shows high early push-out bond strength which did not deteriorate in contact with blood (68). Furthermore it was not affected by the irrigating solutions used (69) indicating material stability.

Conclusions

Biodentine™ is a second generation hydraulic calcium silicate material that is composed mainly of tricalcium silicate and it also contains zirconium oxide radiopacifier and some additives. It is scientifically engineered for a specific purpose to

be used as a dentine replacement material. The research undertaken so far shows that Biodentine™ performs well as a dentine replacement but also for other clinical applications. Thus it certainly is more than just dentine in a capsule.



Josette Camilleri

B.Ch.D., M.Phil., Ph.D., FICD, FADM, FIMMM, FHEA (UK)
 School of Dentistry,
 Institute of Clinical Sciences
 College of Medical and Dental Sciences
 The University of Birmingham
 Birmingham
 U.K.

Biography

Professor Josette Camilleri obtained her Bachelor of Dental Surgery and Master of Philosophy in Dental Surgery from the University of Malta. She completed her doctoral degree, supervised by the late Professor Tom Pitt Ford, at Guy's Hospital, King's College London.

She has worked at the Department of Civil and Structural Engineering, Faculty for the Built Environment, University of Malta and at the Department of Restorative Dentistry, Faculty of Dental Surgery, University of Malta. She is currently a senior academic at the School of Dentistry, University of Birmingham, U.K. Her research interests include endodontic materials such as root-end filling materials and root canal sealers, with particular interest in mineral trioxide aggregate, Portland cement hydration and other cementitious materials used as biomaterials and also in the construction industry.

Josette has published over 100 papers in peer-reviewed international journals and her work is cited over 4000 times. She is the Editor of "Mineral trioxide aggregate. From preparation to application" published by Springer in 2014. She is a contributing author to the 7th edition of "Harty's Endodontics in Clinical Practice" (Editor: BS Chong) and "Glass ionomer cements in Dentistry" (Editor: SK Sidhu). She is an international lecturer, a reviewer and a member of the scientific panel of a number of international journals including the Journal of Endodontics, Scientific Reports, Dental Materials, Clinical Oral Investigation, Journal of Dentistry, Acta Odontologica Scandinavica and Acta Biomaterialia.

References

1. Camilleri J. Characterization and hydration kinetics of tricalcium silicate cement for use as a dental biomaterial. *Dent Mater.* 2011 Aug;27(8):836-44.
2. Camilleri J, Sorrentino F, Damidot D. Investigation of the hydration and bioactivity of radiopacified tricalcium silicate cement, Biodentine™ and MTA Angelus. *Dent Mater.* 2013 May;29(5):580-93.
3. Camilleri J, Kralj P, Veber M, Sinagra E. Characterization and analyses of acid- extractable and leached trace elements in dental cements. *Int Endod J.* 2012 Aug; 45(8):737-43.
4. Vallés M, Mercadé M, Duran-Sindreu F, Bourdelande JL, Roig M. Influence of light and oxygen on the color stability of five calcium silicate-based materials. *J Endod.* 2013 Apr;39(4):525-8.
5. Camilleri J. Color stability of white mineral trioxide aggregate in contact with hypochlorite solution. *J Endod.* 2014 Mar;40(3):436-40.
6. Marciano MA, Duarte MA, Camilleri J. Dental discoloration caused by bismuth oxide in MTA in the presence of sodium hypochlorite. *Clin Oral Investig.* 2015 Dec;19(9):2201-9.
7. Grech L, Mallia B, Camilleri J. Investigation of the physical properties of tricalcium silicate cement-based root-end filling materials. *Dent Mater.* 2013 Feb;29(2):e20-8.
8. Kaup M, Schäfer E, Dammaschke T. An in vitro study of different material properties of Biodentine™ compared to ProRoot MTA. *Head Face Med.* 2015 May 2;11:16.
9. Grech L, Mallia B, Camilleri J. Characterization of set Intermediate Restorative Material, Biodentine™, Bioaggregate and a prototype calcium silicate cement for use as root-end filling materials. *Int Endod J.* 2013 Jul;46(7):632-41.
10. Camilleri J. Hydration characteristics of Biodentine™ and Theracal used as pulp capping materials. *Dent Mater.* 2014 Jul;30(7):709-15.
11. Camilleri J, Grech L, Galea K, Keir D, Fenech M, Formosa L, Damidot D, Mallia B. Porosity and root dentine to material interface assessment of calcium silicate-based root-end filling materials. *Clin Oral Investig.* 2014;18(5):1437-46.
12. Kurun Aksoy M, Tulga Oz F, Orhan K. Evaluation of calcium (Ca²⁺) and hydroxide (OH⁻) ion diffusion rates of indirect pulp capping materials. *Int J Artif Organs.* 2017 Jul 8:0. doi: 10.5301/ijao.5000619. [Epub ahead of print]
13. Arias-Moliz MT, Farrugia C, Lung CYK, Wismayer PS, Camilleri J. Antimicrobial and biological activity of leachate from light curable pulp capping materials. *J Dent.* 2017 Jun 20. pii: S0300-5712(17)30151-3. doi: 10.1016/j.jdent.2017.06.006. [Epub ahead of print]

