EndoSequence® BC Sealer™ and Root Repair Material (RRM™) Research Bibliography

Biocompatibility/Cytotoxicity
Subject: BC Sealer Cytotoxicity vs. AH Plus and MTA
Significance/Conclusion: Concluded that BC Sealer™ is highly biocompatible and that it is significantly less cytotoxic than AH Plus.

Subject: Biocompatibility of RRM (Syringable Paste and Putty)
Significance/Conclusion: Concluded that both versions of RRM™ are highly biocompatible and comparable to MTA.

Subject: Cytotoxicity/Biocompatibility of RRM™ compared to MTA (gray and white).
Significance/Conclusion: Concluded that cell viability is similar to both gray and white MTA in fresh and set conditions.

Ruparel, Ruparel, Chen, Ishikawa, Diogenes. Direct Effect of Endodontic Sealers on Trigeminal Neuronal Activity Published Online: March 20, 2014 DOI: http://dx.doi.org/10.1016/j.joen.2014.01.030
Subject: Evaluation of the effect of sealers on peripheral nociceptors. A post-operative sensitivity study.
Significance/Conclusion: Concluded that ZOE and AH Plus in their fresh form evoked greater CGRP release than the control groups. Conversely, EndoSequence BC Sealer reduced basal GCRP release at all concentrations tested.

Subject: Comparison of the cytotoxicity, inflammatory response, osteogenic effect and the signaling mechanisms of the sealers tested.
Significance/Conclusion: iRoot SP (aka BC Sealer) showed lower expression of inflammatory mediators and enhanced osteoblastic differentiation of PDLCs.

Subject: Cytotoxicity and Proinflammatory Cytokine Production of RRM™ compared to MTA.
Significance/Conclusion: Concluded that RRM™ and MTA showed similar Cytotoxicity and Cytokine Production.

**Subject:** Cytotoxicity comparison of **RRM™** vs. popular pulp capping agents (White MTA, Dycal and UltraBlend Plus).

**Significance/Conclusion:** Concluded that RRM™ was the most biocompatible of the group (“after exposure to the 8-day elutes, the respective percentage of cell survivability was 91% (Brasseler), 88% (MTA-Angelus), 76% (Ultrablend Plus), and 37% (Dycal)").

Hui-min Zhou, PhD, Tian-feng Du, DDS, PhD, Ya Shen, DDS, PhD, Zhe-jun Wang, DDS, PhD, Yu-feng Zheng, PhD, and Markus Haapasalo, DDS, PhD. In Vitro Cytotoxicity of Calcium Silicate–containing Endodontic Sealers. *JOE* 2015; (41(1):56-61.

**Subject:** Cytotoxicity evaluation of bioceramic sealers vs. AH Plus (control).

**Significance/Conclusion:** Concluded that BC Sealer was significantly less cytotoxic than MTA-Fillapex and AH Plus.


**Subject:** Direct pulp cap performance comparison (healing and bridge formation) of MTA vs. RRM Putty in dogs.

**Significance/Conclusion:** Concluded that BC RRM Putty performed favorably and as good as MTA. Both MTA and RRM performed excellent. Both groups exhibited bridge formation and an absence of pulpal inflammation.


**Subject:** Cytotoxicity and mineralization evaluation of BC RRM Putty and white MTA on human dental pulp cells (hDPSCs).

**Significance/Conclusion:** Concluded that both BC RRM Putty and White MTA were highly biocompatible and facilitated odontoblastic differentiation of hDPSCs at a similar and favorable level.

Siyi Liu, MD, Sainan Wang, PhD, and Yanmei Dong, PhD; Evaluation of a Bioceramic as a Pulp Capping Agent In Vitro and In Vivo. *JOE*. 2015 (In press)

**Subject:** In Vitro and In Vivo evaluation of BC RRM Putty as a pulp capping agent using hDPSCs as compared to MTA.

**Significance/Conclusion:** Concluded that BC RRM Putty is an excellent pulp capping material and exhibited favorable results for biocompatibility, hDPSCs proliferation and mineralization (bridge formation).


**Subject:** Clinical outcome study of BC RRM Putty for apical surgery and evaluation of prognostic factors influence on the success/performance of BC RRM Putty.

