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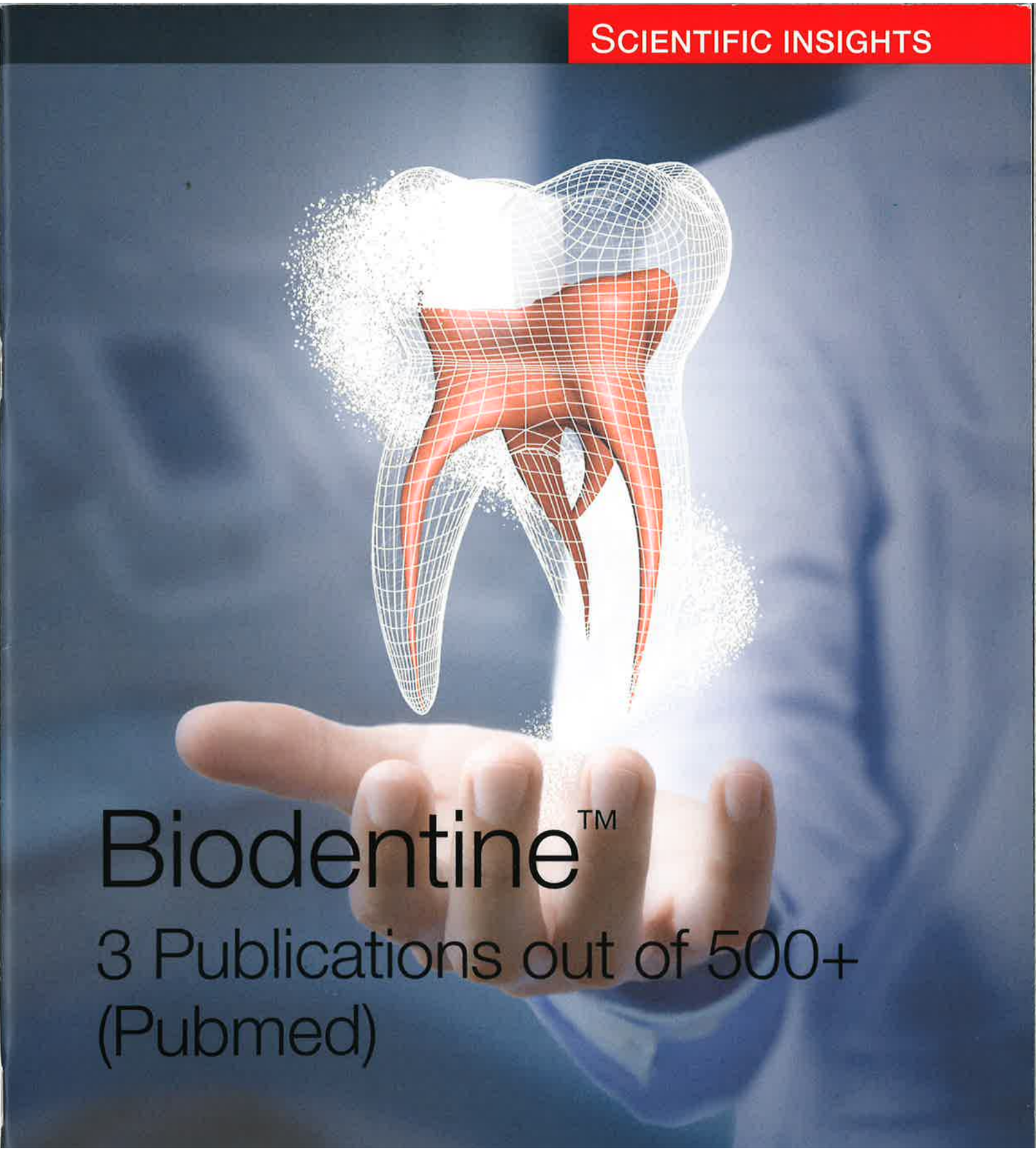

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DENTAL RESTORATIVE MATERIALS (M ÖZCAN, SECTION EDITOR)

Recent Trends in Tricalcium Silicates for Vital Pulp Therapy

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Abstract

Purpose of Review Tricalcium silicates are considered as materials of choice for vital pulp therapy. Recent development improved their mechanical and bioactive properties and broadened their clinical application fields. Incorporating resins to tricalcium silicates further decreased the setting time and simplified clinical procedures but raised questions about their potential toxicity.

Recent Findings Tricalcium silicates represent an added value in vital pulp therapy. This is ascribed to the pulp high regeneration potential, material byproducts production upon hydration and growth factor release from target cells. Adding resins to tricalcium silicates decreases their hydration and subsequently leads to pulp toxicity.

Summary Tricalcium silicates can be successfully used for vital pulp therapy in a broad range of clinical applications. Although long-term clinical studies are still required with these new materials, adding resins to tricalcium silicates is responsible for pulp disorganization and toxicity and cannot be recommended for direct pulp capping.

Keywords Light-cured tricalcium silicates · Direct pulp capping · Hydration byproducts · Pulp regeneration

Introduction

For a long time, direct pulp capping has been performed in immature permanent teeth with traumatic/iatrogenic pulp exposure while carious exposure was managed by pulpotomy or pulpectomy. Tricalcium silicate development rendered direct pulp capping more predictable in mature permanent teeth [1••], and even in teeth with carious exposure [2]. This appears to be due to multiple factors including the material properties, the resulting hydration reaction byproducts, the pulp high regeneration potential and finally, the material bioactivity that induces and stimulates the target tissue regeneration capacity.

Tricalcium silicate materials are known to provide a sealing barrier protecting the underlying pulp from potential toxicity of the applied restorative material and from remnant bacteria or their toxins. This effect may be attributed to the alkaline pH produced locally by the pulp capping material. Over the past decades, significant trends in tricalcium silicates technology have been reported with the release of multiple new materials.

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Mineral Trioxide Aggregate and Derivatives

Mineral trioxide aggregate (MTA) (Dentsply Tulsa, Tulsa, OK, USA) has been and is still among the most widely used direct pulp capping materials. It is refined from Portland cement and composed of tricalcium silicate, dicalcium silicate, tricalcium aluminate, tetracalcium aluminoferrite, gypsum, and bismuth oxide [3••]. The material sets by hydration and is indicated for perforation repair, root end filling [4], one-visit apexification, pulp capping, and regenerative endodontics [5].

MTA as pulp capping material presents a good sealing ability and induces tubular dentin bridge formation within 6 weeks with no signs of inflammation [6, 7•]. However, in spite of its well-demonstrated biocompatibility, MTA has some drawbacks related to its long setting time (2 h 45 min), weak mechanical properties, difficult handling properties [5], and tooth staining when used for regenerative endodontics due to the presence of bismuth oxide as a radio-opacifier [8].

Several modifications were made to overcome MTA drawbacks and various derivatives/alternatives have been developed to improve MTA properties. MTA Angelus (Angelus, Londrina, PR, Brazil), Micro Mega MTA (MM MTA) (Micro Mega, Besançon, France), and Bioaggregate (Innovative Bioceramics, Vancouver, BC, Canada) are among the recently developed MTA derivatives. All three materials are provided in the form of powders and liquids but with similar composition and properties to MTA. It should be noted

though that MM MTA has a shorter setting time (20 min) due to the presence of calcium carbonate. They induce differentiation of human dental pulp cells and mineralization [9]. Although few clinical trials were published with MM MTA and Bioaggregate, all three materials have the same clinical indications: perforation repair, root end filling, and pulp capping [10]. The setting time of these materials is, however, still not short enough for clinical applications and tooth staining was still observed with the materials when used in regenerative endodontics mainly due to the presence of Bismuth oxide as radiopacifier.

Recent Trends in Tricalcium Silicate Technology

Recent advancement in tricalcium silicate technology has taken two distinct directions. The first towards developing tricalcium silicate-based materials with shorter setting time and strong mechanical properties and the second towards improving the handling properties and reducing setting time by developing light-cured materials. This led to the development of Biodentine as a permanent bulk dentin substitute and TheraCal as calcium silicate-resin based hybrid pulp capping material.

Biodentine Has Strong Mechanical Properties

Biodentine is a recently released tricalcium silicate-based material (Septodont, Saint Maur des Fosses, France). Although Biodentine is mainly composed of tricalcium silicates and dicalcium silicates (Table 1), it has a reduced setting time (12 min) due to the addition of calcium chloride as a setting accelerator. Mechanical properties are also improved thanks to the use of a finer particle size, reduced water content, and the presence of a water-reducing polymer [11].

Table 1 Biodentine composition

Powder	Function
Tricalcium silicate	Main core material
Dicalcium silicate	Second core material
Calcium carbonate and oxide	Filler
Iron oxide	Shade
Zirconium oxide	Radiopacifier
Liquid	
Calcium chloride	Setting accelerator
Hydrosoluble polymer	Water-reducing agent

Biodentine as a Permanent Bulk Dentin Substitute

Due to these improved mechanical properties, Biodentine can be applied as permanent dentin substitute without any dentin surface conditioning treatment. Indeed, when it was applied as a bulk restorative material and marginal leakage was investigated, Biodentine sealing was similar to Resin-modified Glass ionomer cement Fuji II LC. When Biodentine was fluorescence-labeled and applied onto the dentin surface, tag-like fluorescent extensions were observed within dentin tubules under the material indicating that sealing appears to occur by micromechanical retention to the dentin [12]. Additionally, different composite resins can be applied on top of this material for final restorations [13]. Thus, Biodentine provides a hermetic sealing preventing marginal leakage. It is not toxic and has been reported to induce proliferation, migration, and odontogenic differentiation of human dental pulp stem cells [11, 14, 15]. Its application directly onto the pulp of extracted and cultured human third molars demonstrated an induction of mineralization within the pulp which had normal histology. When used for direct pulp capping in human teeth and compared to MTA, a complete dentinal bridge formation was obtained with both materials after 6 weeks with mild to absent pulp inflammatory reaction [6, 7•]. Recent data have also demonstrated that Biodentine reduces tumor necrosis factor alpha-induced TRPA1 expression in odontoblast-like cells in vitro by reducing the expression of the transient receptor potential channel A1 and reducing its functional activity [16]. When applied in dentin cavities, Biodentine may reduce nociception and inflammation. Indeed, histological examination has demonstrated either an absence or a mild inflammatory reaction [1••, 7•]. The inflammation degree within the dental pulp is of prime importance as the pulp is located within rigid dentinal walls. Consequently, a severe inflammatory reaction may be deleterious to the dental pulp leading to its necrosis.

Thus, its unique properties and capacity to interact with both soft and hard tissues make Biodentine an ideal permanent bulk dentin substitute, representing a real advancement for a wide range of applications in endodontics, restorative, and pediatric dentistry (Table 2). Additionally, when used in pulp regenerative procedures, no tooth staining was observed due to the incorporation of zirconium oxide as a radiopacifier [8, 43].

Biodentine and MTA mineralization induction potential may be due to calcium ion (Ca^{++}) release and calcium hydroxide ($Ca(OH)_2$) formation during the setting hydration reaction [44•]. It has also been demonstrated that when these materials are applied onto pulp cells, transforming growth factor beta 1 (TGF-β1) is released. This factor is involved in guiding pulp stem cell migration to the material application site and their subsequent differentiation into odontoblastic cells [45, 46].

Table 2 Biodentine clinical applications

Crown		Root
Temporary enamel restoration [17, 18•]	Permanent dentin substitute in: Deep/large carious lesions [17, 18•] Deep cervical/radicular lesions [19–21] Indirect pulp capping [17, 22] Direct pulp capping [6, 7•, 23] Pulpotomy [24–29] Partial pulpotomy [1••, 30]	Root canal/furcation perforations [31, 32] External resorption [33] Internal resorption [34] Regenerative endodontics [35] Apexogenesis after traumatic exposure [36, 37] Apexification [38–40] Retrograde root canal obturation [41, 42]

Overall, these mechanisms explain how a dentin bridge can form under tricalcium silicate-based materials.