References

14. Gong V, França R. Nanoscale chemical surface characterization of four different types of dental pulp-capping materials. *J Dent*. 2017 Mar;58:11-18.
15. Katge FA, Patil DP. Comparative Analysis of 2 Calcium Silicate-based Cements (Biodentine™ and Mineral Trioxide Aggregate) as Direct Pulp-capping Agent in Young Permanent Molars: A Split Mouth Study. *J Endod*. 2017 Apr;43(4):507-513.
16. Kim J, Song YS, Min KS, Kim SH, Koh JT, Lee BN, Chang HS, Hwang IN, Oh WM, Hwang YC. Evaluation of reparative dentin formation of ProRoot MTA, Biodentine™ and BioAggregate using micro-CT and immunohistochemistry. *Restor Dent Endod*. 2016 Feb;41(1):29-36.
17. Nowicka A, Wilk G, Lipski M, Kolečki J, Buczkowska-Radlińska J. Tomographic Evaluation of Reparative Dentin Formation after Direct Pulp Capping with Ca(OH)₂, MTA, Biodentine™, and Dentin Bonding System in Human Teeth. *J Endod*. 2015 Aug; 41(8):1234-40.
18. Hashem D, Mannocci F, Patel S, Manoharan A, Brown JE, Watson TF, Banerjee A. Clinical and radiographic assessment of the efficacy of calcium silicate indirect pulp capping: a randomized controlled clinical trial. *J Dent Res*. 2015 Apr;94(4):562-8.
19. Chang SW, Lee SY, Ann HJ, Kum KY, Kim EC. Effects of calcium silicate endodontic cements on biocompatibility and mineralization-inducing potentials in human dental pulp cells. *J Endod*. 2014 Aug;40(8):1194-200.
20. Luo Z, Kohli MR, Yu Q, Kim S, Qu T, He WX. Biodentine™ induces human dental pulp stem cell differentiation through mitogen-activated protein kinase and calcium-/ calmodulin-dependent protein kinase II pathways. *J Endod*. 2014 Jul;40(7):937-42.
21. Poggio C, Arciola CR, Beltrami R, Monaco A, Dagna A, Lombardini M, Visai L. Cytocompatibility and antibacterial properties of capping materials. *ScientificWorldJournal*. 2014;2014:181945.
22. Abdelmegid FY, Salama FS, Al-Mutairi WM, Al-Mutairi SK, Baghazal SO. Effect of different intermediary bases on micro-leakage of a restorative material in Class II box cavities of primary teeth. *Int J Artif Organs*. 2017 Mar 16;40(2):82-87.
23. Hashem DF, Foxton R, Manoharan A, Watson TF, Banerjee A. The physical characteristics of resin composite-calcium silicate interface as part of a layered/ laminate adhesive restoration. *Dent Mater*. 2014 Mar;30(3):343-9.
24. Camilleri J. Investigation of Biodentine™ as dentine replacement material. *J Dent*. 2013 Jul;41(7):600-10.
25. Meraji N, Camilleri J. Bonding over Dentin Replacement Materials. *J Endod*. 2017 Aug; 43(8):1343-1349.
26. Koubi G, Colon P, Franquin JC, Hartmann A, Richard G, Faure MO, Lambert G. Clinical evaluation of the performance and safety of a new dentine substitute, Biodentine™, in the restoration of posterior teeth - a prospective study. *Clin Oral Investig*. 2013 Jan;17(1): 243-9.
27. Hebling J, Lessa FC, Nogueira I, Carvalho RM, Costa CA. Cytotoxicity of resin-based light-cured liners. *Am J Dent*. 2009 Jun;22(3):137-42.
28. Camilleri J, Laurent P, About I. Hydration of Biodentine™, Theracal, and a prototype tricalcium silicate-based dentin replacement material after pulp capping in entire tooth cultures. *J Endod*. 2014 Nov;40(11):1846-54.
