Biodentine™ | Biodentine™ XP*

Indirect Pulp Treatment with Biodentine™**

Scientific summary

Dr Amre Atmeh
BDS, LDS, MSc, PhD
Associate Professor &
Consultant Endodontist - UAE

septodont

* CE for Biodentine™ XP was obtained on the basis of equivalence with Biodentine™.
** Biodentine™/Biodentine™ XP have additional indications. Please refer to the Instruction for Use for the full list.

A Word from the Author

Whether in the research lab or in the clinic, my experience with Biodentine™ spans nearly 15 years. This has given me closer insight into this bulk-fill hydraulic calcium silicate material.

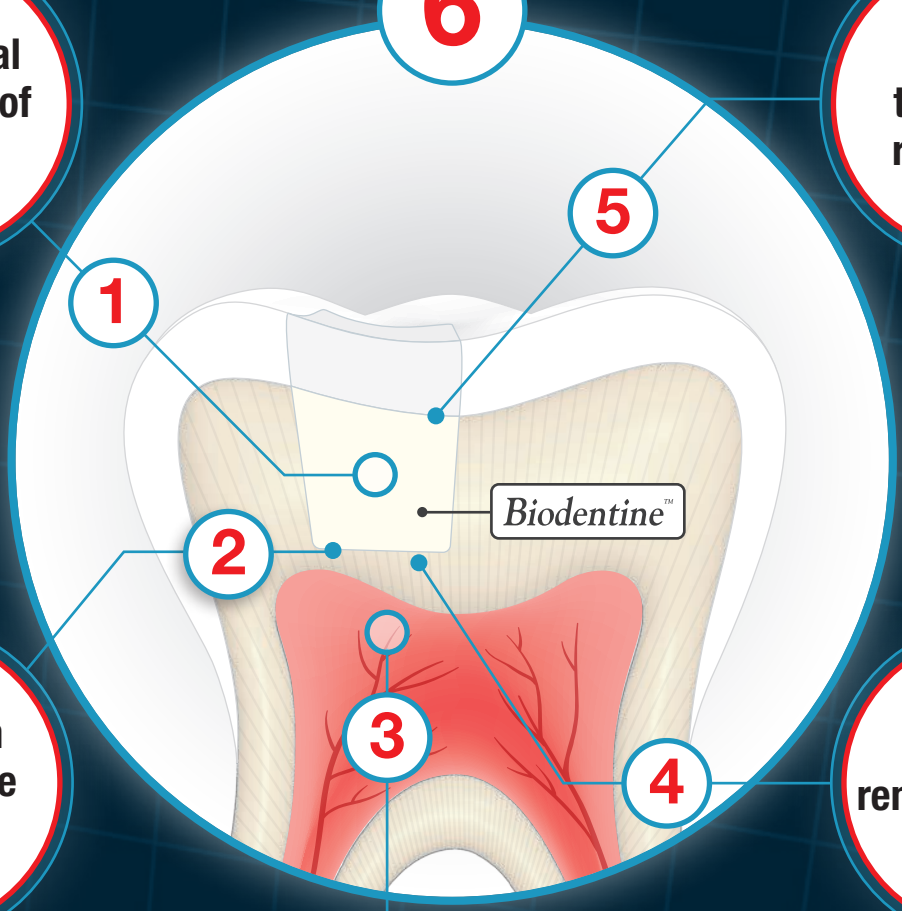
Biodentine™ has been shown to provide a comprehensive solution whenever the dental pulp is concerned. This has become of particular importance in an era where biologically driven approaches in the management of dental caries and pulpal diseases are advocated. This summary provides an evidence-based explanation of the role of Biodentine™ as an indirect pulp capping material. It covers this role from different aspects that relate directly to the clinician's practice. In this summary, a comprehensive review of the scientific literature was conducted, including more than 100 peer-reviewed articles published about Biodentine™ as an indirect pulp capping material since its introduction.

This scientific summary is hoped to provide more insights into the capabilities of Biodentine™ as a solution rather than merely a material within the clinicians' armamentarium in their practices.

Dr Amre Atmeh

Content summary

Clinical success in indirect pulp treatment



1. Mechanical protection of the pulp
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What is **indirect pulp treatment** in the management of deep caries?