Biodentine as a Temporary Enamel Substitute

In addition to its use as a permanent dentin substitute, clinical trials have demonstrated that Biodentine can also be used as a temporary enamel substitute for up to 6 months. In this situation, Biodentine is applied as bulk substitute of both the missing dentin and enamel. Its use in mature and immature teeth demonstrated that Biodentine can be shaped like dentin with burs before permanent restoration with resin [17, 18•].

Calcium Silicate-Resin Hybrid Material for Direct Pulp Capping

Recent advancement made in tricalcium silicate technology is based on combining tricalcium silicates with resins, as in TheraCal™-LC. The aim of this technology is to take advantage of MTA biocompatibility while avoiding its drawbacks: weak mechanical properties and the long setting time (2 h 45 min). This technology ensures an easier clinical procedure by its decreased setting time following photo polymerization and a ready to use syringe containing the material. While many studies were performed on Biodentine in vitro [11–16] and in multiple clinical applications in vivo [1••, 2, 7•, 8, 17, 18•, 24], those performed on TheraCal are scarce and mainly performed on its toxicity [47, 48••] and hydration in vitro [44•]. Only one clinical study with direct pulp capping in humans has been published [1••].

The material combines Portland cement (Type III), fumed silica, barium sulfate, bismuth oxide, and resins (Table 3). It sets by light curing (20 s by 1-mm increments) and the material is indicated as liner in deep cavities under composite restorations and for direct pulp capping [44•]. Thus, opposed to tricalcium silicates where the setting reaction is hydration, the initial setting reaction of materials containing resins such as TheraCal is light curing. Calcium silicate-based cements hydration assessment is usually performed under standardized conditions in vitro. However, it is difficult to relate in vitro conditions to in vivo situations since the replication of environmental conditions is difficult to achieve. Nevertheless, use of extracted molars allowed investigating the material hydration under conditions very close to the in vivo conditions. Indeed, Biodentine and TheraCal were applied directly onto the pulps of freshly extracted human third molars. After restoring the teeth by application of self-etching adhesive resin (Xeno III) and a composite resin (SDR), the teeth were cultured by suspension in the culture medium. Scanning electron micrographs of the materials were examined in different areas: within the biomaterial, at the biomaterial/dentin interface, at the biomaterial/composite resin interface, and at the biomaterial/pulp interface. Overall, this experimental work demonstrated a lack of hydration of TheraCal while Biodentine hydration was complete. Investigation of calcium ion release and by ion chromatography and hydration byproducts with X-ray diffraction analysis showed a high calcium ion release and a significant peak in calcium hydroxide formation with Biodentine. In contrast, less calcium ions were released and a calcium hydroxide peak was absent with TheraCal due to the lack of its hydration [44•].

It has been repeatedly demonstrated that resin polymerization is never complete and it is considered that 1.5–5% of the monomers remain free within the material. When they reach the pulp, they have significant toxic effects. Direct application of TheraCal onto the pulp may even lead to a higher

Table 3 TheraCal composition

TheraCal composition	(% by weight)
Portland cement (Type III)	44
Fumed silica	7
Barium sulfate	3
Bismuth oxide	3
Resins and initiator	43

percentage of free monomers due to the humid environment. Additionally, the material contains 43–45% of resin. Up-to-date, no studies reported on TheraCal polymerization degree or monomers release. However, TheraCal induces toxicity to cultured pulp cells [47, 48••] and when applied on entire teeth and cultured for 2 weeks, it has been shown to induce pulp disorganization and dispersed mineralization. In contrast, Biodentine application directly onto the pulp induced a mineralized matrix formation with the molecular characteristics of dentin and normal pulp histology [48••]. Another study confirmed these differences between tricalcium silicates with and without resin. Indeed, 8 weeks after TheraCal, MTA ,or Biodentine application in partial pulpotomy, histological examination demonstrated a disorganized pulp tissue and either absence or dispersed mineralization with TheraCal while normal pulp histology and dentin bridge formation were observed with Biodentine and MTA [1••]. These data clearly indicate harmful effects of the resin-containing material on the dental pulp.

Tricalcium Silicates Bioactive Properties

Tricalcium silicates are qualified as bioactive materials because of their capacity to elicit a specific response in the target tissue such as mineralization, creating a link between the material and the underlying target tissue. They have also been used for constructing bone scaffolds to treat bone defects. Human bone marrow-derived mesenchymal stem cells cultured in tricalcium silicate-based scaffolds demonstrated osteogenic differentiation with a higher expression of bone markers such as alkaline phosphatase, osteopontin, Runx2, bone sialoprotein II, and bone morphogenetic protein 2 [49]. This may be due to the presence or release of silicon ions, which is an important element for young bone mineralization as their release induces osteoblast cells to produce bone [50]. Recently, it has also been shown to induce osteoblastic differentiation of bone marrow stromal cells [51]. This may explain the successful outcome of MTA and Biodentine when used to seal furcation perforations, with good bone regeneration in the periapical area and a complete regeneration of the pulp floor [32].

Silicon ion effects are less studied in the dental pulp; however, the presence of this ion may also be involved in the mineralization process. Indeed, when Biodentine was applied as a direct pulp capping material in extracted and cultured human third molars, a significant number of mineralized foci were produced within the pulp under the material. Molecular markers of the dentin such as collagen I, osteonectin, and dentin sialoprotein were expressed in the mineralized foci. Cells in contact with these mineralized foci expressed odontoblast markers such as nestin and dentin sialoprotein. Interestingly, small particles of tricalcium silicates were entrapped within these mineralized foci indicating that the material itself may be involved in the odontoblastic differentiation and mineralization [45, 48••].

It should be noted, however, that the major part of tricalcium silicate studies in the dental pulp focused on the materials' clinical effects, their byproducts, and the release of growth factors from pulp cells (Fig. 1).

Tricalcium Silicate Byproducts

Tricalcium silicate materials such as MTA and Biodentine set on hydration leading to byproducts formation. These byproducts have been extensively studied showing their significant role in the materials' bioactivity.

Hydroxyl Ions

Release of hydroxyl ions (OH^-) during the hydration reaction leads to an alkaline pH in the surrounding environment inhibiting bacterial growth [52] which significantly contributes to the material sealing ability as demonstrated with Biodentine [12, 13]. While a necrotic zone forms between the material and underlying tissue due to the alkaline pH, this necrotic zone protects the underlying pulp from additional pH increase and allows the initiation of pulp regeneration. This necrotic zone has been reported to be thick with calcium hydroxide but it is rather thin with MTA and Biodentine [1••].

Calcium Ions

Calcium ion release is among the most frequently reported hydration byproduct. Different calcium concentrations have been reported to be released depending on the material used and the experimental protocol. This ion seems to be involved in the mineralization process as it induces differentiation of human dental pulp cells and an enhanced mineralized matrix nodule formation was found with higher Ca ion concentrations [44•, 53]. High Ca ion release has been reported with MTA and Biodentin while a lower level was found with TheraCal [44•]. These in vitro properties appear well correlated with the material activity at cellular [45, 54], histological [55–57], as well as clinical levels [6].

Calcium Hydroxide

Calcium hydroxide has long been used for pulp capping with a well-demonstrated ability to induce dentin bridge formation [7•]. X-ray diffraction analysis after setting demonstrated a significant peak of calcium hydroxide with Biodentine and another experimental tricalcium silicate-based material, but an absence of this peak was noted with TheraCal [44•]. This is in line with the

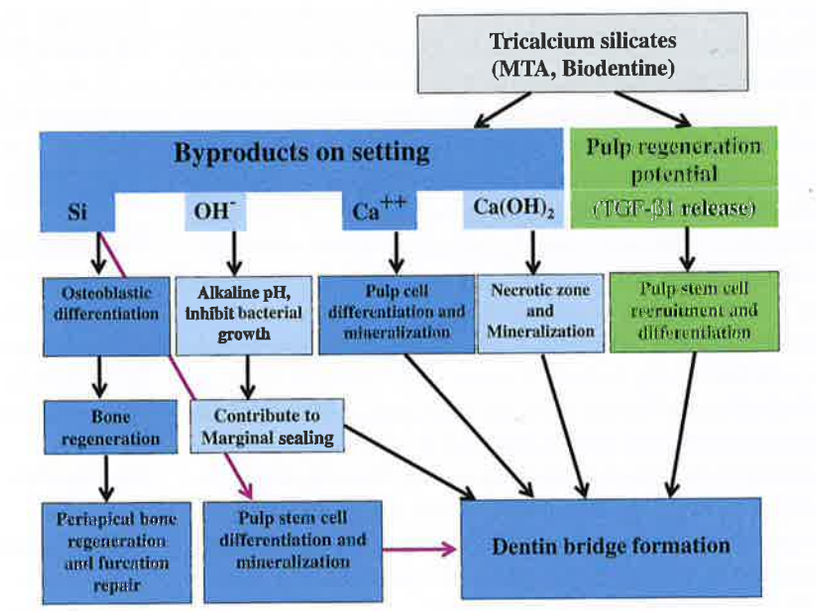

Fig. 1 Tricalcium silicate interaction with target tissues. Tricalcium silicates induce cell differentiation directly due to the presence of silicium ions in their composition. On hydration, byproducts such as hydroxile (OH^-), calcium ions (Ca^{++}), and calcium hydroxide Ca(OH)2 are produced. These play a significant role by their antibacterial activity and induction of mineralization. Interaction of tricalcium silicates, such as MTA and Biodentine with the pulp, induce release of TGF-β1 which guides pulp stem migration and differentiation. All these contribute to bone regeneration and dentin bridge formation

clinical finding demonstrating dentin bridge formation with Biodentine and MTA [1••, 7•] and its absence with TheraCal [1••].

Pulp Regeneration Potential and TGF-β1 Release

The dental pulp has a high regeneration potential due to the presence of both stem cells capable of dentin-pulp regeneration and pulp fibroblasts involved in multiple processes regulating the pulp inflammation and regeneration. Indeed, in addition to the current knowledge on stem cell regeneration potential, pulp fibroblasts secrete growth factors involved in the induction of pulp neo-angiogenesis which represents a pre-requisite to the pulp regeneration process [58]. Recent works demonstrated that pulp fibroblasts synthesize and locally produce innate system complement bioactive components and this synthesis and production increases after mechanical, microbial, or chemical injury to the pulp fibroblasts [59•]. Indeed, while the complement component C3a induces mobilization and proliferation of stem cells [60], another complement component, C5a, guides stem cell migration and neuron sprouting towards the pulp injury site leading to pulp regeneration after injury [61, 62]. Additionally, the dental pulp is also involved in regulating the degree of pulp inflammation and in controlling bacteria growth by expressing receptors such as the toll-like receptors which recognize pathogens and initiate the pulp inflammatory reaction while producing antibacterial agents such as nitrogen oxide [63, 64]. Furthermore, pulp fibroblasts synthesize a complex structure of complement proteins called membrane attack complex (MAC), which fix on the membrane of cariogenic bacteria leading to their destruction [65•]. This has been demonstrated by preparing co-cultures of fibroblasts with cariogenic *Streptococcus mutans* or *Streptococcus sanguinis*. Immunofluorescence revealed MAC synthesis by the fibroblasts within 30 min and its direct fixation on *S. mutans* and *S. Sanguinis*. MAC fixation on these cariogenic bacteria led to a significant decrease in their viability [65•].

This pulp antibacterial potential and pulp regeneration capacity is best demonstrated in fractures of mature teeth with pulps exposed to the oral environment for up to 8 days. Indeed, an interesting paper published on four clinical cases with fractured teeth demonstrated that, after the superficial layer of the exposed pulp and the surrounding tissue were excised to a depth of 2 mm, Biodentine application directly over the exposed pulp preserved pulp vitality and initiated dentin bridge formation. This was further demonstrated during the 18 months follow-up where no spontaneous pain was observed; the pulp showed signs of vitality and absence of periapical radiolucency [30].

