VILNIUS UNIVERSITY
FACULTY OF MEDICINE

Dentistry Programme

Institute of Dentistry

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INTEGRATED STUDY MASTER'S THESIS

Preventive Endodontics in Mature Teeth: The Importance of Avoiding Root Canal Treatment

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Vilnius, 2024.

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List of Abbreviations

Abbreviation	Meaning
Aδ fibers	A-delta fibers
AAE	American Association of Endodontists
BMP	Bone Morphogenic Protein
BR	BioRaCe rotary file
$Ca(OH)_2$	Calcium hydroxide
CHX	Chlorhexidine
dECM	Dentin extracellular matrix
EDTA	Ethylene-diamine tetra-acetic acid
EPT	Electric pulp test
ESE	European Society of Endodontology
GIC	Glass ionomer cement
HEMA	2-hydroxyethyl methacrylate
HF	Nickel titanium hand K-file
IL-1	Interleukin-1
LDF	Laser doppler flowmetry
MeSH	Medical Subject Heading
MTA	Mineral trioxide aggregate
NaOCl	Sodium hypochlorite
PAMPs	Pathogen-associated molecular patterns
PCEM	Pulpotomy using calcium-enriched mixture
PMTA	Pulpotomy using mineral trioxide aggregate
PO	Pulse oximetry
PRISMA	Preferred Reporting Items for Systematic Review and Meta-Analyses
PRRs	Pattern-recognition receptors
RCT	Root canal treatment
RMGIC	Resin-modified glass ionomer cement
ROI	Reactive oxygen intermediates
TGF-ß1	Transforming growth factor beta-1
TNF	Tumor necrosis factor
VPT	Vital pulp therapy
WO	WaveOne reciprocating single file

SUMMARY

Relevance of the problem: Tendencies in a shift of clinicians' preferences from an invasive to conservative treatment approach of pulpal conditions were observed due to negative effects of traditional root canal treatment, including changes in tooth structure, biomechanical behaviour and fracture resistance, advanced comprehension of dental pulp's healing capabilities and introduction of hydraulic calcium silicate-based cements. Accurate diagnosis and preservation of pulp vitality are of major significance concerning prevention of inadequate treatment procedure, maintenance of biomechanical properties and fracture resistance of teeth. Therefore, analysis regarding clinical effectiveness of both, vital pulp therapy and root canal treatment, is required to evaluate the role of preventive endodontic therapies in mature teeth and their importance in avoiding root canal treatment, as an alternative if amenability of the pulp is ensured.

Aim and Objectives: The purpose is to conduct a literature review on the currently available studies evaluating preventive methods in endodontics taking their comparison to root canal treatment into consideration and highlighting their importance in avoiding root canal treatment in mature teeth.

Materials and Methods: A systematic literature search was conducted applying identified Medical Subject Headings (MeSH terms) and text-words in the medical database PubMed restricting language to English and German and publication year to 10 years. Following exclusion of duplicates, a two-phase strategy was employed as initially only title and abstract of articles were screened excluding unsuitable studies, followed by appraisal of full text of articles with regards to exclusion and inclusion criteria.

Results: In total, 43 studies were considered eligible and included in this review. Adapted approaches or treatment protocols of vital pulp therapy methods presented higher success rates than conventional methods. However, outcome of vital pulp therapy can be affected by various patient, intra- and postoperative factors. Compared to calcium hydroxide, the gold standard, application of hydraulic calcium silicate-based cements in vital pulp therapy entailed more favourable outcomes. Comparable clinical effectiveness of vital pulp therapy and root canal treatment was observed.

Conclusion: Higher or comparable success rates to root canal treatment suggest vital pulp therapy as an advantageous alternative treatment modality in mature teeth. However, root canal treatment is the only available approach when the pulp is not amenable to vital pulp therapy, or the latter presented a negative outcome.

Keywords: Pulpotomy, Dental pulp capping, Root Canal Therapy, Pulp Capping and Pulpectomy Agents, Vital pulp therapy, Mature teeth

Content

1. Introduction

For a long time, the prevailing view was that root canal treatment (RCT) was the only therapeutic option after opening the pulp chamber in mature teeth, in terms of managing pulp inflammation.

However, procedure of RCT entails the total loss of the dental pulp's functions. A healthy pulp is characterized by forming dentin, transmitting signals through pain receptors and proprioceptors, responding immunologically to the invasion of bacteria and their metabolites and forming tertiary dentin as a defence mechanism [1]. Various studies reported several disadvantages of RCT, as it reduces tooth resistance, making endodontically treated teeth more prone to fracture than vital teeth [2]. Such teeth require an occlusal load providing a 2,5 times higher force compared to vital teeth to provoke a proprioceptive reaction [3]. Moreover, geometrical changes due to endodontic cavity and mechanical preparation of root canals may occur, leading to a raised prevalence of fractures [3]. Physicochemical changes in dentin may occur as irrigating solutions diminish flexural strength and microhardness and imbalance of organic and inorganic elements [4].

Nowadays, there is a new approach towards the preservation of pulp vitality of teeth with mature apices due to advances in research. A vital pulp can be exposed due to three reasons: caries, iatrogenic or traumatic exposure. A carious lesion refers to an opened pulp before the establishment of full caries removal, whereas mechanical exposure is associated with a pulp that is opened by accident during preparation. Traumatic exposure describes exposed pulp following injury or a traumatic event [5]. The goal of vital pulp therapy (VPT) is the maintenance of pulp vitality by preventing pulpitis from progressing to pulpal necrosis or apical periodontitis, hence eliminating the need for root canal treatment [6]. Methods of VPT comprising indirect pulp capping, direct pulp capping, and partial or full pulpotomy are not new procedures, but have only been used in the treatment of mature primary teeth to maintain pulp vitality and immature permanent teeth to enable apexogenesis [7].

Previously, vital pulp therapy was not considered in treating mature permanent teeth, as an infection induces bacterial spread to the whole pulp and non-recovering insufficient circulation, even after the infection is eliminated [8].

The idea of minimally invasive endodontics was advanced by Gutmann; enhancement of materials' properties as well as a better understanding of the pulp's defense and repair capability. Since pulp vitality is an essential factor in tooth preservation and long-term retention, a shift in treatment preferences of inflamed mature teeth is observed and predicted [8].

The following literature review will investigate the clinical importance of vital pulp therapy in mature teeth based on current scientific literature, comparing it to traditional root canal treatment.

2. Methods

2.1 Systematic literature search

A systematic literature search was conducted using the PubMed database for scientific and medical literature. Identification of Medical Subject Heading (MeSH) terms was established by using keywords of relevance in regard to the thesis topic in the MeSH database of the National Center for Biotechnology Information website (https://pubmed.ncbi.nlm.nih.gov/).
Application of “pulp capping” as an entry term in search yielded the MeSH term “Dental Pulp Capping” and the term “pulpotomy” resulted in the MeSH term “Pulpotomy”. The search using the entry term “Endodontics” entailed several MeSH terms such as “Root Canal Therapy”, “Dental Pulp Capping” and “Pulpotomy”. The entry term “pulp capping agents” generated “Pulp capping and Pulpectomy Agents” as a MeSH term.
The search using the entry terms “Vital pulp therapy” and “Mature teeth” yielded no results, thus these were used as text-words in combination with identified MeSH terms.

The literature search was conducted by combining the identified MeSH terms and text words using the Boolean operator AND as follows:

- (Vital pulp therapy) AND (Mature teeth) (84 results)
- ("Dental Pulp Capping"[Mesh]) AND ("Dentition, Permanent"[Mesh]) (29 results)
- ("Dental Pulp Capping"[Mesh]) AND (Mature teeth) (27 results)
- ("Pulpotomy"[Mesh]) AND ("Dentition, Permanent"[Mesh]) (37 results)
- ("Pulpotomy"[Mesh]) AND (Mature teeth) (64 results)
- (("Dental Pulp Capping"[Mesh]) AND ("Root Canal Therapy"[Mesh])) AND (Mature teeth) (4 results)
- (("Root Canal Therapy"[Mesh]) AND "Pulpotomy"[Mesh]) AND (Mature teeth) (17 results)
- (("Root Canal Therapy"[Mesh]) AND (Vital pulp therapy)) AND (Mature teeth) (22 results)
- ("Pulp Capping and Pulpectomy Agents"[Mesh]) AND (Mature teeth) (18 results)

The search was limited according to the inclusion and exclusion criteria in section 2.2, and its results were presented and selected as explained in section 2.3.