Indirect pulp treatment (capping) is a treatment modality of vital pulp therapy, which aims to preserve the dental pulp during the management of deep carious lesions. According to the European Society of Endodontics (ESE), deep caries refers to lesions that reach the inner quarter of dentine, with a zone of residual hard or firm dentine that can be detected in the radiograph. Unlike in direct pulp treatment, there is no pulp exposure and the pulp remains covered by dentine. **However, protecting the pulp may still be necessary, even in the absence of pulp exposure**. This can be due to pulp irritation caused by the deep caries or by aspects of the operative procedure for caries removal, such as vibration and heat generated by the drilling process.

The idea of protecting the pulp stems from the importance of this tissue in preserving the structure, function, and appearance of the tooth. **Preserving pulp vitality can help extend the tooth's lifespan by delaying more invasive endodontic approaches before it is deemed non-restorable**. The moment the tooth is devitalised, the treatment options become progressively limited due to potential treatment failure and increasing loss of tooth structure. Furthermore, vital pulp therapy can provide a cheaper option, avoiding the need for complex restorative work usually required to protect endodontically treated teeth. Therefore, minimally invasive approaches should be considered for the management of deep caries, which mainly focus on selective caries removal.

Minimally invasive management of dental caries has been widely advocated to preserve the dental tissues. The emphasis is on stimulating the body's natural response, allowing the pulp to react and protect itself through various biological pathways, such as the deposition of tertiary dentine. This is achieved alongside the principal objectives of operative caries management, which include removing the affected tissues, restoring function and aesthetics, and preventing disease progression or recurrence. Therefore, approaches such as selective caries removal have been encouraged. This involves the removal of the outer soft, structurally damaged, infected dentine while preserving the inner, firm, caries-affected dentine. Preserving this layer is particularly valuable in cases with deep carious lesions, where excessive removal of caries may lead to pulp exposure; this would require different management strategies ranging from direct pulp capping to pulpectomy.

While minimally invasive management of deep caries aims to reduce the loss of dental tissues during cavity preparation, indirect pulp treatment aims to increase the chances of preserving pulp vitality following the treatment. This requires biologically based treatment strategies that prioritise the pulp. Such an approach should aim to eliminate bacterial contamination, protect the pulp from new bacterial insult or any other source of irritation, and promote pulpal repair and tertiary dentine formation after removing the diseased tissues. **Therefore, the type of pulp capping material plays a crucial role**. It must fulfil certain requirements, including **mechanical protection of the pulp, proper seal, antimicrobial properties and therapeutic effects on the pulp**. This is particularly important in cases of extensive caries, where the residual thickness of dentine cannot be accurately assessed and pulp exposure cannot be confirmed. For such cases, hydraulic calcium silicate materials are recommended.[1] **However, not all of these materials can deliver the properties required to protect the pulp while acting as a restorative material at the same time**.

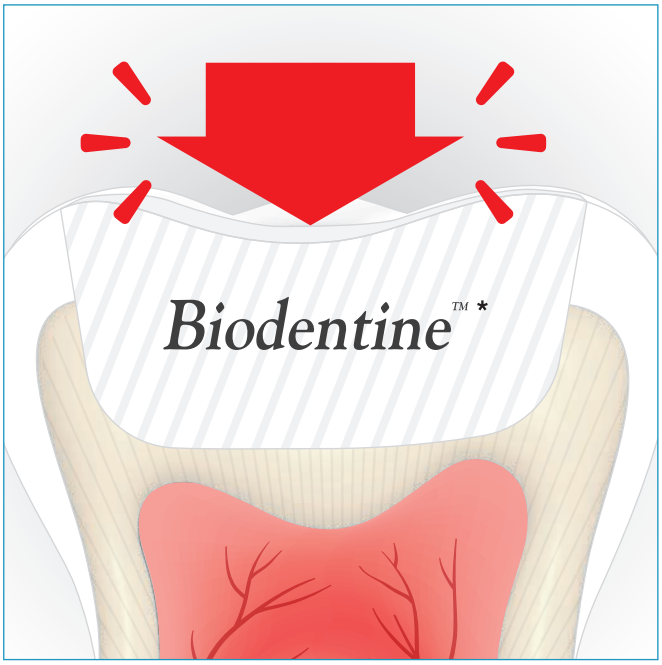
Why Biodentine™ is preferable as an **indirect pulp capping** material?