Tricalcium silicates such as MTA and Biodentine (and their byproducts) not only play a major role in dentin bridge formation but their application on pulp cells also induces a significant increase in TGF-β1 secretion. This has been reported with different sample surface areas indicating that the material can be applied whatever the injury size [45]. Indeed, Biodentine clinical application has reported successful clinical outcome even in pulpotomy, which implies a large pulp injury [24]. This indicates that when Biodentine is applied directly onto the pulp, the underlying pulp cells release TGF-β1. When TGF-β1 was encapsulated into polylactic-polyglycolic microspheres, its controlled release guided pulp stem cell migration. This growth factor has also been reported

to be involved in odontoblastic differentiation leading to dentin bridge formation as reviewed in [66].

Conclusions

There is clear evidence that tricalcium silicate-based materials such as Biodentine and MTA are biocompatible and bioactive and can be applied safely onto the pulp. Their mineralization induction capacity has been well demonstrated in vitro by the induction of mineralized matrix having dentin and odontoblast molecular characteristics. When used for direct pulp capping, dentin bridge formation was obtained. These effects seem to be due to the hydration byproducts on setting such as calcium ions and calcium hydroxide on one hand, and the interaction of the material directly with the pulp cells and the subsequent release of TGF-β1 on the other hand. Indeed, TGF-β1 provides a chemotactic gradient guiding stem cell migration to the material application site, and this growth factor, together with calcium ions and calcium hydroxide, is also involved in odontoblastic differentiation of migrating cells and dentin bridge formation (Fig. 1).

The unique mechanical properties of Biodentine expanded the clinical application field of this material as a permanent dentin substitute in endodontics, restorative, and pediatric dentistry. Additionally, Biodentine is the only tricalcium silicate-based material that can be applied as a temporary enamel substitute. While long-term studies are available for MTA, these are still lacking to cover the different clinical applications with Biodentine.

The presence of resins in direct pulp capping materials such as TheraCal shortens the setting time and its presentation in a syringe as a ready to use product simplifies its clinical application. However, the few studies published on this material demonstrate that TheraCal induces cell toxicity and pulp disorganization without any dentin bridge formation when applied directly onto the pulp.

To conclude, even though long-term clinical investigations are still required to support their wide range of clinical applications, new tricalcium silicate-based materials such as Biodentine represent a significant step-forward in vital pulp therapy. A major requirement for future tricalcium silicate-based material development is a shortened setting time. However, for direct pulp capping purposes, it is clear that adding resins to tricalcium silicates is not a recommended strategy.

Compliance with Ethical Standards

Conflict of Interest Dr. About reports grants from Septodont.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- •• Of major importance

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ORIGINAL ARTICLE

Clinical evaluation of direct pulp capping using a calcium silicate cement—treatment outcomes over an average period of 2.3 years

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Abstract

Objectives This study aims to assess the treatment outcomes of direct pulp capping with a calcium silicate cement (Biodentine) after caries excavation.

Materials and methods A total of 245 teeth of 226 patients diagnosed to be clinical healthy or showing spontaneous pain were directly capped. The teeth were examined 0.19 to 7.4 (mean 2.3 ± 2.04) years after treatment. The following data were recorded: age and sex of the patient, type of tooth and restoration (glass ionomer cement [GIC], amalgam, composite resin, ceramic, gold) and symptoms before or after treatment. The evaluation of the treatment was carried out by sensibility and percussion testing and by the patient's questioning. A positive sensibility test, a negative percussion test, the absence of swelling and discomfort were considered as treatment success. Survival analysis was performed using the Kaplan-Meier, log-rank, Chi-square and Fisher's exact test, respectively.

Results After an average period of 2.3 years, 86.0% of the teeth remained vital; the survival rate after 7.4 years was 83.4%. The treatment outcome was significantly worse for cavities restored with GIC compared to all other restorative materials ($p < 0.05$). All other evaluated factors had no significant influence on the success rate ($p > 0.05$).

Conclusion Exposed pulps of asymptomatic vital permanent teeth and teeth with spontaneous pain before treatment can be successfully capped directly using Biodentine. A subsequent restoration with GIC does not appear to be suitable as it significantly reduces the success of the treatment.

Clinical relevance Direct pulp capping can be done successfully with this type of calcium silicate cement.

Keywords Biodentine · Calcium silicate cement · Direct pulp capping · Treatment outcome

Introduction

Originally, calcium silicate cements like mineral trioxide aggregate (MTA) were developed to seal perforations in the root canal system. However, it soon became obvious that MTA is also suited for maintaining the vitality of the dental pulp [1–3]. The advantages of this calcium silicate-based material over the usually used calcium hydroxide products lie in the higher mechanical strength, lower solubility and tighter sealing of the dentine. Three major disadvantages of calcium hydroxide could thus be avoided when using MTA: dissolution of the capping material as well as the mechanical instability and consequent lack of long-term protection against bacterial microleakage [3]. Despite these advantages, literature is still inconclusive concerning the superiority of MTA over calcium hydroxide suspensions. In some reports, MTA produced better clinical outcomes and showed higher success rates than calcium hydroxide in direct capping [4–6]. Thus, in a meta-analysis, it was stated that direct pulp capping with MTA has a higher success rate, results in a lower pulpal inflammatory response and a more reliable formation of hard tissue than calcium hydroxide. MTA appears to be a suitable substitute for calcium hydroxide in direct capping [7], whereas other systematic reviews [8, 9] and randomised control trials [10] failed to confirm any superiority of MTA and MTA-like materials when covering the exposed pulp tissue in vital pulp therapy.

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Biodentine® (Septodont, Saint-Maur-des-Fossés, France) is another kind of calcium silicate cement. Whereas the composition of MTA is more or less comparable to a refined Portland cement [11, 12], Biodentine consists mainly of pure tricalcium silicate (about 80%) with calcium carbonate as filler (about 15%). Zirconium oxide is added as radiopacifier (about 5%). In contrast to other calcium silicate cements and MTA, Biodentine does not contain dicalcium silicate or metal oxides except the radiopacifier [13, 14]. The liquid consists of calcium chloride in an aqueous solution with an admixture of modified polycarboxylate. The powder is mixed with the liquid in a capsule in a triturator for 30 s. Once mixed, Biodentine sets in about 15 min minimum, presumably up to 85 min [15].

During setting, Biodentine releases calcium ions and calcium hydroxide is formed [16], leading to an alkaline pH in the surrounding tissues, thereby inhibiting the growth of microorganisms [17]. Furthermore, when Biodentine is applied onto pulp cells ex vivo, transforming growth factor beta 1 (TGF-β 1) is released [18, 19]. In vitro Biodentine induces proliferation, migration and differentiation of human dental pulp cells [20–22]. These factors may explain hard tissue formation after direct pulp capping with Biodentine [23]. Thus, histological evaluation in humans revealed a complete hard tissue formation 6 weeks after direct pulp capping with mild to absent pulp inflammatory reactions, comparable to MTA [24, 25]. In addition, Biodentine interacts with dentine leading to a sealing by micromechanical retention [26] and a shear bond strength that is comparable to glass ionomer cements [27]. Different light-curing adhesive resinous lining materials are able to bond on Biodentine [28]. Thus, Biodentine may prevent bacterial leakage [23].

Success rates of direct pulp capping with Biodentine were evaluated in clinical studies in humans to be between 82.6% [29] and 100% [30, 31] and thus partially higher than those given for ProRoot MTA (Dentsply Tulsa Dental, Tulsa, OK, USA) [4–6, 32, 33]. But it had to be kept in mind that the meaningfulness of some of these data for Biodentine [30, 31, 34–36] is limited. Limitations were, e.g. small sample size of mere 12 [34] or 13 [35] patients, short follow-up period of 6 [34] to 12 months [30, 31] and very young patients with permanent teeth but immature root apices [30, 31, 36]. Because of these limitations, these results should be considered with some caution. While long-term studies about direct pulp capping are available for MTA, these are still lacking for Biodentine [23].

Hence, to gain more information about success rates, the aim of this retrospective study was to assess the treatment outcomes of direct pulp capping using Biodentine after iatrogenic pulp exposure during caries excavation. Moreover, the relation of prognostic factors like age, gender, kind of tooth and restoration, arch (mandible or maxilla) and status of the pulp tissue on the likelihood of a favourable treatment outcome of direct pulp capping using Biodentine was evaluated.

Materials and methods

Between 2009 and 2017, 245 teeth of 226 patients were directly capped with Biodentine (Septodont, Saint-Maur-des-Fossés, France) after the pulp tissue had been iatrogenically exposed during deep caries excavation. No pulp capping of traumatically exposed pulps were included in this study.

All treatments were conducted strictly in full accordance with ethical principles, including the World Medical Association Declaration of Helsinki (version 2008). The patients received a thorough explanation of the clinical procedures and possible complications. The treatments were undertaken with the understanding and written consent of each patient and according to the above mentioned principles.

Four dentists of the Department of Endodontics in the Dental School of the Westphalian Wilhelms-University Münster, Germany, participated in the study. All of them were visited by one of the authors (TD) before the start of the study and underwent a training program. The participating dentists were calibrated with regard to diagnosis, rubber dam placement, cavity disinfection, haemostasis, mixing and application of Biodentine and definitive restoration.

The following clinical parameters were assessed as part of the preoperative diagnosis before direct pulp capping was performed: sensibility test with CO_2, general pain and pain on percussion. A pulp was considered to be "clinically healthy" if it did not show spontaneous pain or pain on percussion, if the sensibility test was positive and the triggered pain not lingering. Furthermore, pulp bleeding after exposure could easily be stopped within 5 min. Teeth with "spontaneous pain" were defined as teeth where the sensibility testing was positive, discomfort before and/or subsequent to direct pulp capping was reported by the patient (spontaneously pain), no pain or uncertain pain on percussion, and pulp bleeding could be stopped within 5 min.

A tooth was considered to have an "irreversible pulpitis" if the patient complained about spontaneous pain and/or pain on percussion, pain exacerbated by cold stimuli, lasting from a few seconds to several hours and if the pulp bleeding after exposure could not be stopped within 5 min. Teeth diagnosed to have an "irreversible pulpitis" were excluded from direct pulp capping.

All patients were treated under consistent, standardised and aseptic conditions: local anaesthesia (Septanest; Septodont, Saint-Maur-des-Fossés, France), use of rubber dam from the beginning of the treatment, disinfection of rubber dam and tooth surfaces with NaOCl (3%), cavity preparation using a high-speed handpiece with diamond instruments under copious water cooling, excavation with a slow speed handpiece with sterile stainless steel bud burs, cavity cleaning and haemostasis with cotton pellets soaked with NaOCl (3%) and caries-free dentine before direct pulp capping. The following parameters were used to assess caries-free status of the

dentine: hardness on probing, dentine colouration and the unique sound of unaffected dentine on probing ("cri dentinaire"). However, during caries excavation, efforts were made not to expose the pulp tissue.

For direct pulp capping, Biodentine was mixed strictly according the manufacture's instruction, applied to the exposed pulp tissue and the surrounding dentine with a minimum layer thickness of 1.5 mm, leaving a dentine margin of at least 1.5 mm wide for the final restoration [37]. Biodentine was allowed to set for 3 min and then covered with a thin layer of a self-etching, self-bonding flowable composite resin (Vertise flow; Kerr, Orange, CA, USA) [28]. Subsequently, the cavities were eventually restored with composite resin (Estelite Sigma Quick; Tokuyama Dental, Yamaguchi, Japan) in combination with a self-etching dentine adhesive (OptiBond XTR; Kerr, Orange, CA, USA), amalgam (Vivacap; Ivoclar Vivadent, Schaan, Liechtenstein), glass ionomer cement (Ketac Fil; 3M Espe, Seefeld, Germany) or Biodentine due to time constraints. Temporary fillings with glass ionomer cement and Biodentine were supposed to get replaced in the near future and were done without a Vertise lining.