**Significance/Conclusion:** Concluded that BC RRM is suitable for root end filling (92% success rate) and that none of the prognostic factors affected the success.
Ian Chen, DDS, MS, Bekir Karabucak, DMD, MS, Cong Wang, DDS, Han-Guo Wang, DDS, PhD, Eiki Koyama, DDS, PhD, Meetu R. Kohli, BDS, DMD,* Hyun-Duck Nah, DMD, PhD, and Syngcuk Kim, DDS, PhD. Healing after Root-end Microsurgery by Using Mineral Trioxide Aggregate and a New Calcium Silicate-based Bioceramic Material as Root-end Filling Materials in Dogs. JOE. 2015 (in press).

Subject: The purpose of this study was to compare healing after root-end surgery by using grey mineral trioxide aggregate (MTA) and EndoSequence Root Repair Material (RRM) as root-end filling material in an animal model (dogs).

Significance/Conclusion: Like MTA, RRM is a biocompatible material with good sealing ability. However, in this animal model RRM achieved a better tissue healing response adjacent to the resected root-end surface histologically. The superior healing tendency associated with RRM could be detected by CBCT and micro CT but not periapical radiography.

Wafaa K, Siham A JOE 2015 April (Online) Can Mineral Trioxide Aggregate and Nanoparticulate EndoSequence Root Repair Material Produce Injurious Effects to Rat Subcutaneous Tissues?

Subject: Evaluation of effect of implantation of MTA and BC RRM into Rats.

Significance/Conclusion: Concluded that MTA and BC RRM caused an inflammatory effect. The MTA group was significantly more injurious. Given the long term research on the excellent biocompatibility of MTA this study shows that BC RRM is even more friendly with the tissue than MTA (within the parameters of this study).


Significance/Conclusion: Bioceramic-based sealer had less cytotoxicity and genotoxicity and similar antibacterial effect against E. faecalis in comparison with AH Plus sealer.

Mineralization/Osteogenic/Pulp Cells/Pulp Capping


Subject: Evaluation of the mineralization ability of BC RRM Putty compared to MTA.

Significance/Conclusion: Concluded that RRM Putty outperformed MTA in terms of ALP activity and odontoblastic-differentiation associated gene expressions (mineralization). Given RRM Putty’s favorable handling and mineralization performance in this study it can be concluded that RRM Putty is an excellent pulp capping material.

Zhang W, Li Zhi, Peng, B. Effects of iRootSP (aka BC Sealer™) on Mineralization-related Genes Expression in MG63 Cells. JOE. 2010; 36(12); 1978-1982

Subject: Cytotoxicity and Osteoconductivity of BC Sealer vs. AH Plus

Significance/Conclusion: Concluded that BC Sealer was nontoxic and able to induce mineralization and odontoblastic cell differentiation in hDPCs (human dental pulp cells) at a higher level than mineral trioxide aggregate (MTA).

Subject: The aim of this study was to conduct a comparative assessment on the surface morphology and the cell adhesion capacity of iRoot BP Plus (aka BC RRM Putty), iRoot FS (aka BC RRM Fast Set Putty), ProRoot MTA, and Super-EBA on both fibroblast and osteoblast-like cell models. Furthermore, the time-course in vitro cytotoxicity of these materials was accessed.

Significance/Conclusion: Concluded that BC RRM-Fast Set Putty™ is extremely biocompatible and non-cytotoxic. Furthermore, BC RRM exhibited the fastest set time and the best cell adhesion capacity of all the materials tested including ProRoot®.

doi:10.1111/iej.12439

Subject: Direct pulp cap performance comparison (healing and bridge formation) of MTA vs. RRM Putty in dogs.

Significance/Conclusion: Concluded that BC RRM Putty performed favorably and as good as MTA. Both MTA and RRM performed excellent. Both groups exhibited bridge formation and an absence of pulpal inflammation.

doi:10.1111/iej.12393

Subject: Cytotoxicity and mineralization evaluation of BC RRM Putty and white MTA on human dental pulp cells (hDPCs).

Significance/Conclusion: Concluded that both BC RRM Putty and White MTA were highly biocompatible and facilitated odontoblastic differentiation of hDPCs at a similar and favorable level.

Siyi Liu, MD, Sainan Wang, PhD, and Yanmei Dong, PhD; Evaluation of a Bioceramic as a Pulp Capping Agent In Vitro and In Vivo. JOE. 2015 (In press)

Subject: In Vitro and In Vivo evaluation of BC RRM Putty as a pulp capping agent using hDPCs as compared to MTA.