29. Jeanneau C, Laurent P, Rombouts C, Giraud T, About I. Light-cured Tricalcium Silicate Toxicity to the Dental Pulp. *J Endod*. 2017 Dec, volume 43, Issue 12.
30. Bakhtiar H, Nekoofar MH, Aminshakib P, Abedi F, Naghi Moosavi F, Esnaashari E, Azizi A, Esmailian S, Ellini MR, Mesgarzadeh V, Sezavar M, About I. Human Pulp Responses to Partial Pulpotomy-Treatment with Theracal as Compared with Biodentine and ProRoot MTA: A Clinical Trial. *J Endod*. 2017 Nov, Volume 43, Issue 11.
31. Laurent P, Camps J, About I. Biodentine™ induces TGF-β1 release from human pulp cells and early dental pulp mineralization. *Int Endod J*. 2012 May;45(5):439-48. doi: 10.1111/j.1365-2591.2011.01995.x. Epub 2011 Dec 22.
32. Collado-González M, García-Bernal D, Oñate-Sánchez RE, Ortolani-Seltenerich PS, Álvarez-Muro T, Lozano A, Forner L, Llana C, Moraleda JM, Rodríguez-Lozano FJ. Cytotoxicity and bioactivity of various pulpotomy materials on stem cells from human exfoliated primary teeth. *Int Endod J*. 2017 Feb 7. doi: 10.1111/iej.12751. [Epub ahead of print]
33. De Rossi A, Silva LA, Gatón-Hernández P, Sousa-Neto MD, Nelson-Filho P, Silva RA, de Queiroz AM. Comparison of pulpal responses to pulpotomy and pulp capping with Biodentine™ and mineral trioxide aggregate in dogs. *J Endod*. 2014 Sep;40(9):1362-9.
34. Juneja P, Kulkarni S. Clinical and radiographic comparison of Biodentine™, mineral trioxide aggregate and formocresol as pulpotomy agents in primary molars. *Eur Arch Paediatr Dent*. 2017 Aug 5. doi: 10.1007/s40368-017-0299-3. [Epub ahead of print]
35. El Meligy OA, Allazzam S, Alamoudi NM. Comparison between Biodentine™ and formocresol for pulpotomy of primary teeth: A randomized clinical trial. *Quintessence Int*. 2016;47(7):571-80.
36. Grewal N, Salhan R, Kaur N, Patel HB. Comparative evaluation of calcium silicate- based dentin substitute (Biodentine™) and calcium hydroxide (pulpdent) in the formation of reactive dentin bridge in regenerative pulpotomy of vital primary teeth: Triple blind, randomized clinical trial. *Contemp Clin Dent*. 2016 Oct-Dec;7(4):457-463.
37. Togaru H, Muppa R, Srinivas N, Naveen K, Reddy VK, Rebecca VC. Clinical and Radiographic Evaluation of Success of Two commercially Available Pulpotomy Agents in Primary Teeth: An in vivo Study. *J Contemp Dent Pract*. 2016 Jul 1;17(7):557-63.
38. Rajasekharan S, Martens LC, Vandenbulcke J, Jacquet W, Bottenberg P, Cauwels RG. Efficacy of three different pulpotomy agents in primary molars: a randomized control trial. *Int Endod J*. 2017 Mar;50(3):215-228.
39. Kusum B, Rakesh K, Richa K. Clinical and radiographical evaluation of mineral trioxide aggregate, Biodentine™ and propolis as pulpotomy medicaments in primary teeth. *Restor Dent Endod*. 2015 Nov;40(4):276-85.
40. Cuadros-Fernández C, Lorente Rodríguez AI, Sáez-Martínez S, García-Binimelis J, About I, Mercadé M. Short-term treatment outcome of pulpotomies in primary molars using mineral trioxide aggregate and Biodentine™: a randomized clinical trial. *Clin Oral Investig*. 2016 Sep;20(7):1639-45.
41. Niranjani K, Prasad MG, Vasa AA, Divya G, Thakur MS, Saujanya K. Clinical Evaluation of Success of Primary Teeth Pulpotomy Using Mineral Trioxide Aggregate®, Laser and Biodentine™- an In Vivo Study. *J Clin Diagn Res*. 2015 Apr;9(4):ZC35-7.