1. Mechanical protection of the pulp

The dental pulp is naturally protected by an outer shell of hard dental tissues. Comprised of enamel and dentine, this structure ensures that the pulp is sealed from external irritation and well-protected from the mechanical forces applied to the tooth during mastication. However, this "ultimate" protection can be breached and compromised when the hard protective tissues are lost to caries or trauma. Dentine can be further compromised due to extensive or excessive removal during deep caries management or removal of the pulp roof during complete pulpotomy.

The primary function of pulp capping materials has conventionally been related to their effects on the pulp, whether applied directly or indirectly. Calcium hydroxide was once considered the gold-standard capping material due to its antimicrobial properties and therapeutic effects on the pulp. However, calcium hydroxide liners were far from ideal, mainly due to their high solubility and poor mechanical properties, which required additional protection by a dentine replacement material. **Consequently, hydraulic calcium silicates become the gold-standard pulp capping materials in modern dentistry**.

Fig.1 - Resistance to occlusal forces



Due to their poorer handling and mechanical properties, most hydraulic calcium silicate cements cannot be used as dentine replacement materials on their own. **That is not the case with Biodentine™, which provides reliable handling, shorter setting time, and higher strength**. As a restorative material with a thick, viscous consistency, Biodentine™ can be packed with sufficient plasticity to adapt well to cavity walls and irregularities, and to better conform to the dentine surface.[2] When compared to mineral trioxide aggregate (MTA), Biodentine™ exhibited better adaptation to dentine with a significantly lower percentage of void volume and interfacial debonding.[3]

Hydraulic calcium silicate cements set via a hydration reaction when the powder is mixed with water. The calcium silicate particles in the powder dissolve to create calcium silicate hydrate, bonding the solid components together into a paste that hardens over time.[4] Compared to other calcium silicate cements, this setting reaction happens faster in Biodentine™. This is closely related to the high purity, high tricalcium silicate content, and the inclusion of calcium carbonate. More impor-

*Biodentine™ is a permanent dentine substitute; and enamel substitute for up to 6 months.

tantly, the liquid component also features calcium chloride and solubilising polymers, decreasing the water required for the hydration reaction. This controlled water-to-cement ratio is essential for optimal viscosity and handling properties of the mixed cement.[5]

Biodentine™ exhibits exceptional mechanical properties for a pulp capping material. The material quickly hardens during the setting period, continuing to increase in strength for several weeks. After just one week, Biodentine™ has been shown to reach a compressive strength of up to 194 MPa when stored in fluids that mimic saliva[6], a strength comparable to that of glass ionomer cement (GIC).[7] Therefore, unlike other hydraulic calcium silicate cements, **Biodentine™ can act as a coronal bulk fill material (Bio-Bulk Fill) in addition to its function as an indirect pulp capping material**.

2. Interaction with dentine and seal

In coronal restorations, the interface represents the area of contact between the restorative material and the dentine. At this interface, the material can interact with the dentine surface to exert chemical, physical or even biological effects, such as a mechanical seal or an active exchange of minerals between the two substrates.

When Biodentine™ is mixed, the setting process creates a highly alkaline and ion-rich solution, mainly consisting of calcium hydroxide. When this fresh mixture is applied to a cavity, the solution can leach into the dentine. This has two effects: it causes alkaline etching, which can modify the structure of the interfacial dentine, and it promotes the transfer of ions.[8]

Alkaline etching

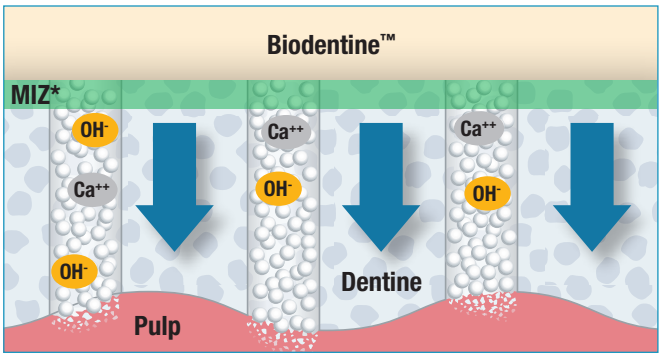
Biodentine™'s natural alkaline etching effect enhances its bond with dentine, improves the quality of the seal, and even promotes dentine remineralisation. The highly alkaline paste targets the organic collagen component of dentine (unlike acid etching that targets inorganic mineral content) and facilitates greater water and mineral transfer into the dentine. This modified dentine layer has been observed using various imaging techniques, including confocal laser scanning imaging, two-photon autofluorescence and second-harmonic generation imaging.[8] It can be compared to the ion exchange layer found in dentine under GIC, which forms via acid etching.