2.2 Inclusion and exclusion criteria

Research studies, published in the last 10 years, comprising of clinical study, clinical trial, controlled clinical trial, comparative study, and observational study investigating vital pulp therapy in mature teeth were included.

Language limitations were set to English and German language. Studies in languages other than English or German, which were not focusing on prevention in endodontics in mature teeth, as well as incomplete research studies such as editorials, comments, study protocols and abstracts were excluded.

2.3 Study selection

The systematic literature search yielded 302 results which were screened for their eligibility based on the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) statement guidelines.

At first, the results applying different search combinations were investigated for duplicates, followed by the exclusion of 149 duplicates. The title and abstract of the remaining studies underwent screening considering inclusion and exclusion criteria. Thus, 92 studies were excluded as considered not suitable. Afterwards, the full texts of initially included studies were screened according to inclusive and exclusive criteria, resulting in the exclusion of 47 studies. In addition, reference mining of the identified articles was performed and detected 33 other scientific papers and enriched the findings. Finally, 43 remaining studies were included in this review.

2.4 Data extraction

The following data was extracted from the included studies:

- Authors
- Year of publication
- Aim of the study
- Type of sample
- Number of samples
- Outcome parameters
- Outcome results
- Conclusion

3. Vital pulp therapy

3.1 Etiopathogenesis of pulp inflammation

Pulpal diseases are attributed to etiological factors, including irritants of mechanical, chemical, or microbial origin [9]. The risk of mechanical pulp irritation depends on the extent of tooth structure removal, as dentinal permeability increases along with a reduction of distance to the pulp. Previously, antibacterial agents, such as phenol, silver nitrate, alcohol, chloroform and various others, used for dentin sterilization and ingredients of restoration materials were suspected to be responsible for pulp irritation, by causing inflammatory changes due to their cytotoxicity which led to refusing their application nowadays [9]. Trauma by impact injuries may lead to pulp inflammation. Potential of maintaining pulp vitality is higher in mild to moderate traumatic injuries compared to those of severe nature [9].

While Gram-positive bacteria are predominantly found in the microflora of various carious lesions, Gram-negative anaerobic bacteria are increasingly present in deeper lesions, leading to the infiltration of the dental pulp with inflammatory cells [1].

Invasion by microorganisms represents the main cause of inflammation in pulp tissue, which reacts initially by innate immune response followed by focal accumulation of chronic inflammatory cells [9].

Progression of caries disease influences infiltrate’s character and intensity. Superficial caries trigger chronic inflammatory cells located in pulp, but definite pulp response occurs if caries are detected in primary dentin. Caries affecting primary dentin evoke innate and adaptive immuno-inflammatory responses by toxins and byproducts of bacteria, enacting in both antigenic and non-antigenic mode, to invade dentinal tubules [10].

Pathogens are recognized through the interaction of pattern-recognition receptors (PRRs) with pathogen-associated molecular patterns (PAMPs), which induce host defence involving early humoral and cellular mechanisms [1,9,11]. These PRRs are expressed in odontoblasts, pulp fibroblasts, leukocytes, and pulpal stem cells [1]. Both G-protein coupled receptors and Toll-like receptors participate in the innate immune response which triggers the cellular phagocytic functions against pathogens. Adhesion molecules on vascular endothelial cells are upregulated, supporting the recruitment of leukocytes to the site of infection. Therefore, adherence of G-protein coupled receptors to chemokines, lipid mediators or bacterial proteins leads to the extravasation of white blood cells, which produce bactericidal substances. These activated leukocytes promote the generation of reactive oxygen intermediates (ROI), supporting bacterial clearance from tissues [9,11]. The immune response is strengthened through the synthesis and release of proinflammatory cytokines, tumor necrosis factor (TNF) and interleukin-1 (IL-1) caused by bacterial products [9,11].

Another characteristic of the pulp's defensive reaction is the formation of tertiary dentin acting as a mineralized barrier and separative layer to prevent bacterial migration [1,8]. Tertiary dentin can be of reparative or reactionary type, depending on its derivative. Therefore, both can be differentiated by genesis and nature [1,10].

Demineralized dentin affected by caries solubilizes bioactive molecules, especially transforming growth factor beta-1 (TGF-ß1), the most abundant non-collagenous protein present in the dentin matrix. Reactionary dentin is formed as odontoblasts respond to TGF-ß1 by raising their secretory activity. In addition, occlusion of dentinal tubules by deposited calcium phosphate causes sclerosis, forming less permeable dentin [1].

Contrary to that, dentinogenesis of reparative dentin differs as stronger stimulation results in the death of odontoblasts and the deposition of minerals by other cells such as pulp fibroblasts or others from the stem cell pool. The source of osteodentine formation leading to mineral deposition is not yet determined [1].

However, localized acute inflammation or abscess may develop if tooth is left untreated [9].

Consequently, an inflamed pulp remains inflamed or necrotizes either eventually or rapidly, which is dependent on the following factors: the virulence and host resistance of the microorganism, the circulation of inflammatory fluids preventing the rise of intra-pulpal pressure, and the amount of circulation and lymphatic drainage [9].

3.2 Diagnostic methods of pulpal status

To establish a baseline, various classifications of pulpal conditions and their proposed treatment in vital pulp therapy have been described.

Pulpal conditions can be classified into healthy pulp, reversible pulpitis, and asymptomatic or symptomatic irreversible pulpitis [12]. This diagnostic terminology is currently based on clinical findings and treatment prognosis. A normal pulp is healthy, thus presents without symptoms and responds normally to pulp testing. Reversible pulpitis describes a clinical diagnosis established by findings of subjective and objective origin indicating the pulp's reparative potential, whereas irreversible pulpitis implies the incapability of a vital inflamed pulp to heal [6].

Diagnostic tests involving sensibility and vitality tests are used in clinical practice to distinguish between pulpal diseases. However, they are limited in terms of accuracy because they are based on their inherent ability to differentiate between health and disease [13].

Pain originating from the dental pulp is transmitted through two different nerve pathways. Fast pain conduction is carried out by myelinated A-delta fibers (Aδ fibers), leading to localized rapid and sharp pain, whereas slow pain conduction by unmyelinated C-fibers presents an unlocalized pain. The pain response of Aδ fibers and its immediate cessation is provoked by the application of a cold stimulus. The severity of inflammation is measured through a cold test, leading to an exaggerated and lingering response as C-fibers are sensitized and hypersensitive due to inflammation [7,13].

In contrast, a hot stimulus evokes a more intense pain presenting as brief, rapid and disappearing after a short amount of time [7,13]. It should be noted that heat application longer than five seconds may cause biphasic stimulation of A-delta and C fibers leading to lingering pain [13].

Electric pulp tests (EPT) measure a value by directly triggering response of A-delta fibers as the applied electric current shifts ions within dentinal fluid, depolarizing and generating action potential in A-delta fibers. The established value does not represent a quantitative measure of pulpal status but refers to function and response ability of some A-delta fibers [13].

Nevertheless, sensibility tests assess ability of the nerve to respond to a stimulus, but not its vitality as it refers to integrity of vascular supply. Symptoms provoked by sensibility tests allow practitioners to differentiate between health and disease, whereas level of inflammation or threshold of irreversibility appear more challenging to identify due to arbitrariness and subjectivity of measurements [13]. A systematic review by Mejàre et al (2012) concluded that lack of sufficient evidence impedes accurate reflection of true status of pulp by symptoms and responses [14]. It has been shown that age and gender play a role in relaying the pulp's response to the stimuli. Additionally, the experience of the clinician also translates into the accuracy of test results [15].