References

42. Camilleri J. Staining Potential of Neo MTA Plus, MTA Plus, and Biodentine™ Used for Pulpotomy Procedures. *J Endod.* 2015 Jul;41(7):1139-45.
43. Rehman K, Saunders WP, Foye RH, Sharkey SW. Calcium ion diffusion from calcium hydroxide-containing materials in endodontically-treated teeth: an in vitro study. *Int Endod J.* 1996;29(4):271-9.
44. Chong BS, Pitt Ford TR. The role of intracanal medication in root canal treatment. *Int Endod J.* 1992;25(2):97-106.
45. Walia T, Chawla HS, Gauba K. Management of wide open apices in non-vital permanent teeth with Ca(OH)₂ paste. *J Clin Pediatr Dent.* 2000;25(1):51-6.
46. Caronna V, Himel V, Yu Q, Zhang JF, Sabey K. Comparison of the surface hardness among 3 materials used in an experimental apexification model under moist and dry environments. *J Endod.* 2014 Jul;40(7):986-9. doi: 10.1016/j.joen.2013.12.005. Epub 2014 Jan 17.
47. Simon S, Rilliard F, Berdal A, Machtou P. The use of mineral trioxide aggregate in one-visit apexification treatment: a prospective study. *Int Endod J.* 2007;40(3):186-97.
48. Khetarpal A, Chaudhary S, Talwar S, Verma M. Endodontic management of open apex using Biodentine™ as a novel apical matrix. *Indian J Dent Res.* 2014;25(4):513-6.
49. Bajwa NK, Jingarwar MM, Pathak A. Single Visit Apexification Procedure of a Traumatically Injured Tooth with a Novel Bioinductive Material (Biodentine™). *Int J Clin Pediatr Dent.* 2015;8(1):58-61.
50. Martens L, Rajasekharan S, Cauwels R. Endodontic treatment of trauma-induced necrotic immature teeth using a tricalcium silicate-based bioactive cement. A report of 3 cases with 24-month follow-up. *Eur J Paediatr Dent.* 2016;17(1):24-8.
51. Vidal K, Martin G, Lozano O, Salas M, Trigueros J, Aguilar G. Apical Closure in Apexification: A Review and Case Report of Apexification Treatment of an Immature Permanent Tooth with Biodentine™. *J Endod.* 2016;42(5):730-4.
52. Evren OK, Altunsoy M, Tanriver M, Capar ID, Kalkan A, Gok T. Fracture resistance of simulated immature teeth after apexification with calcium silicate-based materials. *Eur J Dent.* 2016;10(2):188-92.
53. Niranjana B, Shashikiran ND, Dubey A, Singla S, Gupta N. Biodentine™-A New Novel Bio-Inductive Material For Treatment of Traumatically Injured Tooth (Single Visit Apexification). *J Clin Diagn Res.* 2016;10(9):ZJ03-ZJ04.
54. Schembri Wismayer P, Camilleri J. Why biphasic? Assessment of the effect on cell proliferation and expression. *J. Endod.* 2017 43(5):751-759.
55. Camilleri J, Sorrentino F, Damidot D. Characterization of un-hydrated and hydrated BioAggregate™ and MTA Angelus™. *Clin Oral Investig.* 2015 Apr;19(3):689-98.
56. Bakhtiar H, Esmaili S, Fakhr Tabatabayi S, Ellini MR, Nekoofar MH, Dummer PM. Second-generation Platelet Concentrate (Platelet-rich Fibrin) as a Scaffold in Regenerative Endodontics: A Case Series. *J Endod.* 2017 Mar;43(3):401-408.
57. Topçuoğlu G, Topçuoğlu HS. Regenerative Endodontic Therapy in a Single Visit Using Platelet-rich Plasma and Biodentine™ in Necrotic and Asymptomatic Immature Molar Teeth: A Report of 3 Cases. *J Endod.* 2016 Sep;42(9):1344-6.