Besides the structural changes, the alkaline conditions were linked to the release of matrix proteins, which may initiate various reactionary mechanisms aimed at protecting the dental pulp.[9]

Ion transfer

Calcium, silicon, hydroxyl and carbonate ions are transferred into the dentine thanks to fluid movement between the cement and dentine. This process is aided by the alkaline etching, which increases water absorption by the affected dentine. During the initial days, the release of calcium ions is at its highest, a process enhanced in Biodentine™ by the calcium chloride present in its liquid.[10] **Interfacial dentine beneath Biodentine™ was observed to absorb calcium, silicon and carbonate ions leaching**

Fig.2 - Alkaline etching and ion transfer



*Mineral infiltration zone

from the cement.[11] After one week, calcium and silicon ions may penetrate approximately 74 µm and 46 µm, respectively, while the carbonate ion is detected at around 48 µm depth.[8,12]

The combined effects of alkaline etching and ion transfer result in the formation of an interfacial dentine layer called the "mineral infiltration zone." This is associated with the formation of tag-like structures within the dentinal tubules, resulting from the flow of the paste into open dentinal tubules. Such changes confirm the interactive nature of the dentine-Biodentine™ interface and help to explain its comparable bond strength to dentine in comparison with GIC.[13] **This interaction could also enhance the seal in the interface area, contributing to the protection of the pulp from irritation caused by leakage**. Although dye leakage studies have limitations, they have shown a similar performance of the dentine-Biodentine™ interface compared with composite[14] and GIC.[15] The glucose diffusion test revealed no significant difference in microleakage between Biodentine™ and resin-modified GIC.[16]

All these factors play an essential role in the quality of the seal provided by Biodentine™ as an indirect pulp capping material. This is necessary to protect the pulp from external leakage and irritation, which could be linked to other types of bulk restorations, such as composites, that might suffer from polymerisation shrinkage and increased leakage.

3. Pulpal therapeutic effects, even with no exposure

Whether applied close to the pulp in deep cavities or in direct contact with it after exposure, bioactivity is an essential property for pulp capping materials. This complements their role in protecting the pulp, acting as a physical barrier that provides mechanical protection and a good seal. Bioactivity is particularly necessary when the pulp is vulnerable under the stresses of bacterial invasion and multi-source irritation associated with caries and its management. Deeper carious cavities mean progressively thinner dentine, which causes more irritation to the pulp as the bacteria get closer and irritants gain easier access. This can worsen the inflammatory response in the affected pulpal tissues and increase the associated symptoms presented as pain. The mechanical removal of caries, which generates heat and vibration, can also affect the pulp and worsen its status, pushing it beyond the limits of vitality. **The material should therefore stimulate pulpal responses** to help in the healing process **and provide further protection** for the remaining pulpal tissues.

Calcium hydroxide liners were traditionally used as indirect capping materials because their therapeutic properties helped the pulp cope with such stresses. Their antimicrobial activity protected against bacterial insult, and their bioactive effects resulted in the formation of tertiary dentine and a hard, protective tissue barrier. This minimised the influence of caries, providing the conditions for the pulp to heal.[17]

Calcium silicate cements produce calcium hydroxide as part of the hydration reaction, exerting similar therapeutic benefits. In fact, because Biodentine™ releases calcium hydroxide at lower concentrations over a longer period, the therapeutic effects on the pulp are found to be more favourable.[18] Further, the potential toxicity of calcium hydroxide in higher quantities is avoided.

The invaluable therapeutic effects of Biodentine™ on the pulp are not present in conventional restorative materials like composites. Using bulk-fill composite materials

near the pulp may in fact be associated with further irritation due to the use of acid etching and the monomer content of the adhesive bonding agent.

When applied to dentine, the ion-rich solution that leaches from the fresh mixture of Biodentine™ can permeate through the open dentinal tubules, gaining access to the pulp and exerting its therapeutic effects. These effects can be indirect or direct, combining to influence the pulp at molecular and cellular levels *(Fig.2*).