In 2018, all 226 patients (245 teeth) who received direct pulp capping with Biodentine in the past years were examined. A questionnaire was completed by one dentist (CH), who was not involved in the patients' treatment, with questions on the patients' age at date of treatment and gender, type of affected tooth and restoration, spontaneous symptoms or pain on percussion and/or palpation, sensibility of the tooth, date of treatment and if the patient visited another dentist as well. The sensibility test was performed using CO_2. Also, possible discolouration in comparison to neighbouring teeth was recorded. In addition, the oral cavity was inspected and the periodontal pocket depths were measured. Teeth with periodontal probing depths of more than 3 mm were excluded from the study in order to avoid interference from the periodontal and endodontic damage.

The treatment outcome was considered to be "favourable" when the following criterions were found: positive sensibility test to CO_2, no general pain, no pain on percussion or palpation and no swelling. These teeth were considered to be "clinically healthy". Teeth were considered to show an "unfavourable treatment outcome" if they did not respond to pulp sensibility test, pain on percussion or palpation and/or swelling was visible. If teeth underwent root canal treatment or were extracted, they were also assessed as "unfavourable treatment outcome". A radiological follow-up examination was not performed due to ethical reasons.

The data were statistically analysed using descriptive statistics including minimum and maximum values, standard error and mean values. The Kaplan-Meier statistics were used to calculate the survival rate. To compare the qualitative variables, Chi-square and Fisher exact test was performed. The log-rank test was used to determine p values which are considered as significant when $p < 0.05$.

Results

The follow-up period was 0.19 to 7.4 years after direct pulp capping with a mean follow-up period of 2.3 (± 2.04) years. After the mean follow-up period of 2.3 years, 219 of the 245 teeth showed a favourable treatment outcome (89.39%), whereas 26 teeth (10.61%) showed an unfavourable treatment outcome. The likelihood of having a favourable treatment outcome after 2.3 years was 86.0%. Out of the teeth with unfavourable treatment outcome, most teeth became non-vital during the first year of examination. Likewise, the cumulative survival rate decreased from 92.8% after 1 year to 86.9% after 2 years.

In total, 28 teeth (11.43%) showed an unfavourable treatment outcome 7.4 years after direct pulp capping. The Kaplan-Meier function allowed analysing the cumulative survival rate of the pulp tissue over 7.4 years by calculating the likelihood of having a favourable treatment outcome within the examination period. This function showed that the survival rate descended to 83.4% after 3.4 years. The survival rate remained at that level and did not decrease further until the end of examination period. Hence, the likelihood of having a favourable treatment outcome after 7.4 years still was 83.4% (Fig. 1).

Out of 245 teeth, 236 were diagnosed to be "clinically healthy" whereas 9 teeth showed "spontaneous pain" before the treatment. None of the 28 teeth having an unfavourable treatment outcome after 7.4 years showed "spontaneous pain" before direct pulp capping. Hence, the clinical parameter "spontaneous pain" had no significant impact on the treatment outcome.

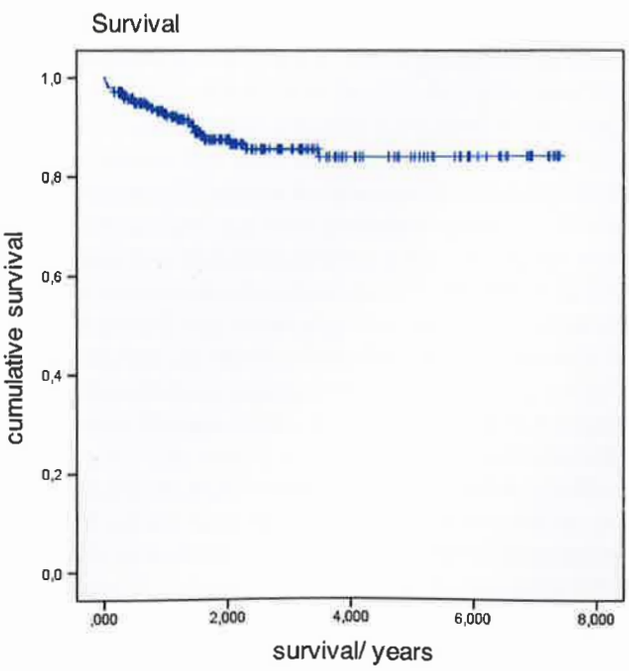

Fig. 1 Cumulative survival after direct pulp capping (Kaplan-Meier function)

The age of the patients at the time of direct pulp capping ranged from 10 to 88 years with a mean age of 42.02 (± 17) years. For further analysis, the patients were grouped in five age cohorts (Table 1). The youngest cohort showed the highest cumulative survival rate of 100% after 2.3 (± 2.04) years, whereas the oldest cohort showed the lowest cumulative survival rate with 76.2%. Nevertheless, no significant difference between age and favourable treatment outcome was found ($p > 0.05$) (Fig. 2).

The distribution between the sexes was balanced: 55.1% of the included patients were males ($n = 135$) and 44.9% ($n = 110$) females. This difference was not significant ($p > 0.05$). A total of 64.5% ($n = 158$) of the treated teeth were in the maxillary arch and 35.5% ($n = 87$) in the mandible arch. There was no statistically significant difference between the two arches ($p > 0.05$) with regard to treatment outcome. A total of 6.94% ($n = 17$) of the capped teeth were incisors, 5.71% ($n = 14$) canines, 32.7% ($n = 80$) premolar teeth and 54.47% ($n = 134$) molar teeth. Table 2 shows a more detailed distribution of the teeth. The type of tooth had no statistically significant influence on treatment outcome ($p > 0.05$).

Directly after pulp capping, 93.88% of the teeth were restored with composite resin ($n = 230$), 2.44% with amalgam ($n = 6$), 2.86% with glass ionomer cement ($n = 7$) and 0.82% with Biodentine ($n = 2$). At the time of follow-up, eight of the composite resin fillings were replaced by ceramic (3.3%) and six by gold (2.45%) restorations. A total of 88.16% ($n = 216$) of the teeth were restored with composite resin. Teeth that were long-term restored with glass ionomer cement showed significantly more unfavourable treatment outcomes than teeth restored with all other materials ($p < 0.05$). Thus, the type of restoration material exerted a significant impact on treatment outcome (Fig. 3). All other factors like age, gender, symptoms before the treatment, the location (arch) and type of tooth did not influence the results significantly ($p > 0.05$).

None of the teeth treated with Biodentine, which were determined to be vital at the end of the observation period, showed discolouration.

Table 1 Cumulative survival rate after 2.3 years for each age cohort (at the time of direct pulp capping)

Age (years)	*N*	Percent	Cumulative survival rate after 2.3 years
< 20	17	6.9%	100%
20–30	65	26.5%	93.3%
30–40	37	15.1%	92.4%
40–60	82	33.5%	82.5%
> 60	44	18.0%	76.2%
Sum	*245*	*100%*	–

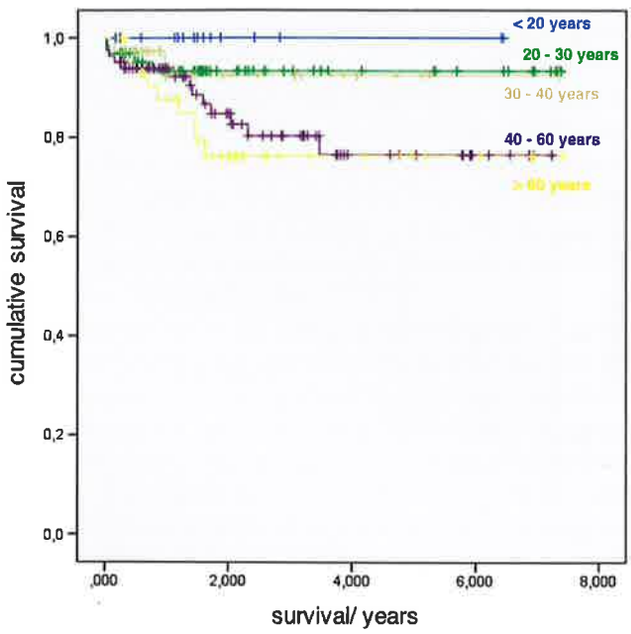

Fig. 2 Survival after direct pulp capping according to age

Discussion

Discussion of methods

The correct diagnosis of the pulp tissue status before direct pulp capping plays an important role in the outcome of vital pulp therapy, thus assessing the degree of infection and inflammation of the pulp tissue is required [38]. On principle, it is challenging to assess the pulpal health accurately through clinical tests and to distinguish between altered and healthy pulps [39]. In order to receive information about the status of the pulp, a sensibility test using CO_2 was performed. Electric pulp test was not used in the present study, because CO_2 cold test was found to be significantly more reliable than electric pulp test [40]. Heavily restored and crowned teeth are known to transmit electrical current to adjacent teeth and gingiva if not isolated properly. Hence, electric pulp test has a low sensitivity [39].

The sensibility test with CO_2 aims to determine the ability of the pulp to respond to a stimulus, in this case

Table 2 Distribution of treated teeth with regard to the arches

Teeth	Maxilla		Mandible	
	N	Percent	*N*	Percent
Molars	75	30.6%	59	24.1%
Premolars	58	23.7%	22	9.0%
Canine	8	3.3%	6	2.4%
Incisors	15	6.1%	2	0.8%
Sum	*156*	*63.7%*	*89*	*36.3%*

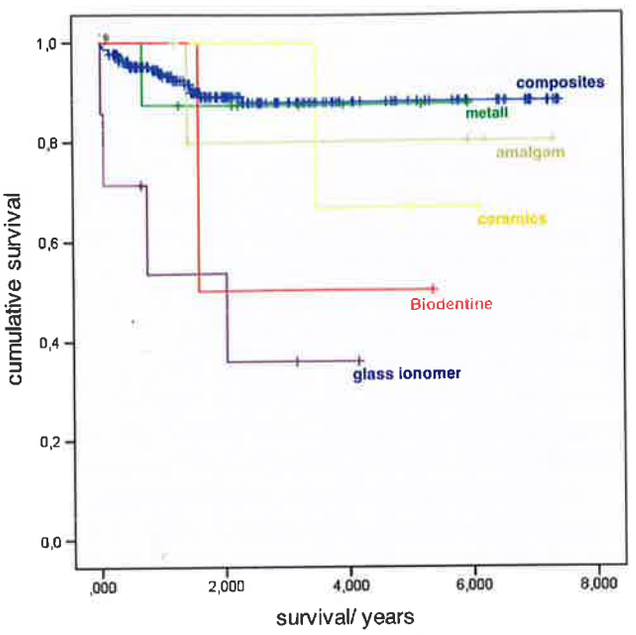

Fig. 3 Survival after direct pulp capping according to restoration

to cold. If pulpal nerve fibres are able to respond to the stimulus, the clinician assesses the pulp to be vital, because a viable blood supply inside the pulp can be expected to keep the nerve fibres alive and functioning. The blood circulation is the most accurate criterion to determine pulp vitality because it gives information whether the pulp tissue is necrotic or vital [41]. Nevertheless, a false positive result may occur, if nerve fibres respond to the stimulus, even though the surrounding pulp tissue has been degenerated [42]. In addition to false positive sensibility testing, one must also expect false negative results. This means that a vital tooth does not respond positively to cold testing, even though the blood microcirculation of the dental pulp is intact. This may occur mainly in recently traumatised teeth, but also in teeth with incomplete root development or teeth with physiological ageing (mineralisation) [42, 43]. A higher occurrence of false negative results (10%) in comparison to false positive (3%) results was reported [44].