On the other hand, vitality tests such as pulse oximetry (PO) or laser doppler flowmetry (LDF) rely on objective measurement of blood flow without dependence on patients' responses [14].

Pulse oximetry is a non-invasive physiometric method using catheter diodes to determine the oxygen saturation of pulpal blood [14].

Laser doppler flowmetry is defined as a non-invasive technique of detecting numbers and velocity of particles in pulpal circulation, thus measuring the health of the pulp. Its higher sensitivity and specificity entail the capability of differentiating between healthy and necrotic pulp which can be useful in sound anterior teeth that underwent trauma, but less in sclerotic teeth or teeth with big restorations, as they commonly lead to false positive and negative results [14].

Both ways of pulp testing are seen as the most reliable in the detection of pulp status, however their comparison suggested PO as the diagnostic test of choice, albeit there are limitations present. Error margins related to determined small blood volume prohibit differentiation between normal and inflamed pulp. In addition, surrounding tissues may interfere, causing inaccurate results and uncertainty about the penetrating ability in mineralized tissue. Furthermore, the costs of devices used for EPT amount to a high price. Contrarily, failures can occur following PO due to the design being unsuitable for dentistry, but adapted dental instruments yield raised sensitivity and specificity numbers compared to EPT and cold tests [14].

Treatment planning is based on the condition of the pulp, however the reliability of clinical diagnosis in comparison with the histologic diagnosis is questioned as various studies detected disparities between clinical and histological status [16].
In 1963, Seltzer et al. showed that the severity of pain is partly related to the severity of inflammatory reaction, but it is also affected by drainage and preceding experiences of the patient [17].
According to the evaluation conducted by Baume et al. (1970), different conditions were found in separate parts of the same pulp after histological examination, thus one diagnosis cannot be established for the complete pulp complex. It was concluded that no histologic diagnosis can be taken based on clinical examination [18].
According to Dummer et al. (1980), no adequate connection between clinical features and pulp histologic condition was observed, concluding that an accurate classification differentiating between all pulpal conditions and the possibility of pulp saving is not possible [19].

In contrast to the previously performed studies, Ricucci et al. (2014) found a high correspondence between clinical and histologic diagnosis predominantly in a healthy pulp and reversible pulpitis which is clinically significant as the applied classification demonstrates a raised possibility of therapy guidance approaching pulp saving [7,16].
In this study, 95 extracted teeth were classified according to determined clinical criteria followed by histologic processing and grouping into healthy, reversible, or irreversible inflammation. This results in a correspondence of 57 out of 59 teeth, thus 96,6% of clinical and histologic diagnosis of normal pulp or reversible pulpitis. Irreversible pulpitis, clinically and histologically, was matched in 27 out of 32 teeth (84,4%) [15,16].
No consideration of teeth defined as clinically healthy was confirmed to be histologically normal due to deviations like present scattered inflammatory cells, fibrosis, hyperemic vessels, and reduced layer of odontoblasts. Therefore, it was advocated that a pulp which has been reversibly inflamed is incapable of demonstrating the same histological signs as a healthy pulp. Nonetheless, pulp tissues with reversible pulpitis are able to function properly after correct therapy [16]. Absence of healthy teeth with uninflamed pulp tissue, except in control group, precludes conclusion about differentiation between healthy teeth and teeth with reversible pulpitis [15].
It is assumed that the differences in the results of all studies compared to those of the study performed by Ricucci et al. (2014) could be associated with varying diagnostic and histologic criteria as well as enhanced methods of histology and histo-bacteriology [16].
Overall, the utilized classification considering the possibility of pulp saving has a high opportunity of guiding the needed treatment in most cases, but there is further research indicated to enhance the

reliability of pulpal diagnosis due to performance of unnecessary therapy of some teeth according to the current parameters [16].

The main issue in diagnostics of pulpal diseases is the absence of reliable standards to use as reference point in clinical work. Currently, combining various clinical tests and symptoms seems to be the most effective method, but including molecular diagnosis in the future to confirm true pulpal diagnosis will be needed. Limited scientific evidence referring to the accuracy and reproducibility of diagnostic tests suggests low effectiveness of diagnostics of pulp. Lacking evidence for detecting true pulp condition and prognostic signs prohibits reliable estimation of the outcome of vital pulp therapy [15]. Therefore, evaluation of bleeding extent following exposure of pulp can aid in enhancing the reliability of diagnosis. Weak bleeding is seen in non- and superficially inflamed pulps, whereas more severe bleeding is observed in deeply inflamed pulp tissue. The amount of bleeding determines the level of inflammation, as in irreversible pulpitis, prolonged or severe bleeding is noted. Healing potential is estimated to be worse in case of severe or persistent bleeding. Hence, the bleeding threshold contraindicating vital pulp treatment has not yet been investigated [15]. The unsuccessful arrest of bleeding within a reasonable period of time indicates the shift in therapy from partial pulpotomy to full pulpotomy, then to pulpectomy [20].

Overall, choice of treatment procedure of pulpitis is dependent on the clinically non-determinable degree of bacterial infection. While correlation of clinical and histologic findings is notably poor, depth of caries lesion and histological response to caries does correlate. The highest reliability of diagnosis is accomplished by assessing the bleeding extent after pulp exposure. The presence of serous, purulent, or bloody exudate or the absence of haemorrhage contraindicates the maintenance of pulp vitality [15].

Scientific evidence suggests that the pulp-dentinal complex of teeth diagnosed with irreversible pulpitis may have reparative potential, indicating revision of the currently used classification system to prevent root canal treatment if the uninflamed/reversibly inflamed part of the pulp might regenerate itself after correct treatment. It was found that unnecessary root canal treatment of some teeth diagnosed with irreversible pulpitis was conducted, which was confirmed by histological examination by Ricucci et al. (2014) [21]. It is highly important to preserve pulp vitality, especially in teeth with irreversible pulpitis, to retain structural integrity and immunological functions of the teeth. This will additionally be of lower financial expenses and inconvenience for the patients [10].

Therefore, Wolters et al. (2017) suggested a new diagnostic terminology of pulpal diseases and their treatment. It includes four different types of pulpitis: initial, mild, moderate and severe pulpitis [21,22].

Initial pulpitis is characterized by reacting in a heightened, but not lengthened way to cold test, non-sensitive to percussion and absence of spontaneous pain. Mild pulpitis responds to elevated and lengthened stimuli of cold, hot, and sweet origin lasting up to 20 seconds followed by cessation. According to histological correlation, local inflammation extending to coronal pulp is present. Both initial pulpitis and mild pulpitis are suggested to be managed by indirect pulp capping [21,22].

Furthermore, moderate pulpitis is expressed by clear symptoms and reacts strongly, heightened, and prolonged to cold tests for as long as a few minutes. Such teeth may be sensitive to percussion, and dull aching occurs, but pain is suppressible with medication. Considering the histological status, which corresponds to the findings from above, local inflammation extends to the coronal part of the pulp. However, it is recommended to manage moderate pulpitis by performing partial or full pulpotomy [21,22].

Severe pulpitis is described as severe spontaneous pain and clear pain to hot and cold tests, as well as sharp to dull throbbing pain. It appears to be sensitive to touch and percussion. Patients report suffering from sleep disturbances due to pain, especially aggravated when lying down. Histologically, local inflammation may extend from coronal pulp to root canals. It is proposed to be managed by performing a coronal pulpotomy if no prolonged bleeding occurs in orifices; otherwise, root canal treatment is indicated [21,22].

Nevertheless, practitioners are incapable of establishing the accurate histological status of the pulp and must rely on clinical symptoms and available diagnostic tests based on subjective responses. Assessment of pulpal bleeding extent serves as the only reliable way to evaluate the inflammatory status of the pulpal complex. Therefore, additional scientific investigations and more affordable resources are needed to ensure a more precise diagnosis of inflamed pulp tissues [13]. A combination of commonly used sensibility tests has long been the standard practice for most experienced clinicians and continues to be to this day.