Indirectly, freshly mixed Biodentine™ can affect the pulp through the release of dentine matrix proteins[19], stimulated by the high pH of the cement. These work as signalling molecules that act on pulp cells to trigger different reparative pathways, including the formation of tertiary dentine.[20]

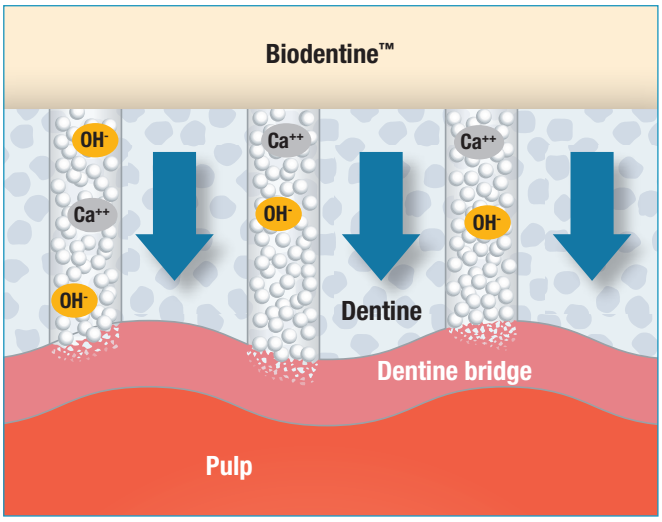
On the other hand, Biodentine™ can directly affect the pulp through the release of ions, which trigger cellular signalling and activation of gene expression of growth factors.[21] This also stimulates the formation of a hard mineralised tissue within the pulp for further protection.[17]

When cultured pulp cells were subjected to Biodentine™ extract, they responded favourably, exhibiting cell proliferation, migration, and attachment, which are important during pulp repair after indirect pulp capping. Opposite responses were observed when using calcium hydroxide, which can be cytotoxic in high quantities, and resin-based calcium silicate materials, which can irritate the pulp.[19,22]

Besides its therapeutic effect on the pulp, Biodentine™ can exert antimicrobial properties attributed to the alkaline pH (12) that limits bacterial proliferation. This effect relies on the release of calcium and hydroxil ions that increase the pH, which found to disrupt the biofilm at the dentin-pulp complex [19,23,24]. The antimicrobial effectiveness of Biodentine™ relies on its release of calcium ions and increased pH[23,24], the latter of which was found to disrupt the biofilm at the dentine-pulp complex.[19]

In conclusion, **the combined pulpal therapeutic effects and antimicrobial properties of Biodentine™ make it the most suitable for indirect pulp treatment during deep caries management**. Inducing pulpal repair and creating unfavourable conditions for bacterial growth and invasion are both beneficial for pulp healing and repair after caries management. This may not only be advantageous in treating pulp affected by deep caries, but it may also prevent postoperative pulp irritation resulting from the operative procedure or postoperative shrinkage of composite restorations.

Fig.3 - Pulpal therapeutic effects



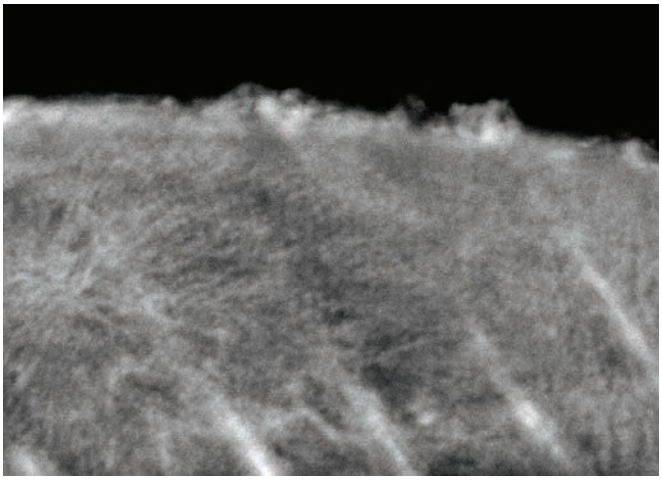
4. Dentine remineralisation

Dental caries results from the chemical dissolution of hard dental tissues (enamel or dentine) caused by the acids produced by bacterial metabolism in the biofilm (dental plaque). Dissolution (or demineralisation) occurs when the pH in the biofilm drops below a certain level, leading to a progressive loss of tissue and the formation of cavitated carious lesions. **Conversely, remineralisation can occur when the pH rises, potentially reversing the process, halting caries progression, and restoring the mineral content of affected enamel or dentine**. It demonstrates the dynamic nature of caries, where progression or remission depends on the surrounding environment and conditions.