It has to be kept in mind that positive sensibility test (cold test) can give a variety of different diagnoses, depending on the severity and duration of response, and these different responses can guide clinicians to different diagnoses. It was shown that teeth responded positively to cold test leading to a preoperative diagnosis of normal pulp, reversible pulpitis, or irreversible pulpitis [36]. Thus, sensibility testing does not precisely reflect the condition of the pulp as 10% to 16% results of the tests are false [42].

Although the pre- and post-operative diagnosis in this study tried to distinguish between teeth with healthy and with altered pulp tissue, it is clear that an accurate classification, whether the pulp tissue was damaged before or after pulp capping or not, can only be made with a histological examination [39]. However, this method cannot be performed in clinical studies, like the present [45].

Nevertheless, the clinical feedback from the patients and the diagnostic data may not correlate with the histological findings. Histologically chronic inflammation, micro-abscesses, necrosis and an absence of bridge formation can occur in directly capped pulp tissue without any complains by the patients [46]. Despite all its limitations, sensibility tests can provide valuable diagnostic information if performed by an experienced clinician [39].

The present study included nine teeth that showed spontaneous pain before pulp capping. Even though patients experience pain subjectively [47], some authors assume "spontaneous pain" to be a sign of an irreversible process leading to pulp necrosis [48]. On the other hand, Matsuo et al. did not find a significant relationship between spontaneous pain before treatment and a favourable outcome of direct pulp capping [49]. Likewise, all teeth that showed "spontaneous pain" before the treatment in the present study ended up with favourable treatment outcomes after direct pulp capping with Biodentine. Pulp healing can be achieved even after a carious exposure if the inflammation is no more severe than reversible pulpitis [2]. Thus, for MTA, it was reported that direct pulp capping of teeth with reversible pulpitis may be successful [32, 36]. Even teeth with diagnosed irreversible pulpitis and early periapical involvement could be successfully capped with Biodentine in young patients with the mean follow-up of 1.5 years [36]. Biodentine was also successfully used for root pulp capping after pulpotomy in teeth with clinical signs and symptoms of irreversible pulpitis of the crown pulp [50].

It is controversial, whether teeth with irreversibly inflamed pulps should be capped or not. And it has to be kept in mind that in the reported cases, a preoperative irreversible pulpitis was not histologically proven. Nevertheless, caries-induced pulpitis ought to be reversible and the pulp able to heal if caries is removed completely [51].

Beside pain and sensibility testing, the bleeding of the pulp tissue after exposure was assessed to further evaluate the status of the pulp. The degree of pulpal bleeding may be a more reliable way to determine the status of pulpal infection than preoperative sensibility testing and clinical signs and symptoms [49]. The amount of bleeding when exposing the pulp tissue may reflect the level of inflammation of the pulp. Excessive bleeding of the tissue usually indicates a pulp with little or no chance of recovery [52]. With increased bleeding on exposure, the possibility of inflammation of the pulp and irreversible pulpits will rise [49]. The inflammatory response extends deeper into the pulp tissue when carious dentine is present during exposure so that bacteria can penetrate the pulp in comparison to the superficial inflammation when the pulp is just mechanically exposed [53, 54]. Pulps with profuse and lingering bleeding had a significantly poorer outcome than

those with modest bleeding or bleeding of short duration [49]. Clinically, pulp bleeding should be controlled within 5 min [38].

A radiographic assessment was not performed in this study which may be regarded as a limitation. But besides ethical reasons, it must be kept in mind that information gained from radiographs (e.g. width of the periodontal ligament) may not correlate well with the status of the pulp tissue [55]. However, when there is no radiograph, one cannot diagnose the periapical area of the tooth. The result of this study relies mainly on sensibility testing, which have limitations of both false positive and false negative, leading to both under- or overestimation of the unfavourable outcomes.

According to the manufacture's recommendation, the initial setting time of Biodentine is about 12 min. Thus, according to this advice, Biodentine should be allowed to set for 12 min minimum before a permanent restoration can be placed. Nevertheless, in clinical usage, waiting about 12 min for the calcium silicate cement to set can lead to complications. To bypass the long setting time of Biodentine in the present study already 3 min after mixing, Biodentine was covered with a thin layer of a self-etching, self-bonding flowable composite resin (Vertise flow). Vertise flow achieved already 3 min after mixing shear bond strengths on Biodentine that were similar to those after 15 min and 2 days. A longer waiting time after mixing (to let the calcium silicate cement fully set) did not increase the adhesion of the lining materials to Biodentine [28].

Discussion of results

In this retrospective clinical study concerning direct pulp capping with Biodentine, 86.0% of the teeth remained vital after the mean period of 2.3 years. The survival rate decreased to 83.4% after 7.4 years. Hence, the survival rate is in the same range than in a recently published prospective study concerning direct pulp capping with Biodentine [29] and comparable to success rates given for MTA [4–6, 32, 33]. In a retrospective clinical study of direct capping with aqueous suspension of calcium hydroxide under comparable conditions, the survival rate was 78.1% [56]. Therefore, Biodentine may appear to have certain advantages over calcium hydroxide in direct pulp capping.

The highest success rate in the present study was found in the youngest age cohort (10 to 20 years). The success rate decreased with increasing age, but the differences were not statistically significant. Hence, the patient's age did not influence the outcome of direct pulp capping with Biodentine. In accordance, also for MTA, it was claimed that age apparently did not influence the prognosis of direct pulp capping [32, 33, 35]. This is in contrast to a clinical study on Biodentine in which the age of the patient clearly influenced the result of direct pulp capping. Significantly more unfavourable treatment outcomes were observed if direct pulp capping was performed on patients older than 40 years of age [29].

In the present study, the sex of the patient had no impact on treatment outcome, which is in accordance with other studies on Biodentine [29] or MTA [5, 32, 36]. Also, the type of tooth (posterior or anterior) and its position (arch) did not have a significant influence on treatment outcome in the present study, which is in accordance with results on Biodentine [29] and on MTA [5, 32, 36].

The present study did outline a significant effect on the outcomes regarding the type of restoration: glass ionomer cement restorations were significantly more often associated with unfavourable treatment outcome than all other materials. The reason for this finding could be that composite resins and dentine adhesives seal the margin between the restoration and the tooth structure more effectively than glass ionomer cements, thus preventing or reducing the entry of bacteria that may occur at the restoration tooth tissue interface [57]. Glass ionomer cements (GIC) possess a low antimicrobial efficacy [57, 58], whereas the antimicrobial activities of Biodentine and MTA are significantly higher [17]. The negative impact of the time span between direct pulp capping and placement of the permanent restoration was also reported as teeth that were permanently restored more than 2 days after direct pulp capping with MTA had a significantly worse prognosis. It was speculated that bacterial leakage is more likely in temporary restorations [5]. In contrast, a significant difference in the success rate could not be observed compared to teeth which were capped with Biodentine and directly restored with a composite resin filling in the same appointment by Lipski et al. [29]. In 37 out of 112 teeth, Biodentine was used in a two-stage approach, which means that the cavities were restored solely with Biodentine after direct pulp capping for 2 to 3 months and then replaced by a permanent restoration [29]. Nevertheless, the capacity of the restoration to prevent bacterial microleakage may have an influence on the healing of pulp exposures [59], which indicates a permanent and bacteria proof restoration immediately after pulp capping [5, 56]. In this study, the highest amount of unfavourable treatment outcomes occurs within the first year of examination. This is in accordance with other studies using MTA, in which the majority of the failures occurred within the first months up to 1 year after direct pulp capping [4, 32]. In contrast, Parinyaprom et al. did not find a significant influence of the follow-up period and the success rate in MTA capping [36].

Discolouration

In the present study, in none of the cases where direct pulp capping was successful, a tooth discolouration was observed. This is in accordance with other studies that observed a grey tooth staining only after direct pup capping with MTA but no discolouration when using Biodentine [30, 35, 36]. Lipski

et al. [29] reported a yellowish discolouration in 8% of teeth capped with Biodentine. The authors explained this yellow discolouration by new hard tissue formation in the pulp chamber [29]. In contrast, the grey discolouration of the clinical crown of vital teeth capped with MTA may be explained by the fact that MTA contains heavy metal, especially the added radiopacifier bismuth oxide. The heavy metal in contact with NaOCl and/or blood leads to grey tooth discolouration [60]. Due to the fact that Biodentine does not contain any bismuth oxide, discolouration was not observed in Biodentine capped teeth. This low likelihood of discolouration after direct pulp capping seems to be an advantage of Biodentine over MTA.

Comparison to calcium hydroxide

With regard to treatment procedures, patient collective and evaluation methods, the present study is more or less comparable to a previous study, in which an aqueous suspension of calcium hydroxide ($Ca(OH)_2$) instead of Biodentine was used for direct pulp capping [56]. In fact, there were some differences between the two studies that could affect the treatment outcome: in the previous study, cavity cleaning and haemostasis were performed with H_2O_2 (3%), whereas here cotton pellets soaked with NaOCl (3%) were used. Furthermore, after direct pulp capping with $Ca(OH)_2$ zinc oxide phosphate cement or glass ionomer cement served as a subbase, in contrast to self-etching, self-bonding flowable composite resin in this study. These two factors may have additionally influenced the survival rates, while the impact on the result cannot be determined by the methods used. Nevertheless, it is appropriate to compare the results of both studies in a certain extent and looking at the outcomes that have been documented within the first 7 years after treatment. Teeth directly capped with Biodentine showed a survival rate of 83.4% after 7.4 years whereas the survival rate of teeth capped with calcium hydroxide was 78.1%. In both studies, the highest risk of a treatment failure was found in the first year after capping. Compared to calcium hydroxide (90.9%), the likelihood of having a favourable treatment outcome using Biodentine after 1 year was 92.8%.

The examined patients differ in regard to their age, as the mean patients' age in the study using calcium hydroxide was lower (29.3 ± 10.5 years) than in the present study (42.02 ± 17 years). Even though the highest percentage for unfavourable treatment outcome was found in both studies in the group of patients older than 60 years of age, the influence of age on a favourable treatment outcome of direct pulp capping was only significant ($p < 0.05$) when calcium hydroxide was used. However, the success of treatment was not significantly dependent on age in the present study.

Regardless of whether the pulp was directly capped with calcium hydroxide or with Biodentine, in both cases, teeth restored solely with glass ionomer cement showed significantly worse survival rates. Accordingly, the success rates in both studies were significantly influenced by the use of temporary restorations.

Both studies included teeth that were diagnosed to be clinically healthy and teeth that showed spontaneous pain before the treatment. In comparison to the present study using Biodentine, in which no correlation between symptomatic teeth and an unfavourable treatment outcome was found, the study using calcium hydroxide outlined a significant negative influence of spontaneous pain before treatment on the success rates.

Moreover, both studies failed to show any significant influence of sex, tooth position or arch type on treatment outcome.

To the best of our knowledge, this retrospective study is the one with the highest number of patients and the longest observation period concerning direct pulp capping with Biodentine. The success rates are comparable to those reported for MTA. When comparing Biodentine with calcium hydroxide capping, it may be speculated that Biodentine may guarantee higher success rates, especially in older patients and in teeth with spontaneous pain before treatment. A definite restoration after pulp capping with Biodentine is mandatory. Hence, Biodentine is a biocompatible and bioactive material and well suitable for direct pulp capping [23].

Conclusions

From the results of this retrospective study, it may be concluded that using Biodentine for direct pulp capping may lead to high success rates. Tooth discolouration was not observed. The type of coronal restoration had a significant influence on the results. It does not seem appropriate to restore teeth with glass ionomer cement after direct pulp capping due to an increased risk of unfavourable treatment outcome.