3.3 Disadvantages of root canal treatment

In older practices, total caries removal was preferred because it was assumed to be the better option, exposing the pulp instead of leaving softened and infected dentin behind [23].

Nevertheless, a study conducted by Maltz et al. (2012) comparing microbiological infection after conventional and incomplete caries treatment revealed lower levels of infection when infected dentin was sealed instead of fully removed [24].

Vital pulp therapy including indirect pulp capping, direct pulp capping, and pulpotomy serves as an alternative approach to traditional non-surgical root canal treatment and tooth extraction. The latter may induce disturbances in bone development of jaws and adjacent teeth especially in younger patients. In addition, it may change appearance, occlusal relationship, phonetics, and digestive system of the patient [10].

Loss of vitality and root canal treatment are thought to entail modifications in tooth structure, composition, and biomechanics. Considering a weakened collagen network stimulated by dehydration of dentin, a higher number of incomplete bindings in collagen of non-vital teeth in comparison with vital teeth was observed [2].

A vital pulp is characterized by circulating blood flow, including cellular and humoral components and nerve innervation. Injury to pulp complex entails migration of these components to the site of injury to establish elimination of the irritant by mounting an immunoinflammatory response. Sensory nerve fibers are capable of blood flow regulation, wound healing, and immune response [10]. Blood circulation is assumed to set the flow of dentinal fluid under a pressure of 15 cm H_2O (1,47 kPa). However, effects on dentin following removal of blood supply changing fluid flow remain unclear and require further research [2].

Additionally, altered moisture content due to vitality loss affects modulus of elasticity called Young's modulus. This change in moisture has no effect on compressive and tensile strength. Only the change affecting the unbound water is assigned to 9% of lost moisture. Therefore, endodontically treated teeth present higher levels of dehydration in dentin. This dehydration consequently causes dentin to have a higher elastic modulus and is hence more brittle making the roots more susceptible to fracture [2].

No differences in collagen cross-linkage comparing vital and non-vital dentin were found. In contradiction, endodontically treated teeth presented more extensive cross-linkage of collagen [25]. While mechanical removal of pulp tissue has no chemical effects on dentin, irrigating solutions applied in chemo-mechanical debridement interact with dentin, thus modifying its features. A concentration higher than 1% of sodium hypochlorite (NaOCl) up to 5,25% as utilized in chemical preparation during root canal treatment softens dentin if its action time surpasses 10 minutes. Moreover, it modifies the dentin substrate and exhibits proteolysis, decreasing elastic modulus and flexural strength. Chelators, e.g. ethylene-diamine tetra-acetic acid (EDTA), were proven to interact with the mineral content of dentin, causing erosion and softening by depletion of calcium and by acting on non-collagenous proteins [2].

Biomechanical properties of tooth are altered as tissue is lost, especially due to endodontic cavity preparation as vertical coronal walls have higher flexure possibilities, the tooth is less resistant to fracture [2]. Reduced strength of radicular dentin following root canal treatment surpasses that of naturally ageing dentin, thus raising the risk of root fractures with time [25]. Additional preparations of the tooth related to decay, including marginal ridges, entail the highest risk of tooth fracture. The proprioceptive sensitivity of a treated tooth is diminished following the absence of pulp, which leads to a partial loss of its mechanical responsiveness. Root-canal treated teeth exhibit a lower tubule occlusion ratio than non-restored teeth [25]. Therefore, in a non-vital tooth, the altered sense of perception of occlusal forces possibly produces discomfort when the double values of the functional occlusal load for the vital teeth are reached [2].

Overall, preservation of intact tooth structure is of high significance in terms of maintenance of biomechanics and resistance to fracture, which explains the higher rate of mechanical failure of endodontically treated teeth in comparison to vital teeth [2,10].

3.4 Pulp capping

3.4.1 Indirect pulp capping and its variations

In scientific papers, no one standardized definition of indirect pulp capping exists. In German literature, the term “indirect pulp capping” is assigned to caries excavation until reaching a thin caries-free layer close to the pulp, otherwise known as treatment of profound caries, whereas in English literature, it refers to covering a thin layer of affected or infected dentin without completion of the caries removal process and placement of definitive adhesive restoration in the same appointment [3,26]. The latter approach is a one-step selective or partial caries removal procedure and indirect pulp capping without re-entry and entails the risk of irreversible pulpitis due to bacteria remaining or penetrating tissue due to cytotoxic components of restoration materials. In this context, clinicians expect the formation of reactionary dentin, but non-tubular hard tissue deposition is more probable due to the damage extent of odontoblasts [3,26].

Another article points out that only affected dentin can remain in the tooth, but infected dentin must be excavated based on the theory stating that the zone of affected demineralized dentin lies between the outer infected layer of dentin and pulp [27]. Clinical distinction between affected and infected dentin can be a challenge for clinicians. Remineralization of affected dentin followed by formation of reactionary dentin is awaited, while the tooth is temporarily sealed. After 2 months dentin and its level of remineralization is reevaluated taking presence and depth of soft dentin and possible communication with the pulp into account of decision about the need for root canal treatment [27].

This method of indirect pulp capping with re-entry is more commonly known as stepwise caries removal or in other words two-step selective caries removal [26].

The European Society of Endodontology (ESE) proposed definitions of indirect pulp capping and its variations in a statement concerning the management of deep caries and exposed pulps. According to the ESE, indirect pulp capping is defined as a method of one-stage caries removal up to hard dentin followed by the application of biomaterial onto a thin dentin barrier. It is notably more aggressive than one-step selective and stepwise carious tissue excavation as neither soft nor firm carious dentin is left intentionally, thus raising the risk of pulp exposure [28]. One-stage selective caries removal describes an indirect caries excavation technique up to soft or firm dentin before applying biomaterial on dentine barrier and immediately restoring tooth permanently which is time- and cost-effective as clinical and patient time is saved. It is limited due to the possibility of the patient approaching another dentist who detects remaining caries and suggests intervention [28]. Stepwise excavation can be termed as an indirect two-step selective removal approach aiming to alter the cariogenic environment. In the first appointment caries are removed selectively up to dentin of soft texture to a level facilitating temporary restoration [28]. Clinically, active caries appear as soft discoloured and wet tissue, while after 6 to 12 months, retained dentin presents as a drier and harder substance when a tooth is reopened. Finally, caries is excavated up to firm dentin, followed by placement of a final restoration [28].

These variations in indirect pulp capping techniques raise the question regarding the most effective method in clinical practice. Mainly, all approaches share the common aim of excavating caries to the greatest extent possible without exposing the pulp. Comparable results of the one-stage selective and stepwise caries removal approach of caries in the pulpal third were found; however, evidence concerning caries in the pulpal quarter is limited. Residual dentin staying in situ may cause shrinkage of dentin and impairment of coronal restoration, leading to pulpal complications [29]. A meta-analysis of randomized control trials comparing the therapeutic effects of selective and stepwise caries treatment found that selective caries excavation is superior to stepwise method due to increased rate of success and decreased quantity of pulp exposure, pulpitis, or pulp necrosis [30].

3.4.2 Direct pulp capping

Direct pulp capping is defined as the direct coverage of an exposed pulp using a pulp capping material prior to the immediate placement of a permanent restoration [28]. Its main goal is the protection of exposed tissue from bacterial irritation [31]. Following pulp exposure, bleeding is controlled compressing gently with cotton pellet moist with sterile water. Inflamed and infected pulp should be removed, followed by disinfection applying 2% chlorhexidine (CHX) for 2 to 3 minutes before dressing with pulp capping material [32]. Trend in pulp wound lavage utilizing 2,5% NaOCl in aqueous solution due to its selective effect on necrotized and infected soft tissues is visible, thus allowing pulp capping material to exert effects on healthy tissue which increases success rates of direct pulp capping [33].