With the progression of caries and continuous demineralisation, the dental hard tissues begin losing their structure and integrity, resulting in cavitation. As dentine contains a higher amount of organic matter (30-35% vol.), demineralisation does not lead to total loss of its structure, unlike enamel, which is principally composed of hydroxyapatite.[25] This difference in composition means that even with demineralisation, dentine may retain its original collagenous framework to some extent, albeit with a lower mineral content.[26] Clinically, this layer of inner dentine can be identified as "firm" or caries-affected and has the potential to undergo remineralisation. It is located underneath a "soft," irreparable layer of dentine that has lost its collagenous framework due to caries.

For dentine remineralisation to occur, alkaline conditions must be present, and calcium and phosphate ions must be available. Phosphate is usually available in body fluids, but other ions can be obtained from the restorative material. **Biodentine™ releases calcium, hydroxyl and silicon ions, which are transferred from the material to the dentine via water movement**. When enough ions are present, mineral deposits form, creating a sealed environment that allows the affected dentine to remineralise. Indeed properties attributed to the alkaline pH (12) which limits the proliferation of bacteria.

Fig. 4 - Dentine remineralisation



Two-photon fluorescence mode image showing mineral deposits forming within the matrix of demineralised dentine after storage with Biodentine™.

The ability of a pulp capping material to remineralise dentine underneath carious lesions, as Biodentine™ has been proven to do, is invaluable. It is particularly important in minimally invasive caries management, which encourages the selective removal of caries while sparing the firm, mineralisable dentine.

Research on natural or partially demineralised dentine shows that Biodentine™ is comparable to GIC in terms of remineralisation capability.[27-29] However, unlike GIC, Biodentine™ is also proven to induce remineralisation in completely demineralised dentine that has lost its apatite content.[28-30] This is because Biodentine™'s unique remineralisation process promotes new mineral deposition, while GIC depends on the growth of existing apatite crystals.[28,31,32]

5. Bonding to the final restoration

As a dentine replacement material, **Biodentine™ can provide support for the remaining dental tissues in addition to its therapeutic effects on the pulp**. Teeth restored using Biodentine™ exhibited comparable fracture resistance to those restored with alternative restorative materials.[33] Furthermore, primary teeth treated with Biodentine™ as a pulp capping material demonstrated greater strength relative to those treated with MTA.[34,35] However, for the sake of wear resistance, durability, and improved functionality and appearance, Biodentine™ must be covered by an outer enamel restoration – either a direct resin composite or an indirect ceramic restoration.

For bonding to Biodentine™, different adhesive systems can be used. They are principally divided into two categories: etch-and-rinse adhesives and self-etch adhesives. With the **etch-and-rinse method**, a 35-37% phosphoric acid etch can be applied to all bonded surfaces (total etch) or just the enamel (selective etch), before washing and the application of the bonding agent. In the **self-etch approach**, a separate step of acid etching is not necessary; the bonding agent contains acidic monomers (e.g., 10-methacryloyloxydecyl dihydrogen phosphate (10-MDP)) that demineralise and prime the dentine, facilitating the penetration of adhesive resin monomers into the dentine. Some bonding agents can be used in both methods and are therefore described as “universal.”

A combination of micromechanical retention and chemical bonding usually mediates bonding. The micromechanical retention results from the resin tags formed after resin penetration into the microporosities of the bonded surface and polymerisation. Chemical bonding occurs through the formation of chemical bonds between the functional groups of the monomers and the bonded surfaces, such as the chemical interaction between 10-MDP and hydroxyapatite. **The same mechanisms also apply to bonding with the Biodentine™ surface.**[36,37] However, the wettability of the bonded surface should be considered, as water may interfere with the penetration of adhesive resin and the micromechanical retention. The curing stage of Biodentine™ should also be considered; it should not be bonded during its initial setting time, as this is a critical period in which the material establishes its strength.