Age, gender, tooth position, type of tooth, arch type or spontaneous pain before treatment had no influence on the treatment outcome. Therefore, the hypothesis that pulp capping should be avoided in older patients and in teeth with pain or discomfort cannot be confirmed. To evaluate the long-term treatment outcome of direct pulp capping with Biodentine, a prospective clinical study is highly desirable.

Compliance with ethical standards

Conflict of interest Carolin Sabine Harms declares that she has no conflict of interest.

Edgar Schäfer declares that he has no conflict of interest.

Till Dammaschke declares that he has no conflict of interest.

Ethical approval All treatments were conducted strictly in full accordance with ethical principles, including the World Medical Association Declaration of Helsinki (version 2008).

Informed consent The treatments were undertaken with the understanding and written consent of each patient and according to ethical principles, including the Declaration of Helsinki.

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ORIGINAL ARTICLE

Factors affecting the outcomes of direct pulp capping using Biodentine

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Abstract

Introduction This study aimed to evaluate the prognostic value of factors with regard to the treatment outcome of direct pulp capping using Biodentine (Septodont, Saint-Maur-des-Fossés, France), in permanent teeth in which the pulps were exposed during caries removal.

Methods Between 2010 and 2014, 112 teeth with deep carious lesions underwent direct pulp capping. The patients were followed up at 2–3 months and 1–1.5 years with a routine examination on both recall visits. Periapical radiographs were taken at 1–1.5 years. Lack of patient complaints, positive reactions to cold and electric testing, no sensitivity to percussion, and no widening of the periapical ligament indicated success. The Fisher exact test was used for statistical analysis. The significance level was $P = .05$.

Results Eighty-six teeth were available for 1–1.5 years follow-up. The overall success rate was 82.6%. Only age had a significant effect on the pulpal survival rate: the success rate was 90.9% in patients younger than 40 years and 73.8% in patients 40 years or older ($P = .0480$). Sex, initial or secondary caries treatment, occlusal or cervical/proximal caries, delayed placement of permanent filling, tooth position, and arch type did not influence the outcome.

Conclusions A patient's age influenced the outcome of direct pulp capping using this new calcium silicate cement.

Clinical relevance Asymptomatic vital permanent teeth with cariously exposed pulp can be treated successfully by direct pulp capping using Biodentine.

Keywords Biodentine · Carious pulp exposure · Direct pulp capping · Treatment outcome

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Direct pulp capping is a procedure in which a medicament, dressing, or dental material is placed directly over exposed dental pulp to preserve its vitality. Inducing reparative tertiary dentin formation by pulp cells has been widely accepted as the ultimate goal of using capping material [1, 2]. For many decades, calcium hydroxide was the material of choice among the various available pulp-capping agents [1, 2]. However, there are shortcomings when using this material such as its dissolution in tissue fluids and degradation on tooth flexure, the formation of tunnel defects beneath dentinal bridges, and poor sealing [3–6].

An alternative gold standard, mineral trioxide aggregate (MTA), is available as a direct pulp-capping material [7–9]. However, MTA is difficult to use because of its long setting time, poor handling properties, cost, and the potential discoloration of teeth and soft tissue [10–12]. To overcome some of these limitations, other bioactive tricalcium silicate cements have been recently introduced on the market. One material is Biodentine. It consists of a powder and liquid. The powder

primarily contains tricalcium silicate ($3CaO{\cdot}SiO_2$) and dicalcium silicate ($2CaO{\cdot}SiO_2$) and calcium carbonate ($CaCO_3$). Zirconium dioxide (ZrO_2) is a contrast medium. The liquid consists of calcium chloride ($CaCl_2{\cdot}2H_2O$), which is used as a setting accelerator and water-reducing agent in aqueous solution with an admixture of polycarboxylate (i.e., a superplasting agent). Mixing is achieved by using an amalgamator for 30 s at 4000–4200 rpm. The manufacturer has specified the powder to liquid ratio. This allows practitioners to achieve a reproducible material with optimum properties each time. The initial setting time according to the manufacturer is about 12 min. However, Kaup et al. [13] evaluated the final setting time of this material to be 85 min according to ISO 6876:2001. The consistency of Biodentine is similar to that of phosphoric cement [13, 14].

Several in vitro studies have evaluated Biodentine [14–17]; however, few histologic studies have been conducted to evaluate the pulp response of this calcium silicate cement in animal teeth [18–20] and in human teeth [21, 22]. A survey of the available literature shows that a few isolated clinical investigations have been published that include the use of Biodentine for direct pulp capping in permanent teeth, but no studies have an adequate sample size or long-term data [23–26].

This study aimed to evaluate the prognostic value of factors with regard to treatment outcome of direct pulp capping using the new calcium silicate cement Biodentine in permanent teeth in which the pulp was exposed during caries removal. The tested null hypothesis was that the following factors would not influence the results of direct pulp capping using Biodentine: (1) sex, (2) age of <40 years or ≥ 40 years, (3) anterior or posterior tooth, (4) maxilla or mandible, (5) initial or secondary caries treatment, (6) occlusal or proximal/cervical caries localization, and (7) immediate restoration (> 1 day) or delayed placement of a permanent filling (2–3 months).

Material and methods

All patients in this study were referred for routine conservative treatment at the Department of Pediatric Dentistry of Pomeranian Medical University of Szczecin (Szczecin, Poland), the Department of Preclinical Conservative Dentistry and Preclinical Endodontics of Pomeranian Medical University of Szczecin (Szczecin, Poland), the Department of Pediatric Dentistry of Silesian Medical University (Zabrze, Poland), or private dental offices (in Szczecin, Poland) between 2010 and 2014. The treatment was performed by a total of six dentists who had limited their work to conservative dentistry for 10–25 years. Each dentist received training in the use of Biodentine for direct pulp capping to ensure uniformity among the operators.

This study comprised 112 vital teeth with caries-induced pulp exposure, which were obtained from 94 patients (50 female patients and 44 male patients, age 11–79 years). The patients and/or their legal guardians received thorough explanations concerning the clinical procedures and possible complications. All procedures were registered by the local ethical committee of the Pomeranian Medical University (Szczecin, Poland; KB-0012/96/11/15).

Direct pulp capping was indicated when a tooth was exposed on account of caries excavation. However, during the preparation, efforts were made not to expose the pulp. In these patients, the appropriate materials were used for indirect capping. Only teeth with signs and/or symptoms of reversible pulpitis were included. Teeth exhibiting reversible pulpitis had provoked pain of short duration that was relieved on the removal of the stimulus (i.e., cold, heat, or compressed air). Teeth were excluded that exhibited signs and/or symptoms of irreversible pulpitis such as prolonged unbearable pain or pain disturbing night sleep, lack of response to cold (K ltespray, M&W Dental GmbH, Büdingen, Germany; Aethylum Chloratum, Filofarm, Bydgoszcz, Poland) and electrical pulp testing (Vitality Scanner Pulp Vitality Tester, SybronEndo, Orange, CA or Gentle Pulse Analog Pulp Tester, Parkell, Edgewood, NY), a sinus tract or swelling, percussion pain, periodontal inflammation, radiographic evidence of calcification of the pulp chamber or canals, internal/external resorption, or furcal/periapical radiolucency. Furthermore, no treated patient took corticosteroids or statins or was pregnant before or during this study.

After local anesthesia, teeth were isolated and disinfected with 0.2% chlorhexidine before caries removal. Round diamond burs and high-speed handpiece with copious water spray were used to remove enamel. Rose burs and a low-speed handpiece under water/air spray coolant were used to remove carious dentin. When the pulp was exposed by the caries excavation process, the cavity was rinsed with sterile saline and a cotton pellet soaked with 2% sodium hypochlorite, 2% chlorhexidine, or sterile saline, which was left at the pulpal wall of the cavity. Teeth with excessive uncontrollable bleeding were excluded from the study. After controlling the bleeding, Biodentine was mixed according to the manufacturer's instructions and applied on the exposed pulp. Cavities were restored directly without provisional filling (i.e., one-stage treatment) or restored provisionally (i.e., two-stage treatment). The decision depended on the patient's time availability.

For the one-stage group, Biodentine was placed with a flat hand instrument over the exposed pulp and surrounding dentin and then lightly condensed with a ball burnisher to achieve a thickness of 2–3 mm. After 12–20 min of Biodentine hardening, a glass ionomer cement was used as the base (Ketac Bond, 3M ESPE, Seefeld, Germany; Fuji Triage, GC Corporation, Tokyo, Japan; ChemaDent G-J-P NR 3,

Chema-Elektromet Rzeszów, Poland; and Vitrebond, 3M ESPE, Seefeld, Germany). The cavities were restored with a light-cured resin composite (Herculite XRV, Kerr, Bioggio, Switzerland; Gradia, GC Corporation, Tokyo, Japan; Charisma, Heraeus Kulzer Inc., Armonk, NY; N'Durance, Septodont, Saint-Maur-des-Fossés, France; Synergy D6, Coltène/Whaledent Inc., Cuyahoga Falls, OH; and Spectrum, Dentsply Caulk, Milford, DE). All materials were applied in accordance with the manufacturer's directions with dedicated bonding systems. Prelude (Danville, Carlsbad, CA) was used with composite materials which had no their own bonding system.

For class II cavities, a thin metallic matrix was carefully wedged with wooden wedges. After checking the occlusion/articulation, the final finishing was performed. For the two-stage treatment group, Biodentine was applied for direct pulp capping and for temporary restorations. For class II cavities, a metallic matrix was also used. After hardening the material (12–20 min), the occlusion was gently checked. A carving instrument was used for occlusal adjustment. At the subsequent visit (2–3 months after capping), the Biodentine material was partially removed with round diamond burs on a high-speed handpiece with copious water spray to maintain a minimum cement thickness of 2–3 mm to protect the pulp, and restored with a resin composite filling (i.e., the same process as for the one-stage treatment).

Follow-up examination

The patients were followed up at 2–3 months and 1–1.5 years. All patients had a routine examination during both recall visits. A periapical radiograph was taken at 1–1.5 years. One patient had cone-beam computed tomography but no periapical radiographs. Two blinded observers independently examined the radiographs and reached a consensus for all teeth. Periapical pathology was diagnosed if the apical part of the periodontal ligament was at least twice as wide as in other parts of the roots and the lamina dura was absent. In addition, the pulpal space was checked for calcific alterations in comparison with the adjacent teeth, which had not been pulp-capped. The teeth that exhibited pulpal vitality and did not show any clinical or radiographic signs and/or symptoms of irreversible pulpitis and pulp necrosis/apical periodontitis were considered a treatment success. The teeth with no response to the pulp vitality test and teeth that exhibited clinical or radiographic signs and/or symptoms of irreversible pulpitis or necrosis/apical periodontitis were considered treatment failures. The assessment included tooth crown discoloration. The color of the treated tooth and the adjacent teeth was compared during visual examination. If the patient was not examined at these intervals, a telephone interview was attempted. Patients who dropped out of the study refused to participate in the recall.

Statistical analysis

The Fisher exact test was used for analysis with a significance level of $P < .05$.

Results

Among the 112 teeth included in this study, 91 teeth (81.2%) were examined at 2–3 months and 86 teeth (76.4%) at 1–1.5 years (the median follow-up period was 14.7 months).

At the time of treatment with direct pulp capping, the patients' age ranged 11–79 years with a median age of 44 years. The overall success rates for the 2–3-month and 1–1.5-year recall groups were 100 and 82.6%, respectively. Of the 86 teeth recalled at 1–1.5 years, the outcome was deemed as a failure in 15 (17.4%) teeth. Nine of the failed teeth received subsequent root canal treatment, five teeth showed evidence of pulp necrosis at follow-up, and one tooth (a third molar) was extracted. The pulp space in five teeth was substantially obliterated, but the teeth were responsive to vitality testing and did not show any signs of clinical or radiographic failures (i.e., no complaints of pain or tenderness to percussion or palpation, no evidence of periradicular bone or external/internal root resorption on radiographs); therefore, the outcome was considered a success in these teeth.