Reported variations in the success rate of direct pulp capping, as confirmed by Cushley et al. (2021), demonstrate that applied pulp capping material influences long-term outcomes [34].
Consequently, Bjørndal et al. (2019) proposed a classification of pulp capping strengthening the need for improved technique after microbial pulp exposure which was approved by the European Society of Endodontology. Therefore, direct pulp capping is sub-grouped into pulp capping class I and II [31].
Class I refers to the traditional pulp capping method indicated in traumatized teeth with superficially exposed pulps and teeth with iatrogenically exposed pulps. Preoperatively, there is no deep carious lesion present, thus status of the pulp is considered healthy and relatively free of inflammatory processes. Pulp exposure should be superficial, preferably less than 1 mm and localized in coronal third of pulp chamber ideally connecting to a pulp horn [31].
In class II pulp capping the conventional treatment protocol is adjusted as used in teeth with preoperatively exposed pulp due to deep carious lesions. It includes operating with microscope-guided caries removal, attaining haemostasis within 5 minutes, disinfecting with 5,25% NaOCl, completing therapy by “restoring the pulp roof” with hydraulic calcium silicate-based cements [31].
Bogen et al. (2008) and Marques et al. (2015) observed high success rates, 97,96% and 91,3%, when following protocol of direct pulp capping (class II) [35,36]. Contrarily, in randomized control trials by Bjørndal (2017) a 5% survival rate at 5 years of teeth treated utilizing conventional approach, was reported [37].
Therefore, the enhanced technique of direct pulp capping (class II) is a more promising modality in managing carious exposed pulps.

3.5 Pulpotomy

Pulpotomy, a minimally invasive method of vital pulp therapy, is characterized by the removal of coronal pulp tissue followed by coverage of radicular tissue using an adequate pulp capping material to ensure pulp protection from injuries and promote healing. Its main purpose is the prevention of bacterial penetration by excavation of inflamed tissue located in the pulp chamber [38]. There are two distinct types of pulpotomy, partial and full pulpotomy, considering the amount of removed tissue from the crown of the tooth [39].
Reported advantages of pulpotomy in permanent teeth in comparison with traditional root canal treatment are the following: maintenance of tooth vitality, intra-radicular tooth structure,

neurosensory performance and proprioception, cost-effectiveness compared to root canal treatment, minimal invasive approach, and treatment being less technique sensitive [38,39]. Performance of pulpotomy does not cause mechanical compromise, thus diminishing side effects such as discoloration, residual inflammation of periapical tissues, and fracture [38].

3.5.1 Partial pulpotomy

Vital mature teeth which do not present signs and symptoms of irreversible pulpitis can be primarily treated in a more conservative manner with partial pulpotomy compared to full pulpotomy. If hemostasis is not achieved, progression to full pulpotomy may be required [40].

Partial pulpotomy, also named Cvek pulpotomy, refers to the amputation of coronal pulp up to 1 to 3 mm, followed by placement of lining material and permanent restoration [38]. According to Cvek, it is an aseptic surgical removal of exposed pulp and dentin surrounding the exposure site to a depth of 1,5 to 2 mm [27]. Partial pulpotomy is defined by the ESE as post-exposure removal of a small portion of the coronal pulp tissue prior to biomaterial placement on remaining pulp tissue and permanent restoration [28].

Shallow pulpotomy mainly aims to acquire a clean surgical wound in non-infected pulp connective tissue surrounded by mineralized non-infected dentin, thus performed to preserve remaining coronal and radicular pulp tissue. It is based on the principle of selective eradication of diseased pulp segments where inflammation and microbial colonization occurred and removal of soft dentin, potentially infected, around the exposure site as well as dentine spicules with tubules which could harbour bacteria, thus preventing transportation into the pulp [20].

Compared to direct pulp capping, it has the positive aspects of removing superficially inflamed pulp tissue and providing space for sealing the cavity, and in comparison, with full pulpotomy, Cvek pulpotomy provides benefits including preservation of cell-rich coronal pulp tissue, assuring continued deposition of cervical dentin and decreasing likelihood of root canal treatment [39,41].

3.5.2 Full pulpotomy

Mature teeth diagnosed with irreversible pulpitis expressing symptoms such as severe spontaneous or prolonged pain with enhanced lingering responses to sensibility testing can be indicated for full pulpotomy treatment. This treatment alternative can also target vital mature teeth with pain on percussion or with radiographic findings of widened periodontal ligament space [40].

Complete or cervical pulpotomy involves excavating the full coronal pulp, followed by directly applying biomaterial such as hydraulic calcium silicate-based cements to exposed pulp tissue at the level of the root canal orifices before placing the restoration [28].

According to the ESE, if hemostasis is not managed during the span of five minutes, and the tooth presents with signs and symptoms of irreversible pulpitis, the clinician can proceed with a full coronal pulpotomy to the level of the root canal orifices and can control the bleeding using cotton pellets soaked with NaOCl or CHX [28]. There are controversial statements regarding the duration of bleeding control time ranging from 2 to 25 minutes at which a more radical approach is advocated [42]. These time variations in achievement of hemostasis do not act as a determining factor of pulpotomy outcome. However, it is contraindicated to perform pulpotomy in teeth bleeding persistently beyond 10 minutes [40].

This procedure is also a good alternative to a partial pulpotomy for practitioners without advanced magnification equipment. If bleeding is still not arrested after full pulpotomy and if the tooth is restorable, root canal treatment is indicated. The application of hydraulic calcium silicate-based cement and immediate definitive restoration is required to prevent further microleakage [28].

Careful clinical and radiographic monitoring following full pulpotomy is required at 6 months and 1 year respectively. The tooth should be assessed at regular intervals if the tooth presents lasting symptoms or uncertainty regarding healing prevails. The tooth treated with full pulpotomy should not be responsive to cold and electric pulp sensibility testing [28,40].

A potential complication of total pulpotomy in mature permanent teeth is the occurrence of apical periodontitis due to pulp canal obliteration. However, this is a consequence of pulp infection due to microleakage in the coronal restoration or improper pulp disinfection during the procedure as well as the canal obliteration itself [28,40].

3.6 Indications and contraindications of vital pulp therapy in mature teeth

Previously, indications of vital pulp therapy were limited due to the assumption of the pulp’s healing incapability when it comes to diagnosis of irreversible pulpitis, thus it was only applied in teeth diagnosed with reversible pulpitis [8].

Indirect pulp capping is indicated in symptom-free teeth with deep caries, but healthy pulp reacting in normal way to pulp tests. A healthy pulp presents a mild to moderate transient response to cold and electrical stimuli subsiding within seconds after removal of stimulus, and no reaction to hot stimulus. Such teeth include both teeth with a thin sound dentin layer and teeth in which a thin carious layer of dentin is left intentionally to prevent pulp exposure [26]. While some papers encompass teeth with reversible pulpitis as possible to manage by indirect pulp capping, other scientific papers present this pulpal condition as contraindicated for indirect pulp capping [3,26]. In the guide to clinical endodontics provided by the American Association of Endodontists (AAE) presenting evidence-based recommendations to general practitioners and endodontists, indications of indirect pulp capping took only permanent teeth with immature apices into account [43].

According to the latest guide from AAE in 2013 indications of direct pulp capping are [43]:

- Mechanically exposed clinically vital and asymptomatic pulp
- Controlled bleeding at the exposure site
- Exposure allows pulp capping material to directly contact the vital pulp tissue
- Exposure under dental dam isolation
- Maintaining of adequate seal of the coronal restoration
- Informing patient that root canal treatment may be indicated in the future

No information about status of teeth considering apex formation was given.

Considering the same guide, the indications of pulpotomy are as follows [43]:

- Exposure of vital pulps or irreversible pulpitis of primary teeth
- Emergency procedure in permanent teeth until accomplishment of root canal treatment
- Interim procedure for permanent teeth with immature root formation to allow apexogenesis

No information about status of teeth considering apex formation was given.