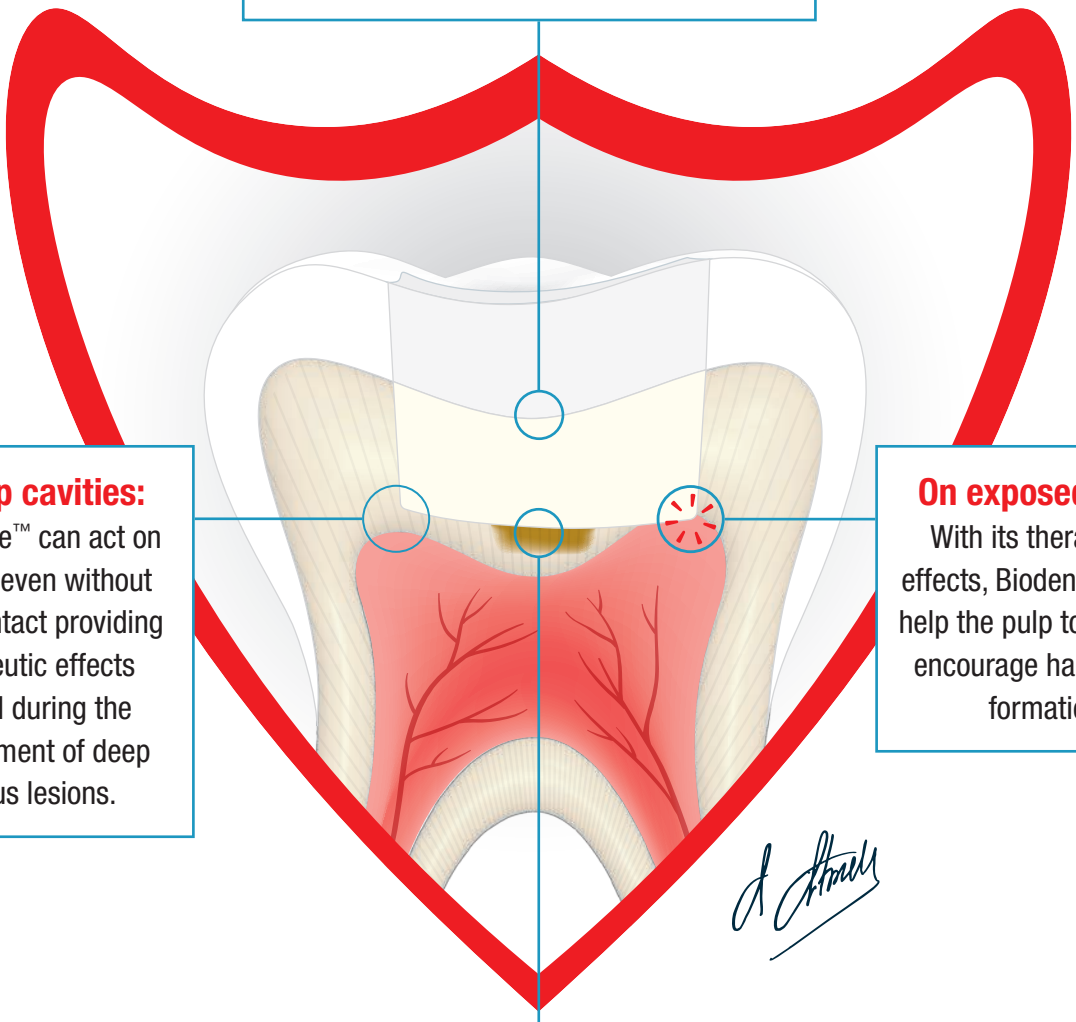
For Biodentine™, most studies have indicated that the timing of bonding to composite, whether in the same visit (after at least 12 minutes of mixing) or a second visit (after 1-14 days of application), has no effect on the bond strength.[38-42]

Furthermore, **numerous studies have demonstrated that the adhesive system used, whether etch-and-rinse or self-etch, has no effect on the shear bond strength**.[36,38,43-46] However, it should be noted that if bonding is performed using an etch-and-rinse method in the same visit, the acid etching should be selective to enamel after 12 minutes of mixing the cement, as etching fresh Biodentine™ can adversely affect its setting reaction.