The outcome was not influenced by the following parameters: sex, initial or secondary caries treatment, occlusal or cervical caries localization, delayed placement of permanent filling, tooth position, and arch type. Thus, the null hypothesis was accepted for these factors.

However, the patients' age did influence the outcome; therefore, the null hypothesis concerning this parameter was rejected (Table 1). Figure 1 shows examples of the treated teeth.

The follow-up visit at 2–3 months showed no obvious crown discoloration of the treated teeth. However, 6 of 71 teeth with vital pulp seemed to be yellower than the adjacent teeth after 1–1.5 years. There was no gray discoloration of the teeth.

Discussion

This study aimed to identify the significant prognostic factors of treatment success in direct pulp capping using a new calcium silicate-based cement, Biodentine. Thus, no control groups using calcium hydroxide and/or MTA were included. Our study investigated similar prognostic factors that were

Table 1 Outcome of direct pulp capping with Biodentine with regard to the study variables

Studied variables	Success		Failure		*P* value
	n	%	*n*	%	
Age					
< 40 years	40	90.9	4	9.1	.0480
≥ 40 years	31	73.8	11	26.2	
Sex					
Female	40	83.3	8	16.7	1
Male	31	81.6	7	18.4	
Tooth location					
Maxilla	34	87.2	5	12.8	.3963
Mandible	37	78.7	10	21.3	
Tooth type					
Anterior	10	76.9	3	23.1	.6911
Posterior	61	83.6	12	16.4	
Caries treatment					
Initial	39	88.6	5	11.4	.1608
Secondary	32	76.2	10	23.8	
Caries location					
Occlusal	19	95.0	1	5.0	.1749
Proximal/cervical	52	78.8	14	21.2	
Time before permanent restoration					
Direct	42	85.7	7	14.3	.4031
2–3 months	29	78.4	8	21.6	

used in previous clinical studies that assessed the effectiveness of calcium hydroxide and/or MTA [27–34]. Several factors were investigated: sex, age, primary or secondary caries, occlusal or proximal/cervical caries, delayed placement of permanent filling, size of exposure, tooth position, and arch type. However, the outcomes indicated that only age had a significant effect on the survival rate of vital pulps.

Age

Patient age may have a role in the survival rate after direct pulp capping [27–33]. In the present study, the age-dependent success of treatment was statistically significant ($P = .048$). A success rate of 90.9% occurred in patients younger than 40 years and 73.8% in patients 40 years and older. This finding is in accordance with that of Cho et al. [27], who reported that age had significant effects on the survival rate: patients younger than 40 years had a better success rate than older patients. Dammaschke et al. [30] reported significantly lower favorable treatment outcomes for direct pulp capping in the oldest age cohort (i.e., > 60 years), compared to patients younger than 40 years old. Hørsted et al. [31] found significant differences between the youngest patients (i.e., 10–29 years) and the oldest patients (i.e., 50–79 years). However, some studies could not confirm an influence of age on the success or failure of pulp-capped teeth [29, 35].

The higher success rate for patients younger than 40 years than for patients 40 years old and older can be explained by the high capacity of pulp tissue in young patients. Indirect comparison of the weighted pooled success rate in teeth with an open apex (i.e., higher healing capacity of the pulp tissue) or closed apex showed statistically more successful outcomes in teeth with incomplete root development [36]. However, further clinical studies with a higher number of patients are needed to re-evaluate the age-related influence on treatment outcome after pulp capping with Biodentine.

Sex

Available studies show a patient's sex has no significant effect on the treatment outcome of direct pulp capping [27–35]. In the present study, the success rates, as expected, also did not differ between female and male patients.

Tooth type and location

The type of tooth (anterior vs. posterior) and location (mandible vs. maxillary arch) showed no significant difference in the survival rate. This finding is in accordance with the findings of various studies [27, 30, 32, 34]. Some authors state that the anterior teeth had a higher failure rate of treatment outcome than the posterior teeth [31, 37]. However, other studies showed more favorable treatment outcome in the anterior teeth than in the posterior teeth [38].

Primary caries versus secondary caries

In the present study, teeth with primary caries demonstrated a higher success rate (88.6%), compared to teeth with secondary caries (76.2%). However, no statistically significant difference existed ($P = .1608$). The influence of this factor on the success of direct pulp-capping treatment was studied only by Marques et al. [33], who used MTA and reported 88.9% treatment success in teeth with secondary caries, compared to 94.7% treatment success in teeth with primary caries. However, in the cited study, the difference was also not statistically significant.

Caries location

The exposure site (occlusal vs. cervical/proximal) could affect the survival rate. Cho et al. [27] reported a better survival rate when the exposure site was limited to the occlusal side than when it was on the axial side. Treatment failure occurred

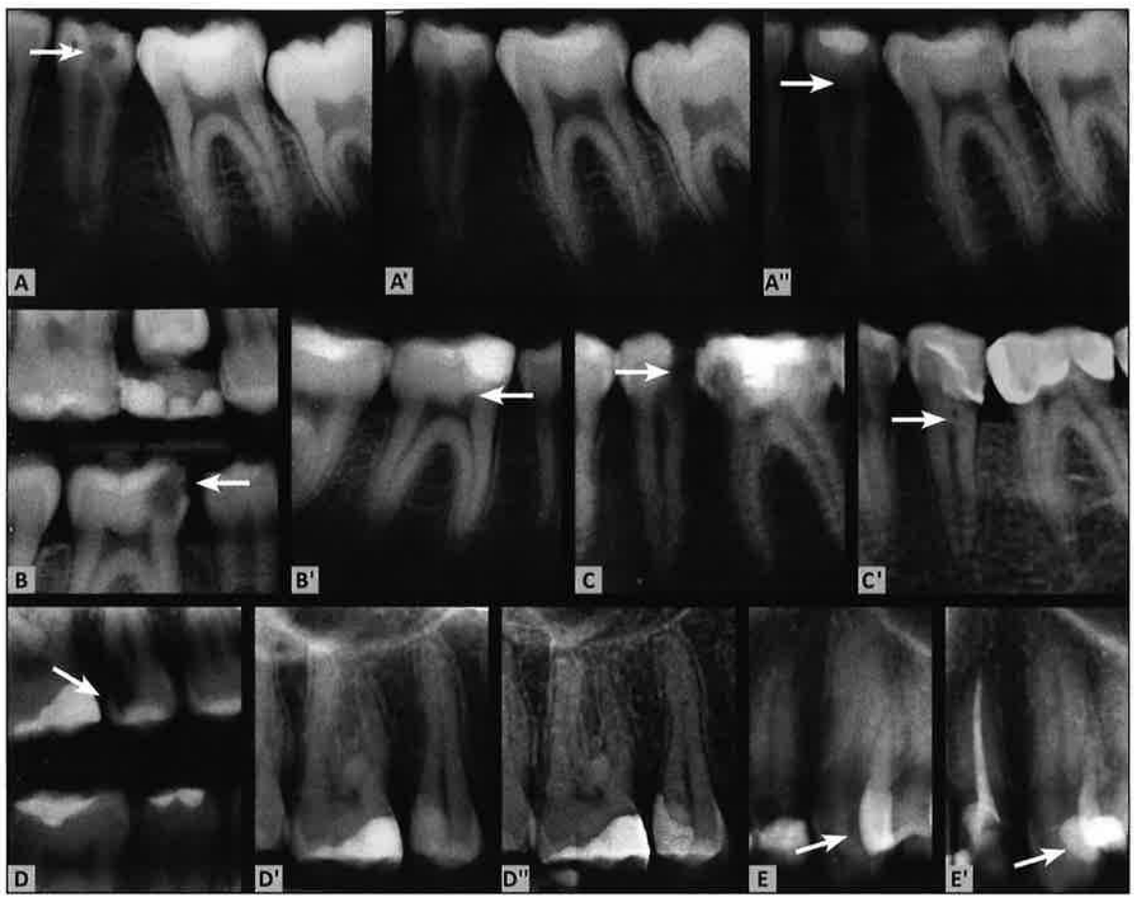

Fig. 1 (A) The preoperative periapical radiograph shows a deep carious lesion in the second mandibular premolar (arrow). (A′) Postoperative radiograph taken directly after the application of Biodentine for pulp capping and for temporary restoration. (A″) Follow-up radiograph after 18 months. There is dentine bridge formation and the development of the tooth (arrow). (B) The bitewing radiograph shows a deep carious lesion on the first mandibular molar (arrow). (B′) The periapical radiograph after 18 months after direct capping does not show any pathological findings on tooth 46. There is dentine bridge formation (arrow). (C) The preoperative radiograph of the mandibular premolar shows a deep carious lesion (arrow). (C′) The follow-up radiograph at 12 months shows dentine bridge formation (arrow). (D) The preoperative bitewing radiograph shows a deep carious lesion in the second maxillary premolar (arrow). (D′) The postoperative radiograph taken directly after the application of Biodentine for pulp capping and for temporary restoration. (D″) The follow-up radiograph at 14 months. (E) The preoperative periapical radiograph of the maxillary canine shows a deep carious lesion on the distal surface (arrow). (E′) The periapical radiograph at 12 months after direct capping does not show any pathological findings of this tooth

because of difficulty of isolating axial exposure from contaminants rather than because of pulp exposure on the occlusal side, completing caries removal, applying the pulp-capping material, or sealing the cavity. Jang et al. [34] observed that two thirds of treatment failures involved restorations of teeth with class V cavities caused by root caries; the failure rate was 50%, which was the highest rate, compared to the groups with class I, II, or III cavities. The sealing quality of a class V restoration may be reduced because of insufficient cavity volume for capping material and permanent restoration and tensile stress under occlusal loading. In the present study, no statistically significant difference was evident between occlusal and cervical/proximal exposure. This confirms the findings of a study by Pereira and Stanley [39], who did not detect any difference for treatment success based on the site of exposure.

Time span before permanent restoration

Some research shows that the time span before the placement of a permanent restoration after pulp capping has a major impact on the healing of an exposed pulp; a permanent restoration protects the tooth structures more effectively from microleakage, compared to a temporary filling [28]. Barthel et al. [32] reported a significantly higher failure rate in teeth with a temporary restoration, compared to a permanent amalgam, composite, or gold cast restoration.

Multivariate analyses in another study [29] confirmed an increased risk of failure after pulp capping for all teeth in which a permanent restoration was performed with a delay of 2 days or more. In the present study, 49 teeth were immediately restored with permanent filling after direct pulp

capping. In 37 teeth, the final restoration was applied after 2–3 months. The treatment success rate was 78.4% in the group for whom Biodentine was used as a temporary filling and 85.7% in the group with immediate placement of the final restoration (the difference was not statistically significant $P = .4031$). The lack of significant differences between teeth that were restored immediately after pulp capping and teeth temporarily filled with Biodentine for 2–3 months can be explained by the relatively good physical properties of this new tricalcium silicate cement. Koubi et al. [40] determined how long Biodentine can remain as a restorative material submitted to occlusal chewing force. Koubi et al. found that this material can be used for up to 6 months. However, in our study, some restorations were discontinuous (but without the exposure of dentin) and seemed to be more yellow after 2–3 months, compared to their color directly after restoration. The discoloration of fillings may be because of their lower abrasive wear resistance, the porosity of Biodentine, and the absorption of dyes from saliva.

Some authors suggest delaying final restorations after pulp capping. According to these authors, placing the final restoration immediately after direct pulp capping complicates subsequent procedures when the teeth need root canal treatment [41]. Matsuo et al. [35] suggest that 3 months is sufficient for tentative prognoses and for determining the need for final restorations. In the aforementioned cited studies, the permanent restoration materials provided a long-term bacteria-tight seal (glass ionomer cements or resin-bonded zinc oxide eugenol cement).