Recent scientific research entailing more knowledge about healing ability of pulp and emergence of hydraulic calcium silicate-based cements widened range of indications. Therefore, irreversible pulpitis was taken into account as well [8].

Traditional direct pulp capping is applicable for small defects less than 0,5 mm with non-caries exposed pulps. Hydraulic calcium silicate-based cements allowed direct pulp capping of exposed pulps more than 1 mm due to better dentin bridge formation [8].

Pulpotomy is indicated in permanent vital teeth: with deep carious lesions and pulp exposure, diagnosed with either reversible or irreversible pulpitis, with or without periapical rarefaction, is restorable, and periodontium does not present with advanced disease, and absence of soft tissue swelling or sinus tract, patient does not present with contributory medical history, hemostasis is achievable following complete pulpotomy [41].

Indications of partial pulpotomy include an exposure bigger than 1 mm in size and no success in bleeding control to enable direct pulp capping. In contrast, total pulpotomy is indicated in cases of inflammation characterized by an extension deep in coronal pulp tissues when irreversible pulpitis is indicated by symptoms [8,38].

Overall, dentists should choose vital pulp therapy as the first treatment modality, if possible, to preserve vitality of teeth [8].

3.7 Pulp capping materials

Throughout history, several pulp capping materials were introduced during the process of finding the ideal pulp capping material which can be utilized in vital pulp therapy.

According to Cohen and Combe, the ideal pulp capping material should entail the following properties [22,44]:

- Stimulation of reparative dentin formation
- Maintenance of pulp vitality
- Bactericidal and bacteriostatic activity
- Adherence to dentine and other restorative materials
- Resistance to forces during final restoration delivery and mastication forces
- Release of fluoride
- Be sterile and radiopaque
- Bacterial tight seal

Additionally, it is crucial that the pulp capping materials fulfill the following essential aspects [32]:

- Immediate protection of exposed pulp before formation of mineralized bridge
- Non-toxicity and biocompatibility
- Bioactive properties triggering the formation of a mineralized barrier between the material used and the pulp undergoing treatment

In 1756, direct pulp capping was carried out and documented for the first time by Phillip Pfaff using gold foil. Subsequently, a wide range of agents were introduced and suggested for application in pulp capping procedures [22,44,45].

3.7.1 Calcium hydroxide

Calcium hydroxide ($Ca(OH)_2$) was considered the golden standard in pulp capping due to its ability to stimulate tertiary dentine formation ever since it was introduced by Hermann in 1920. It is well known for its high pH value and potent antibacterial effect, eliminating bacterial infiltration and future injuries to pulpal tissue. Nowadays, calcium hydroxide acts as a reference point to compare emerging materials to [45].

In previous years, there was much uncertainty around calcium hydroxide's ability to trigger pulp tissue repair [5]. It has recently come to light that a variety of proteins are found in the dentin matrix. These proteins, especially Bone Morphogenic Protein (BMP) and TGF-ß1, proved to be of importance during pulp capping, due to their capability to promote pulp repair, by being solubilized by calcium hydroxide. $Ca(OH)_2$ acts initially by forming superficial pulp necrosis, followed by firm necrosis, resulting in minor irritation and stimulation of the pulp's defence and repair mechanisms. These include cellular differentiation, extracellular matrix secretion and subsequent mineralization entailing the development of reparative dentin [5].

Nevertheless, aqueous calcium hydroxide presents some disadvantages as its setting depends on the composition of the paste and is incomplete very often, along with gradual resorption after placement, leading to porosity in neo-dentine and creating empty micro-space. This is known as tunnel defects, causing microleakage which leads to a decrease in tooth vitality and calcification. A tunnel defect can be described as a patency from the exposure site through reparative dentin to the pulp, possibly with the presence of capillaries and fibroblasts [45,46].

A cement type of calcium hydroxide with preferred setting characteristics was developed in which the drawbacks of aqueous calcium hydroxide were eliminated. Its efficacy in direct pulp capping was examined in studies yielding relatively low success rates [45]. A study conducted by Al-Hiyasat et al. (2006) demonstrated different success rates considering cause of exposure. Evaluation of x-rays after 3 years showed that outcome of mechanically affected teeth (92%) presented higher success rate than of carious teeth (33%) [47]. Another study by Barthel et al. (2000) brought to attention that the success rate decreased throughout the years as the treatment outcome after 5 and 10 years, considering radiographs and pulp vitality tests was evaluated. Numbers were accounted for 37% after 5 years and 13% after 10 years. Mostly, failures were expressed in an asymptomatic manner as well as pulp necrosis and slow calcification [48].

3.7.2 Mineral trioxide aggregate

Alternatively, development of mineral trioxide aggregate (MTA) at Loma Linda University and its introduction in the 1990s induced changes in endodontics. It was commercially available as ProRoot MTA, later in two forms either grey or white MTA. ProRoot MTA Gray is composed of Type I Portland cement (75%), bismuth oxide (20%) and calcium sulfate dihydrate (5%). Portland cement itself consists of tricalcium silicate, dicalcium silicate, tricalcium aluminate, tetracalcium aluminoferrite, magnesium oxide, sulfate, and free calcium oxide. Both bismuth oxide and calcium sulfate play a role in setting modification and influence the energy attenuation of photons in an X-ray beam by absorbing and deflecting them, thus lowering their intensity. Its composition is different from its successor's called ProRoot MTA White as tetracalcium aluminoferrite was removed and calcium silicates were added [5,22,45].

Similarities between the action mechanism of calcium hydroxide and MTA were observed, being that $Ca(OH)_2$ arises as a byproduct out of MTA's hydration and results in pulp necrosis following contact with pulp [45]. Therefore, formation of calcium hydroxide contributes to biocompatibility of MTA [5].

Benefits of MTA encompass high pH value, antimicrobial activity, sealing ability, radiopacity, biocompatibility and bioactivity, and aid in the creation of mineralized tissue. MTA demonstrates effective antibacterial activity in facultative bacteria but not in strictly anaerobic microorganisms, resulting in controversy about its antibacterial effect. Comparative studies evaluating dentin bridge formation of MTA and calcium hydroxide showed more uniformity and thickness in the MTA group [5,45].

Despite its advantages, negative aspects cover long setting time, poor handling, and discoloration of tooth. The prolonged time required for sufficient setting forces practitioners to provide treatment in two appointments, which entails a raised risk of bacterial contamination. The sand-like texture of MTA following a mixture of water and coarse particles complicates delivery and condensation in the area of application. The size and distribution of particles influence setting time and handling characteristics. Changes in tooth color induced by both gray and white MTA were reported, despite the formulation of white MTA excluding substances responsible for dental dyschromia [32,45]. The color of white MTA was altered upon contact with dental structures. Interaction of bismuth oxide, a constituent of MTA, and collagen in the dentin matrix results in grayish discoloration of the tooth, indicating the need for replacement of bismuth oxide as a radiopacifier [49]. Factors influencing the discolouration property of white MTA comprise blood contamination, contact with sodium hypochlorite and light, and oxygen presence. However, clear reason and mechanism related to colour changes require further investigations [32,45].

Analysis of released growth factors from dentine by $Ca(OH)_2$ and MTA as well as effects on dentin extracellular matrix (dECM) by Tomson et al. (2017) demonstrated that dECM is rich in potent signaling molecules which stimulate proliferation and chemotaxis in cells of pulp after being solubilized more by white and gray MTA than $Ca(OH)_2$ [50]. The advantage of MTA to calcium hydroxide in dentinogenesis and hard tissue barrier formation is observed [51].
A study conducted by Kierat et al. (2010) investigating the effectiveness of both materials obtained 88,2% using MTA and 86,7% using $Ca(OH)_2$ reported positive results in direct pulp capping, whereas in indirect pulp capping, 100% positive results in both material groups were observed. In the latter, critically lower toxicity levels using MTA were recorded. Another study by Mente et al. (2010) reported 78% of MTA results and 60% of $Ca(OH)_2$ as successful outcomes after direct pulp capping. In summary, evidence shows that clinical performance of MTA is superior to calcium hydroxide due to better effectiveness, higher success rate and more favorable long-term outcomes. Furthermore, evaluation of pulp tissue response resulted in lower toxicity and pulp inflammation in teeth treated with MTA.