Significance/Conclusion: Concluded that BC RRM Putty is an excellent pulp capping material and exhibited favorable results for biocompatibility, hDPCs proliferation and mineralization (bridge formation).

Retreatability

Subject: Evaluation of the retreatability of BC Sealer vs. AH Plus and other sealers.

Significance/Conclusion: Both BC Sealer and AH Plus were readily retreated using conventional retreatment methods with the ProTaper retreatment instruments.

Subject: The aim of this study was to evaluate the retreatment efficacy and amount of residual sealer in a single canal filled with either EndoSequence BC (Brasseler, Savannah, GA) or AH Plus (Dentsply DeTrey, Konstanz, Germany).

Significance/Conclusion: The present study shows that EndoSequence BC sealer and AH Plus sealer have similar efficacy in dentin penetration and retreatment efficacy.


Significance/Conclusion: Endosequence BC sealer showed similar removal efficacy compared to AH Plus sealer.

Antibacterial Properties

Significance/Conclusion: Bioceramic based sealer was superior to the other materials tested.


Significance/Conclusion: Endosequence root repair material and MTA had superior antibacterial properties against the main cariogenic bacteria compared to the other materials tested.


Significance/Conclusion: EndoSequence BC sealer showed antimicrobial activity against all the microorganisms and proved to be a better choice compared to the other two sealers.


Significance/Conclusion: BC Sealer killed all bacterial within 2 min of contact (fastest), had the strongest antibacterial activity and continued to be effective at killing bacteria for 7 days after mixing/setting. The high pH of BC Sealer makes it extremely effective at killing bacteria.

Lovato, K, Sedgley, M. Antibacterial Activity of EndoSequence Root Repair Material and ProRoot MTA against Clinical Isolates of Enterococcus faecalis JOE. 2011; 37(11); 1542-6.

Subject: Evaluation of the antibacterial properties RRM™ (Syringable and Putty) vs. MTA.

Significance/Conclusion: RRM and MTA both effectively killed E. faecalis. There was no statistical difference between their effectiveness.

Subject: The purpose of this study was to evaluate the antimicrobial effects of root canal sealers on Enterococcus faecalis biofilms in dentinal tubules by using a novel dentin infection model.

Significance/Conclusion: The 3 endodontic root canal sealers had antibacterial effects against E. faecalis in the dentinal tubules. BC sealer and AH Plus had superior antibacterial effects compared with PCEWT. The antibacterial effects of sealers in dentinal tubules continued after setting.


Subject: The aim of this study was to evaluate the pH change, viscosity and other physical properties of 2 novel root canal sealers (MTA Fillapex and Endosequence BC) in comparison with 2 epoxy resin-based sealers (AH Plus and ThermaSeal), a silicone-based sealer (GuttaFlow), and a zinc oxide-eugenol–based sealer (Pulp Canal Sealer).

Significance/Conclusion: The tested sealers were pseudoplastic according to their viscosities as determined in this study. The MTA Fillapex and Endosequence BC sealers each possessed comparable flow and dimensional stability but higher film thickness and solubility than the other sealers tested.

Leakage/Bond Strength/Sealing Ability/Fracture Resistance


Significance/Conclusion: The BC sealer groups had superior push out bond strength compared to the AH Plus groups.


Significance/Conclusion: Bioceramic sealer and epiphany sealed better than AHplus.


Significance/Conclusion: MTA and BC-RRM had similar sealing ability


Significance/Conclusion: All materials showed comparable marginal adaptation at the anatomic apex when used for orthograde obturation of open apices. Application of BC Sealer before the delivery of BC RRM-FS Putty enhanced the quality of adaptation coronal to the apex.
Bolla Nagesh, Eppala Jeevani, Varra Sujana, Bharagavi Damaraju, Kaluvakolanu Sreeha, Penumaka Ramesh. Scanning electron microscopy (SEM) evaluation of sealing ability of MTA and Endosequence as root-end filling materials with chitosan and carboxymethyl chitosan (CMC) as retrograde smear layer removing agents, Vol 19, Issue 2, 2016, 143-146.