58. Khoshkhounejad M, Shokouhinejad N, Pirmoazen S. Regenerative Endodontic Treatment: Report of Two Cases with Different Clinical Management and Outcomes. *J Dent (Tehran).* 2015 Jun;12(6):460-8.
59. Elnaghy AM, Elsaka SE. Fracture resistance of simulated immature teeth filled with Biodentine™ and white mineral trioxide aggregate - an in vitro study. *Dent Traumatol.* 2016 Apr;32(2):116-20.
60. Yoldaş SE, Bani M, Atabek D, Bodur H. Comparison of the Potential Discoloration Effect of Bioaggregate, Biodentine™, and White Mineral Trioxide Aggregate on Bovine Teeth: In Vitro Research. *J Endod.* 2016 Dec;42(12):1815-1818. doi: 10.1016/j.joen.2016.08.020. Epub 2016 Oct 21.
61. Subramanyam D, Vasantharajan M. Effect of Oral Tissue Fluids on Compressive Strength of MTA and Biodentine™: An In vitro Study. *J Clin Diagn Res.* 2017 Apr; 11(4):ZC94-ZC96.
62. Akcay H, Arslan H, Akcay M, Mese M, Sahin NN. Evaluation of the bond strength of root-end placed mineral trioxide aggregate and Biodentine™ in the absence/presence of blood contamination. *Eur J Dent.* 2016 Jul-Sep;10(3):370-5.
63. Tsesis I, Elbahary S, Venezia NB, Rosen E. Bacterial colonization in the apical part of extracted human teeth following root-end resection and filling: a confocal laser scanning microscopy study. *Clin Oral Investig.* 2017 Mar 28. doi: 10.1007/s00784-017-2107-1. [Epub ahead of print]
64. Escobar-García DM, Aguirre-López E, Méndez-González V, Pozos-Guillén A. Cytotoxicity and Initial Biocompatibility of Endodontic Biomaterials (MTA and Biodentine™) Used as Root-End Filling Materials. *Biomed Res Int.* 2016;2016:7926961.
65. Silva LAB, Pieroni KAMG, Nelson-Filho P, Silva RAB, Hernández-Gatón P, Lucisano MP, Paula-Silva FWG, de Queiroz AM. Furcation Perforation: Periradicular Tissue Response to Biodentine™ as a Repair Material by Histopathologic and Indirect Immunofluorescence Analyses. *J Endod.* 2017 Jul;43(7):1137-1142.
66. Katge FA, Shivasharan PR, Patil D. Sealing ability of mineral trioxide aggregate Plus™ and Biodentine™ for repair of furcal perforation in primary molars: An in vitro study. *Contemp Clin Dent.* 2016 Oct-Dec;7(4):487-492.
67. Sinkar RC, Patil SS, Jogad NP, Gade VJ. Comparison of sealing ability of ProRoot MTA, RetroMTA, and Biodentine™ as furcation repair materials: An ultraviolet spectrophotometric analysis. *J Conserv Dent.* 2015 Nov-Dec;18(6):445-8.
68. Aggarwal V, Singla M, Miglani S, Kohli S. Comparative evaluation of push-out bond strength of ProRoot MTA, Biodentine™, and MTA Plus in furcation perforation repair. *J Conserv Dent.* 2013 Sep;16(5):462-5.
69. Guner MB, Akbulut MB, Eldeniz AU. Effect of various endodontic irrigants on the push-out bond strength of Biodentine™ and conventional root perforation repair materials. *J Endod.* 2013 Mar;39(3):380-4.

Septodont - 58 Rue du Pont de Créteil - 94100 Saint-Maur-des-Fossés - France
Tél. : +33 (0)1 49 76 70 00 - Fax : +33 (0)1 48 85 54 01
Please visit our website for more information:
www.septodont.com