3.7.3 Hydraulic calcium silicate-based cements

Hydraulic calcium silicate-based cements can be classified according to their clinical context as proposed by Camilleri et al. (2020). This classification is based on the composition of the materials distinguishing between five types which depend on cement type, radiopacifier, vehicle, and additives [32].
The first type describes a cement composed of Portland cement with or without radiopaque characteristics but does not contain additives and requires being mixed with water, whereas the second type is radiopaque and has additives. Type 1 cements include ProRoot MTA and unradiopacified Portland cement. Type 2 cements such as MTA Angelus, Bio MTA+ and MM-MTA contain specific additives with different goals. The presence of calcium oxide in MTA Angelus improves the early release of calcium hydroxide, while bioactivity is improved through hydroxyapatite in Bio MTA+. Calcium carbonate acting as filler and calcium chloride as accelerator influence mechanical performance and setting time of MM-MTA [32].
Only the vehicle of type 3 differs from type 2. Cements belonging to type 3 are Endoseal or premixed materials such as MTA Fillaplex or TheraCal. Camilleri et al. (2020) found that the setting properties of these cements are dependent on the imbibition of fluids from surroundings [32].
Both type 4 (e.g. Biodentine, BioAggregate) and type 5 (e.g. TotalFill) are based on tricalcium/dicalcium silicate. However, only type 4 is mixed with water. These two types can be referred to as “bioceramics”. The main intention of introducing tricalcium-silicate based materials

was the withdrawal of Portland cement due to presence of aluminium and trace elements including chromium, arsenic and lead. In addition, the level of these trace elements is heightened, thus disregarding international standardized regulations [32].
Exerted effects on biological tissues by increasing OD-21 cell proliferation and biomineralization made Biodentine suitable for usage in pulp capping procedures [52]. It was demonstrated that upon application, Biodentine raised TGF-ß1 secretion from pulp cells and initiated an early form of reparative synthesis of dentin, as shown by Laurent et al. (2011) [53]. Therefore, it is known for its capability to stimulate mineralization and early odontoblastic differentiation. Furthermore, the present setting accelerator enhancing handling characteristics and strength of Biodentine reduces the risk of bacterial contamination. Its cytotoxicity was compared to that of MTA and glass ionomer cement, yielding that MTA and Biodentine are both less cytotoxic [54]. It can protect the pulp, is biologically active, and releases dentin matrix proteins from dentin upon contact, which promotes pulp healing [32].
Drouri et al. (2023) evaluated outcome of indirect and direct pulp capping using Biodentine in mature permanent teeth with deep caries. The success rate was 90% at 1 month, 85% at 3 months and 80% at 6 months which allows conclusion that Biodentine is a suitable material for both indirect and direct pulp capping [55].
Hydraulic calcium silicate-based cements have become the material of choice in vital pulp therapy, owing to their positive characteristics regarding pulp protection, mineralization and cellular differentiation, and the ability to trigger the release of dentin matrix proteins.

3.7.4 Glass ionomer and resin-modified glass ionomer cements

Glass ionomer cement (GIC) is a biomimetic material that can be referred to as a type of acid-base cement. Its formulation includes three main ingredients: water-soluble acid, basic (ion-leachable) glass, and water. It is commonly provided as an aqueous solution of polymeric acid and finely divided glass powder, requiring a mixture to achieve a viscous paste [56].
Similarities in its physical properties to those of dentin were found. GIC is capable of chemically bonding to dentin and releasing fluoride ions, thus participating in the remineralization of dentin. Firstly, an initial rapid release of fluoride, known as an early burst, takes place, followed by continuous lower-level release based on diffusion [56]. Chemical bond to dental structures prevents the diffusion of potentially toxic materials through the dentin to pulp complex [5].
By adding organic monomers, usually 2-hydroxyethyl methacrylate (HEMA), and photoinitiators to the composition of GIC aiming to enhance mechanical properties and setting reaction, resin-modified glass ionomer cements (RMGIC) were introduced [56,57]. The main intention behind the introduction

of resin-modified glass ionomer cement was to overcome instability in the water balance of glass ionomer setting only through acid-base reaction [56]. RMGICs are set using a combination of acid-base reaction and photochemical polymerization [22].

Both types present cytotoxic behaviour when in direct contact with cells, resulting in inflammation, necrosis, and lack of dentin bridge formation [58]. Conventional composition has a lower toxicity than resin-modified formulation as confirmed by Ribeiro et al. (2018) showing that Riva LC (RMGIC) initially exerted more transdentinal toxic effects than Riva SC (GIC) which diminished over time [59].

The efficacy of GIC in indirect pulp capping in teeth indicative of reversible pulpitis was compared to calcium-silicate-based materials, concluding that both materials were clinically effective. However, longer follow-up periods are required to analyze differences in the sensitivity of assessment criteria [57].

No statistically significant difference between RMGIC and calcium hydroxide was found in the application as direct pulp capping materials considering inflammation, fibrosis, formation of reparative dentin and bacterial examination, making RMGIC suitable for managing iatrogenic exposures [60].

Contradictory to all available materials, GIC is the only one capable of adhesive bonding to tooth structure, ensuring permanent sealing.

3.8 Influence factors on the outcome of vital pulp therapy

In earlier practices, the outcome of clinical procedures was dependent on radiographic and clinical evaluation as well as history examination, while nowadays, several aspects related to the patient are also considered [61].

Variations in the success rate of direct pulp capping raised the need to investigate the effects of prognostic factors, which encompass sex, age, exposure site, location of tooth in jaws, tooth type, capping material, and time span prior to permanent restoration, on clinical outcomes [62,63].

No significant effects of patients' sex on outcome of direct pulp capping were detected as there was no difference in survival rate [36,62–64].

Cho et al. (2013) and Lipski et al. (2018) reported better outcomes in a group of patients younger than 40 years and an increase in differences among age groups proportionate to follow-up time [62,63], whereas Mente et al. (2014) and Al-Hiyasat et al. (2006) did not detect an association between patients' age and treatment outcome [47,64]. The increased success rate for younger patients is related to the high capacity of their pulp tissue [63]. However, this controversy could be a result of the analysis of different age groups [62].

There is no significant difference in success rates when considering whether the tooth is anterior or posterior and whether it is located in the maxillary or mandibular arch [48,63].

Permeability of axial dentin is higher compared to pulpal floors of caries class II cavities. Isolation of axial exposure and performance of direct pulp capping appear more challenging for dentists making its management more prone to failure than in occlusal exposures [62]. Moreover, Jang et al. (2015) found that two-thirds of failures were assigned to class V cavities caused by root caries, and it presented the highest rate in comparison with other caries classes [65]. In contradiction, no impact of site of exposure on outcome was confirmed by Lipski et al. (2018) [63].

A systematic review and meta-analysis performed by Cushley et al. (2020) presented variations in success rate of direct pulp capping respective of applied pulp capping material. While $Ca(OH)_2$ succeeded 74% after 6 months, 65% after 12 months and 59% after two or three years, Biodentine - 96%, 86% and 86% and MTA - 91%, 86%, 84% and 81%, respectively, had significantly higher success rates [66].

Higher effectiveness of MTA (85%) compared to calcium hydroxide (52%) in direct pulp capping in mature permanent teeth was observed [67]. This statistically significant difference was also supported by Suhag et al. (2019) presenting success rate of MTA group (93%) and calcium hydroxide (69%) [68].

A pilot retrospective study by Linu et al. (2017) evaluated the outcome of direct pulp capping using hydraulic calcium silicate-based cements, MTA and Biodentine, demonstrating high success rates in both groups, MTA (84,6%) and Biodentine (92,3%). However, discoloration of tooth crowns was observed in the cases treated with MTA. Small sample size of 30 patients and short follow-up period of 1, 3, 6, 12 and 18 months was applied. Therefore, a confirmation by randomized control trials with extended sample size and follow-up time is needed [69]. These findings are in accordance with those of Awawdeh et al. (2018), taking the association between long-term success and left tooth structure and durability of coronal restoration into consideration [70]. Therefore, the selection of pulp capping material plays an important role in the prognosis of direct pulp capping outcomes.