**Significance/Conclusion:** Endosequence showed superior sealing ability compared to MTA.


**Significance/Conclusion:** The Endosequence BC group showed the least dye leakage and the highest leakage was seen in the Zinc oxide Eugenot based sealer.


**Significance/Conclusion:** Endosequence and MTA showed less microleakage than Zirconomer and are more suited for furcation repair.


Subject: Comparison of sealability of BC Sealer with a single cone technique vs AH Plus with a warm vertical technique (continuous wave)

**Significance/Conclusion:** The study concluded that there was no statistical difference in the sealing ability of each material with the associated technique used. Warm vertical is considered by many to be the standard of care because it minimizes the sealer layer and fills the majority of the canal 3 dimensionally with a relatively stable filling material (gutta percha does shrink upon cooling). The warm techniques were developed to overcome the limitations of the sealers at our disposal (prior to BC Sealer, sealers have been known to shrink significantly). This study showed that BC Sealer used with a single cone technique, can provided the same sealability as the more time consuming and technique sensitive continuous wave technique with AH Plus.

Nagas E, Uyanik MO, Eymirli A, Cehreli ZC, Vallittu PK, Lassila LVJ, Durmaz V. Dentin moisture conditions affect the adhesion of root canal sealers. JOE. 2011; 38 (2): 240-4

Subject: Comparison of the push out bond strength (and the assumed sealability) of BC Sealer™ + Gutta Percha vs. AH Plus + Gutta, MTA Fillapex + Gutta and Epiphany + Resilon in a full range of moisture conditions (artificially dry, normal, moist and wet).

**Significance/Conclusion:** BC Sealer exhibited, by far, the highest bond strength in all moisture conditions. Many sealers are negatively affected if water or bleach remains in the canal when the sealer is applied. BC Sealer is hydrophilic and achieves its set by utilizing the moisture naturally present in the dentinal tubules. This study proves that regardless of moisture level in the canal, BC Sealer will achieve its set and it exhibits excellent bonding to the canal walls.


Subject: BC RRM Putty Salability vs. White MTA.

**Significance/Conclusion:** Concluded that BC RRM Putty (aka. iRootBP Plus) has a similar ability to that of white MTA in preventing glucose leakage as a root end filling material.
Ersahan S, Aydin C. Dislocation Resistance of iRootSP (aka BC Sealer), a Calcium Silicate-based Sealer, from Radicular Dentine. JOE. 2010; 36(12); 2001-2
Subject: Comparison of the push out bond strength (and the assumed sealability) of BC Sealer™ vs. AH Plus and Sealapex and EndoRez.
Significance/Conclusion: BC Sealer and AH Plus both exhibited high bond strengths which were significantly higher than Sealapex and EndoRez.

Subject: Evaluation of the fracture resistance of teeth obturated with BC Sealer™ + gutta percha and BC Sealer™ + Silicate Coated Points.
Significance/Conclusion: The negative control for this study was tooth that had not undergone root canal therapy. The study concluded that BC Sealer used in conjunction with Brasseler’s coated/impregnated cones (originally ActivGP Point™ but later updated to BC Points™) actually increased the fracture resistance of the root to a level comparable of the negative control. This type of restorative obturation could represent a significant advancement in root canal therapy.

Subject: The aim of this study was to conduct a comparative assessment on the surface morphology and the cell adhesion capacity of iRoot BP Plus (aka BC RRM Putty), iRoot FS (aka BC RRM Fast Set Putty), ProRoot MTA, and Super-EBA on both fibroblast and osteoblast-like cellsmodels. Furthermore, the time-course in vitro cytotoxicity of these materials was accessed.
Significance/Conclusion: Concluded that BC RRM-Fast Set Putty™ is extremely biocompatible and non-cytotoxic. Furthermore, BC RRM exhibited the fastest set time and the best cell adhesion capacity of all the materials tested including ProRoot®.

Subject: The aim of this study is to compare the corono-apical sealing ability of three single-cone obturation systems using a glucose leakage model.
Significance/Conclusion: Hydrophilic groups have shown significantly lesser leakage as compared to the gold standard hydrophobic gutta-percha obturation system. Futhermore, studies would be required to assess the hydrophilic nature of the recent obturation systems.
Subject: The purpose of this study was to evaluate the push-out bond strengths of MTA Plus Sealer, AH Plus and EndoSequence BC Sealer when they were used in cold single cone technique (SC) and a thermoplastic technique (CW).