Crown discoloration

A potential drawback of the using of MTA for vital pulp therapy is the subsequent development of crown discoloration. Discoloration occurred in 60% of treated teeth when gray MTA was used as the pulpotomy material in primary teeth [42] and in 13.6% of permanent teeth after direct pulp capping with white MTA [33]. Furthermore, gray and white MTAs darken when irradiated with a curing light or fluorescent lamp in an oxygen-free environment and after contact with sodium hypochlorite or chlorhexidine gluconate [43]. The authors suggest that the bismuth oxide component of gray MTA or white MTA is responsible for the gray discoloration. In the present study, when Biodentine with zirconium oxide as radiopacifier was used for direct pulp capping, the tooth discoloration rate was 8%. In all patients, the gross observation of teeth by the naked the eye showed yellow discoloration of crowns (i.e., no gray) in comparison to the adjacent teeth. Five (83.3%) discolored teeth exhibited substantial pulp obliteration. This finding suggested that yellow discoloration of a crown is associated with dentin deposition resulting from stimulation of odontoblasts after the direct capping procedure rather than from the components of Biodentine. This is confirmed by an in vitro study in which Biodentine applied to the pulp chamber for 6 months did not induce a perceptible color change in the tooth structure [43].

Follow-up period

The follow-up period of this study was 1–1.5 years. It is recommended that teeth should be followed after direct pulp capping for longer times to evaluate the long-term success rate. Aguilar and Linsuwanont [36] calculated the pooled success rates of 996 teeth after direct pulp capping, finding 87.5% success at 6 months to 1 year, 95.4% success at 1–2 years, 87.7% success at 2–3 years, and 72.9% success after 3 years. Similarly, Hørsted et al. [31] reported a decrease in the survival rate from 96.7% after 1 year to 81.8% after 5 years. Cho et al. [27] reported a decrease from 89.9% after 1 year to 67.4% after 3 years when MTA was used for pulp capping and from 77.7 to 52.5% when calcium hydroxide cement was used to cap exposed pulps. Furthermore, Barthel et al. [32] reported a failure rate of 44.5% after 5 years and 79.7% after 10 years, whereas Willershausen et al. [44] reported a failure rate of 19.9% after 1 year, 32.0% after 5 years, and 41.3% after 9 years.

In this study, the estimated survival rate for pulps capped with Biodentine was 82.6% after 1–1.5 years of follow-up (median 1.2 years). This result is consistent with that of Mente et al. [29], who reported a success rate of 80.5% for MTA (median follow-up 3.5 years), and the study by Hilton et al. [45], in which the success rate for direct pulp capping using MTA was 80.3% (median follow-up 1.2 years). Recently, Kundzina et al. [46] published a randomized controlled trial comparing MTA and calcium hydroxide. The success rate after direct pulp capping with MTA was 85% after 3 years of follow-up. All of the cited studies confirmed the significant superiority of MTA over calcium hydroxide. However, Schwendicke et al. [47], based on their findings and considering results from non-controlled trials, concluded that dentists can, but do not need to, use MTA instead of calcium hydroxide for direct pulp capping in permanent teeth. Thus, the 1–2 years of adequate postoperative follow-up examination, which has been applied in most studies evaluating the outcomes of direct pulp capping and our study, may well be too short. However, Jang et al. [34] suggested that most failures occur within the first 3 months.

The conventional treatment of deep carious lesions involves complete removal of all infected and affected dentin, followed by tooth restoration. However, when carious tissues are removed, the dentin barrier may be broken, making the cause of the treatment less predictable. It may also require other measures, such as direct pulp capping, partial or full pulpotomy, or in extreme cases pulpectomy [48, 49]. To

minimize the potential complications of the complete removal of carious dentin close to the pulp, alternative treatment options have been proposed, such as selective excavation (the teeth will not be treated further) and stepwise excavation involving the removal of decayed tissue in two steps [49]. In deep cavitated lesions in primary or permanent teeth, selective removal to soft dentine should be performed, though stepwise removal is an option in permanent teeth [50]. Bjørndal et al. [51] found an advantage of stepwise excavation in permanent teeth, as only 17.5% of the pulps were exposed compared to 28.9% after complete excavation. Similar findings were reported by Leksell et al. [52] (18 vs. 40%) and Magnusson and Sundell [53] (15 vs. 53%). Moreover, Bjørndal et al. observed a higher success rate (74.1%) for stepwise excavation at 1 year of follow-up than direct complete excavation (62.4%) when considering exposed pulps with sustained vitality without apical radiolucency.

Aguilar and Linsuwanont [36] performed a systematic review to illustrate the clinical and radiographic success of direct pulp capping, partial pulpotomy, and full pulpotomy in vital permanent teeth with cariously exposed pulp. Overall, the success rate of each procedure was between 72.9 and 99.4%. In the present study, the overall success rate was 82.6% when Biodentine was used for direct pulp capping. However, the comparison presents difficulties, mainly due to differences in terms of case selection. For example, the patients participating in the studies were different ages (e.g., 15–44 years or 11–79 years in the present study).

The current study has some limitations. The treatment was carried out by six dentists, who mainly used saline for rinsing, sporadically sodium hypochlorite or chlorhexidine. Although all solutions are recommended to control hemorrhage [44, 54], sodium hypochlorite has been shown to inhibit the differentiation of odontoblasts from dental pulp stem cells [55] and chlorhexidine may inhibit calcium silicate cement setting [56]. In addition, the restorations were performed as either one-stage or two-stage treatments, and different adhesives and composites were used for permanent restorations. However, the quality of the temporary and final restorations recorded at 2–3 months and 1–1.5 years was acceptable in all cases.

Conclusions

The overall success rate was 82.6% when Biodentine was used for direct pulp capping. However, a patient's age influenced the outcomes of direct pulp capping when using this new silicate cement. Further clinical studies with longer observational time on the use of Biodentine for direct pulp capping are recommended.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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Biodentine™: 3 Publications out of 500+ (Pubmed)

Selection of Publications

Author	Title	Publication	Year
Abdelmegid FY, Salama FS, Al-Mutairi WM, Al-Mutairi SK, Baghazal SO.	Effect of different intermediary bases on microleakage of a restorative material in Class II box cavities of primary teeth	International Journal of Artificial Organs	2017
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	Journal of Conservative Dentistry	2013
Aggarwal V, Singla M, Yadav S, Yadav H, Ragini.	Marginal Adaptation Evaluation of Biodentine™ and MTA Plus in "Open Sandwich" Class II Restorations	Journal of Esthetic Restorative Dentistry	2015
Atmeh A, Festy F, Ee Zhuan C, Watson T.	Dentin-cement interfacial interaction: calcium silicates and polyalkenoates	Journal of Dental Research	2012
Camilleri J, Kralj P, Veber M, Sinagra E.	Characterization and analyses of acid-extractable and leached trace elements in dental cements	International Endodontic Journal	2012
Camilleri J, Sorrentino F, Damidot D.	Investigation of the hydration and bioactivity of radiopacied tricalcium silicate cement, Biodentine™ and MTA Angelus	Dental Materials	2013
Camilleri J.	Characterization and hydration kinetics of tricalcium silicate cement for use as a dental biomaterial	Dental Materials	2011
Camilleri J.	Staining Potential of Neo MTA Plus, MTA Plus, and Biodentine™ Used for Pulpotomy Procedures	Journal of Endodontics	2015
Costa F, Sousa Gomes P, Fernandes MH.	Osteogenic and Angiogenic Response to Calcium Silicate-based Endodontic Sealers	Journal of Endodontics	2016
El Meligy OA, Allazzam S, Alamoudi NM.	Comparison between Biodentine™ and formocresol for pulpotomy of primary teeth: A randomized clinical trial	Quintessence	2016
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	Biomedical Research International	2016
Evren OK, Altunsoy M, Tanriver M, Capar ID, Kalkan A, Gok T.	Fracture resistance of simulated immature teeth after apexication with calcium silicate-based materials	European Journal of Pediatric Dentistry	2016
Gomes-Cornélio AL, Rodrigues EM, Salles LP, Mestieri LB, Faria G, Guerreiro-Tanomaru JM, Tanomaru-Filho M.	Bioactivity of MTA Plus, Biodentine™ and an experimental calcium silicate-based cement on human osteoblast-like cells	International Endodontic Journal	2017
Gong V, França R.	Nanoscale chemical surface characterization of four different types of dental pulp-capping materials	Journal of Dentistry	2017
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	Contemporary Clinical Dentistry	2016
Guneser MB, Akbulut MB, Eldeniz AU.	Effect of various endodontic irrigants on the push-out bond strength of Biodentine™ and conventional root perforation repair materials	Journal of Endodontics	2013
Han L, Okiji T.	Uptake of Calcium and Silicon released from calcium silicate based endodontic materials into root canal dentin	International Endodontic Journal	2011
Jung S, Mielert J, Kleinheinz J, Dammaschke T.	Human oral cells' response to different endodontic restorative materials: an in vitro study	Head & Face Medicine	2014
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	Contemporary Clinical Dentistry	2016
Koubi G, Colon P, Franquin JC, Hartmann A, Richard G, Faure MO, Lambert G.	Clinical evaluation of the performance and safety of a new dentin substitute, Biodentine™, in the restoration of posterior teeth - a prospective study	Clinical Oral Investigation	2012

Author	Title	Publication	Year
Kurun Aksoy M, Tulga Oz F, Orhan K.	Evaluation of calcium (Ca2+) and hydroxide (OH-) ion diffusion rates of indirect pulp capping materials	International Journal of Articial Organs	2017
Kurun Aksoy M, Tulga Oz F, Orhan K.	Tomographic Evaluation of Reparative Dentin Formation after Direct Pulp Capping with Ca(OH)2, MTA, Biodentine™, and Evaluation of calcium (Ca2+) and hydroxide (OH-) ion diffusion rates of indirect pulp capping materials	International Journal of Artificial Organs	2017
Laurent P, Camps J, About I.	Biodentine™ induces TGF-ß1 release from human pulp cells and early dental pulp mineralization	International Endodontic Journal	2011
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.	European Journal of Pediatric Dentistry	2016
Możyńska J, Metlerski M, Lipski M, Nowicka A.	Tooth discoloration induced by different calcium silicate-based cements: a systematic review of in vitro studies	Journal of Endodontics	2017
Nowicka A, Wilk G, Lipski M, Kołecki 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	Journal of Endodontics	2015
Özgül BM, Tirali RE, Cehreli SB.	Effect of Biodentine™ on secondary caries formation: An in vitro study	American Journal of Dentistry	2016
Özyürek T, Demiryürek EÖ.	Comparison of the antimicrobial activity of direct pulp-capping materials: Mineral trioxide aggregate-Angelus and Biodentine™	Journal of Conservative Dentistry	2016
Peng L1,Ye L,Tan H, Zhou X.	Evaluation of theformocresolversus mineral trioxide aggregate primary molar pulpotomy: a meta-analysis	Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology	2006
Schmidt A, Schäfer E, Dammaschke T.	Shear Bond Strength of Lining Materials to Calcium-silicate Cements at Different Time Intervals	Journal of Adhesive Dentistry	2017
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	Journal of Conservative Dentistry	2015
Subramanyam D, Vasantharajan M.	Effect of Oral Tissue Fluids on Compressive Strength of MTA and Biodentine™: An In vitro study	Journal of Clinical Diagnosis and Research	2017
Tsesis I, Elbahary S, Venezia NB, Rosen E.	Bacterial colonization in the apical part of extracted human teeth following root-end resection and lling: a confocal laser scanning microscopy study	Clinical Oral Investigation	2017
Widbiller M, Lindner SR, Buchalla W, Eidt A, Hiller KA, Schmalz G, Galler KM.	Three-dimensional culture of dental pulp stem cells in direct contact to tricalcium silicate cements.	Clinical Oral Investigations	2016

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