Universal bonding systems are most useful when used with a selective etch-and-rinse method that allows bonding to all surfaces, regardless of acid etching. Hence, this approach is recommended where Biodentine™ is to be bonded in the same visit. **If the final restoration will be bonded in another visit, either a total etch-and-rinse or self-etch adhesive can be used**, in which both the enamel and Biodentine™ surfaces will be etched. For this approach, it is recommended that etching time should not exceed 30 seconds; prolonged etching will affect the cement without providing the advantage of enhanced bonding.

If Biodentine™ will be covered by composite at a later visit, it requires no provisional protection by any other temporary restoration, such as GIC. It can be used as a bio-bulk fill material, provided there is no contact with opposing teeth out of occlusion. This is because Biodentine™ can establish adequate strength to support the remaining tissues when fully set.[47] Furthermore, the bond strength between Biodentine™ and GIC is very weak, which does not add any advantage.[48]

Under composite restorations:
Due to its strength as a bulk fill material and low shrinkage, Biodentine™ can be placed under composite restoration to minimize postoperative pain



In deep cavities:
Biodentine™ can act on the pulp even without direct contact providing therapeutic effects needed during the management of deep carious lesions.

On exposed pulp:
With its therapeutic effects, Biodentine™ can help the pulp to heal and encourage hard tissue formation

On carious dentine:
Due to its ability to remineralise dentine, Biodentine is suitable with selective caries removal when placed on firm carious dentine

6. Clinical performance

From a clinical perspective, the success of a dental procedure is determined by specific clinical criteria to evaluate the control or resolution of the disease or problem. As a result, the outcome is primarily assessed based on the success rate. For indirect pulp treatment, the success criteria include the absence of any symptoms or clinical or radiographic signs indicating pulpal or peri-radicular disease. This involves a normal response to pulp tests, normal radiographic appearance of the periapical tissues, and absence of any symptoms that indicate disease progression, such as severe or spontaneous dental pain, localised swelling, or pain on biting.

Clinical studies assessing the success of indirect pulp treatment, using different materials, including Biodentine™, reported high overall success rates ranging from 90% to 100%.[49-52] **A higher rate of success with Biodentine™ was observed compared to calcium hydroxide[50], resin-modified glass ionomer[53], and GIC**. These differences, however, were not statistically significant. When cases of irreversible pulpitis were included, with some exhibiting periapical involvement as assessed by cone-beam computed tomography (CBCT), the overall success rate after 12 months was 83%.[54] Cases with signs of periapical healing were significantly higher in those treated with Biodentine™ compared to those that received GIC as an indirect pulp capping material.

While the results from clinical studies are important, they have considerable limitations, due to the short follow-up durations and the weak correlation between clinical assessments and actual histological changes of the pulp.

On another note, **success is multidimensional, involving not only curing the disease, but also other factors such as the comprehensiveness of the treatment provided, durability, patient satisfaction, and cost-effectiveness**. Therefore, for the complete assessment of the clinical performance of pulp capping materials, such factors need to be taken into consideration. This also applies when choosing an indirect pulp capping material, considering both the clinical success rates of the material and its ability to provide a long-lasting treatment. This ensures that patients receive value for their investment with minimal need for further intervention.

Vital pulp treatment using indirect pulp capping usually involves teeth with deep caries that reach the inner quarter of dentine.[1] Therefore, the effectiveness of indirect pulp capping materials goes beyond their therapeutic impact on the pulp. Along with its therapeutic and biological benefits, **Biodentine™ demonstrates a remarkable combination of mechanical strength, effective sealing, and dentine remineralising potential**, as shown in the previous sections. In comparison to other pulp capping materials that provide only a therapeutic effect, **this makes Biodentine™ a unique, comprehensive and cost-effective solution as both a therapeutic and a dentine replacement material**.

The ability of Biodentine™ to create a strong and durable seal that protects the pulp makes it suitable for application after procedures involving total caries removal, which can be associated with an increased risk of pulp exposure. In contrast, with selective caries removal, Biodentine™ provides the ability to remineralise remaining caries-affected dentine as part of a minimally invasive approach. Unlike Biodentine™, calcium hydroxide liners may suffer deterioration and reduced ability to release calcium hydroxide over a shorter time[56], which may affect their durability and pulpal response.[57] This can also explain the lower postoperative pain reported with Biodentine™, which improves patient experience and satisfaction.[52]

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Septodont
58 rue du Pont de Créteil - 94100 Saint-Maur-des-Fossés - France
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