Significance/Conclusion: BC Sealer showed significantly higher bond strengths than AH Plus and MTA Plus sealer in both cold and warm techniques. The CW obturation technique decreased the bond strengths of both MTA Plus and BC Sealer but BC Sealer (cold and warm) was still higher than AH Plus with warm vertical. Note: This study confirmed that heating bioceramic sealers can effect their bond strength. For non-premixed bioceramics (MTA Plus) the negative effect was shown to be more significant. For premixed bioceramic sealers (BC Sealer) heat did not have a major effect (BC Sealer CW warm still outperformed AH Plus with CW). Furthermore, it is now suggested by Brasseler that BC Sealer be used with a warm vertical technique only at 150C. This study utilized 200C which is warmer than what Brasseler now recommends. For clarification, none of the groups utilized Brasseler’s BC Points which are bioceramic coated and impregnated and have been shown to increase the bond strength when used with BC Sealer.


Subject: The treatments for which mineral trioxide aggregate (MTA)-based materials can be used in dentistry are expanding. Smaller particle size and easier handling properties have allowed the advent of tricalcium silicate sealers including EndoSequence BC Sealer (Brasseler USA, Savannah, GA), QuickSet2 (Avalon Biomed, Bradenton, FL), NeoMTA Plus (Avalon Biomed), and MTA Fillapex (Angelus, Londrina, Brazil). The objective of this study was to measure the tubule penetration with these sealers using continuous wave (CW) and single-cone (SC) obturation techniques.

Significance/Conclusion: Within the limitations of this study, the CW and SC techniques produced similar tubule penetration at both the 1-mm and the 5-mm level with the tricalcium silicate sealers BC Sealer, QuickSet2, and NeoMTA Plus.


Subject: The aim of this study was to evaluate the fracture resistance of teeth filled with 3 different endodontic sealers.

Significance/Conclusion: In contrast to Tech Biosealer Endo, Endosequence BC and AH Plus Jet sealer increased the force to fracture in root-filled single-rooted premolar teeth.


Significance/Conclusion: The push-out bond strength of Bioceramic sealer was highest followed by resin-based sealer and lowest for the MTA-Filapex sealer.


Significance/Conclusion: The push out bond strength of PMTA and ERRMF was significantly increased after exposure to 2.5% NaOCl.

Significance/Conclusion: The use of gutta-percha and a root canal sealer reinforced the root dentin leading to increased fracture resistance in all cases. Bioceramic sealer group exhibited the best results.

Hydrophilicity, Low Contact Angle, Calcium Hydroxide diffusion & Release of Calcium Ions
Significance/Conclusion: “BC Sealer, by far had the lowest contact angle/wetting ability”. The authors attribute the favorable sealing properties of BC Sealer to its “combination of high pH, hydrophilicity, and active calcium hydroxide diffusion”.

Subject: To analyse the effect of commercial and experimental gutta-percha with the additon of niobium phosphate glass on biofilm formation by oral bacteria from human dental plaque. Additional pH and elemental release of the materials were analysed.
Significance/Conclusion: GNB and GBC reduced biofilm formation. GNB had the lowest amount of viable bacteria in biofilms with the highest pH, and high Zn and Na release values after 30 days.

Subject: The aim of the present study was to evaluate the physicochemical properties of a bioceramic root canal sealer, Endosequence BC Sealer. Radiopacity, pH, release of calcium ions (Ca$^{2+}$), and flow were analyzed, and the results were compared with AH Plus cement.
Significance/Conclusion: Endosequence BC Sealer showed radiopacity and flow according to ISO 6876/2001 recommendations. The other physicochemical properties analyzed demonstrated favorable values for a root canal sealer.

Healing
Subject: Compare healing after root-end surgery by using grey mineral trioxide aggregate (MTA) and EndoSequence Root Repair Material (RRM) as root end-filling material in an animal model
Significance/Conclusion: RRM achieved a better tissue healing response adjacent to the resected root-end surface histologically. The superior healing tendency associated with RRM could be detected by CBT and micro CT but not periapical radiography.

Subject: The purpose of this retrospective study was to determine the clinical and radiographic outcome of root-end surgery when EndoSequence BC Root Repair (ES-BCRR) was used as the root-end filling material and to identify any possible prognostic factors that may have affected the healing outcome.

Significance/Conclusion: This current study suggests that ES-BCRR is a suitable root-end filling material to be used in endodontic surgery.


Significance/Conclusion: The overall success rate was 90.9%. The presence of sealer extrusion did not have any significant effect on the treatment outcome. BC used with a single-cone technique is a viable option for obturation.

Color Stability

Subject: Mineral trioxide aggregate (MTA) has been reported to cause tooth discoloration when applied with the esthetic zone. A previous study has shown discoloration of MTA in contact with root canal irrigation solutions. Moreover, there are limited data on color stability of novel calcium silicate-based materials. This study aimed to evaluate color changes of 4 calcium silicate based materials in contact with different irrigation solutions.

Significance/Conclusion: All materials exhibited clinically perceptible discoloration when immersed in sodium hypochlorite and chlorhexidine gluconate. ProRoot White MTA showed a statistically significant difference from Bioaggregate, Biodentine, and white MTA Angelus. Distilled water did not cause any clinically perceptible discoloration of any material. In esthetically critical regions compounds free of bismuth oxide, Biodentine, and BioAggregate can be considered as alternatives to MTA. However, all calcium silicate based materials exhibited clinically perceptible color changes.


Significance/Conclusion: Endosequence RRM putty and Biodentine did not discolor teeth. White and grey MTA and triple antibiotic paste showed the worst chromogenic effect.


Significance/Conclusion: In the absence of blood Biodentine and ERRM showed significantly less discoloration than OrthoMTA

Significance/Conclusion: ERRM and Biodentine did not cause tooth discoloration. ProRoot MTA, white ProRoot MTA and MTA Angelus all caused tooth discoloration.


Significance/Conclusion: Teeth restored with PMTA exhibited progressive discoloration, whereas teeth restored with ERRM maintained color stability over a 4-month period.

Bio-Activity


Significance/Conclusion: ERRM and MTA showed similar proliferation of dentin pulp cells with an increased secretion of angiogenic factors from the cells. Results showed ERRM could replace MTA as a pulp capping agent because it has the same pulp proliferation potential without discoloration.


Significance/Conclusion: MTA and RRM are biocompatible and promote cell proliferation and survival in an ERK-dependent manner.


Significance/Conclusion: ERRM promotes osteoblast differentiation better than MTA and controls with no material in a 3-dimensional culture system.


Significance/Conclusion: EndoSequence was initially irritating. After 6 weeks it displayed more biocompatible characteristics.


Significance/Conclusion: Of all the sealers tested Endosequence showed the lowest cytotoxicity while MTA Fillapex showed the highest cytotoxicity.

Updated 8.10.18

**Significance/Conclusion:** All of the dental cements used in this study are biocompatible with the potential to induce proliferation and osteogenic differentiation of hBMSCs. Therefore, the newly introduced ERRM can be the material of choice in various endodontic applications.


**Significance/Conclusion:** Biodentin (BD) and EndoSequence (ES) promoted greater survival and differentiation of SCAP and the increase of the odontoblastic marker DSPP, whereas MTA appeared to promote greater osteoblastic differentiation. Thus, BD and ES can be considered for regenerative and vital pulp therapies.

**Setting**
Maria Xuereb, Paul Vella, Denis Damidot, Charles V. Sammut, Josette Camilleri.
In Situ Assessment of the Setting of Tricalcium Silicate–based Sealers Using a Dentin Pressure Model, Journal of Endodontics, Volume 41, Issue 1, 2015, Pages 111-124

**Significance/Conclusion:** The dentinal fluid present in the root canal is adequate to allow EndoSequence BC to set inside the root canal.


**Significance/Conclusion:** iRoot fast set had a faster setting time and hydrating process than G-MTA and W-MTA. Machanical properties were similar.


**Significance/Conclusion:** The BC-RRM set with or without the cotton pellet up to a thickness of 6mm.

**Sealer Penetration**

**Significance/Conclusion:** Warn vertical and Single Cone techniques produced similar tubule penetration at both the 1-mm and the 5-mm level with the tricalcium silicate sealers.

**Review article**

**Significance/Conclusion:** Calcium silicate based sealers showed proper physiochemical properties and optimal biologic properties.

Updated 8.10.18