The time span from delivery of treatment until the permanent seal of the tooth is of major influence on the clinical outcome as a permanent restoration provides enhanced protection from microleakage compared to temporary restoration. A higher rate of failure was observed in temporarily restored teeth than in permanently sealed teeth [48]. In contrast, no significant difference between teeth with temporary (78,4%) and permanent (85,7%) restoration was found by Lipski et al. (2018), which is related to the use of Biodentine as a temporary filling material [63]. However, Song et al. (2015)

suggested a delay of permanent restoration to facilitate the conduction of potential subsequent therapies if root canal treatment is required [71].

Various prognostic factors were reported to impact the outcome of tooth following pulpotomy and classified into three groups: patient, intraoperative, and postoperative factors [61].

Patient factors include age, gender, general medical condition, tooth type, stage of tooth development, depth of carious lesion, type of exposure, pulpal diagnosis, and severity of pulpal symptoms [61]. The stage of tooth development and its effect on the outcome of pulpotomy are not relevant as only mature teeth are the focus of this literature review.

Age or gender are seldom chosen as primary outcome variables. Thus, considering currently available evidence, both do not influence pulpotomy outcome as success rates are similar in male and female patients despite their age [61,72]. However, further investigations on both factors and their association with pulpotomy outcome are required [61].

There are uncertainties about the potential effect of systemic diseases on pulpotomy outcome as such patients are either excluded from studies or non-accurate information regarding the medical conditions are given in available research [61].

Most scientific studies investigating pulpotomy either include all types of teeth or are limited to a certain type of teeth such as molars or premolars, however no specific analysis of effect of tooth type on outcome of pulpotomy was found [61]. Kang et al. (2017) concluded that premolars or molars do not serve as prognostic factors of pulpotomy success rate [72].

The depth of the carious lesion is related to the preoperative pulpal status as pulpitis accompanies caries invading tertiary dentin, thus entailing increase in severity of inflammatory response and risk of bacterial invasion to pulp. Therefore, categorization of caries depth into deep caries and extremely deep caries was proposed by Bjørndal et al. (2019) and the ESE to make this distinction of clinical relevance [28,31]. Success rate of partial pulpotomy was affected by extremely deep caries as all failures occurred only in that group [73].

There is no research available which directly compares outcome and its relation to origin of exposure. However, limited conclusions can be drawn from studies analyzing pulpotomy as treatment modality for carious exposure [61]. Systematic reviews reported high success rates in teeth with different pulpal diagnosis and at different follow-up periods indicating no effect of exposure type on outcome [74,75].

Diagnosis of pulp and severity of its symptoms influence selection of treatment [61]. It was shown that full pulpotomy managing irreversible pulpitis presented high success rates like in root canal treatment [76]. A lower success rate of partial pulpotomy (80,8%) in comparison with full pulpotomy

(89,8%) was observed, but this difference is not of statistical significance [77]. More clinical trials focusing on impact of partial pulpotomy in irreversible pulpitis are needed [61].

Intraoperative factors cover type of VPT, isolation, magnification and operator experience, pulpal hemorrhage, pulp disinfection solution, VPT pulp capping material, final restoration, and finally level of pulpal biomarkers [61].

Outcomes of both partial and coronal pulpotomy are similar to those of root canal treatment [76,77]. Isolation, as in the usage of a rubber dam system, is important to ensure an aseptic environment, but its relevance and ineffectiveness is not studied separately. In scientific studies rubber dam isolation is employed, while in daily practice practitioners might not which raises the need for studies assessing outcome of pulpotomy in more pragmatic environment [61].

The influence of magnification and the operator's experience are not evaluated separately in a comparative manner [61]. The ESE recommends using magnification, as better vision will aid in managing exposed pulps [28].

Hemostasis and direct visualization of vital tissues after pulp exposure are essential in treatment selection, but bleeding time itself is not related to outcome as confirmed by Careddu et al. (2021) [61,73].

Generally, sodium hypochlorite should be used in wound disinfection as recommended by the ESE due to its antibacterial and hemostatic characteristics [28,40]. NaOCl disinfects dentin and pulpal structures and detaches biofilm, whereas saline is inferior in pulpal disinfection due to deficient disinfection properties leading to less favorable outcomes in comparison to NaOCl [40].

As explained above, the applied VPT pulp capping material is important. Hydraulic calcium silicate-based cements should be chosen as first line pulp capping material due to their characteristics. However, it is not clear how important they are in the overall success of pulpotomy [61].

Tan et al. (2020) showed that the rate of late failures increased significantly when restoring tooth permanently using glass ionomer cements [78]. Alqaderi et al. (2016) did not detect difference between amalgam and composite as final restoration material [75]. Currently, there is no ideal material. Radiographic and clinical evaluation of material’s integrity in regular intervals is important to ensure long-term success [61].

At the moment, there are no available objective chair-side diagnostics which could be applied in pulp diagnostics and assistance in choice of therapy [61].

Postoperative factors comprise of hard tissue bridge formation, postoperative interval before placing definitive restoration, periodontal condition, and period of follow-up. [61].

Presence of a hard tissue bridge marks a favorable outcome following pulpotomy [73]. Kunert et al. (2015) concluded that dentin bridge affected success positively as it acts as protective layer [79].
In general, recommendations of the ESE include immediate placement of final restoration [28]. As early failure may occur within 6 weeks in pulpotomized teeth, Tan et al. suggested placing an temporary restoration with good seal [78]. If pulp capping materials with long setting time such as MTA are applied, it is advised to arrange the second appointment as soon as possible to avoid potential contamination in case of a two-visit approach [61].
Considering that periodontal disease does not contraindicate pulpotomy, its effect on the outcome is not studied as such patients are either excluded or no related information is given. Research on association between pulpotomy and advanced periodontal disease has yet to be carried out [61].
Teeth following pulpotomy should be followed-up as early or late failures might occur. Early failures occur in the first 3 months after pulpotomy, while late failures occur greater than 6 months after treatment. Therefore, teeth should be assessed at 6 months, 1 year and subsequently every year, if uncertainties about healing, sensitivities or responses to pulp sensibility are present [61].

In summary, gender, exposure site meaning occlusal or proximal caries, delayed placement of a permanent filling, and position of tooth and arch type do not impact the outcome of direct pulp capping, while the age of the patients does [62,63].
No significant influence on pulpotomy outcome by age, gender, type of tooth, intraoperative pulpal hemorrhage is observed. Contrarily, depth of caries, inflammatory status of pulp, pulp capping material, level of pulpal biomarkers, and integrity of final restoration do have an influence on outcome of pulpotomy. The other factors, such as exposure site, periodontal condition, pulp disinfection solution, magnification, experience of operator, isolation, and type of pulpotomy, require further investigations as their effect on the outcome remains unclear [61].

3.9 Comparison of pulpotomy and root canal treatment outcomes

Traditionally, dentists prefer root canal treatment in mature teeth indicative of vital pulp therapy in order to prevent symptoms following pulpotomy as shown by Jin et al. (2023) [80].
To strengthen the shift to vital pulp therapy, it should be mentioned that root canal preparation is a predisposing factor for vertical root fractures leading to an increase in susceptibility. Tavanafar et al. (2015) compared the effect of different instrumentation techniques including nickel titanium hand K-file (HF), BioRaCe rotary file (BR) and WaveOne reciprocating single-file (WO) on vertical root fracture resistance. Statistically significant reduction concerning fracture resistance was seen in all groups. While HF and BR group differed statistically, the WO group did not. All instrumentation

techniques weakened root structure making teeth more prone to fracture under lower load than non-prepared roots [81].

In general, success or failure of pulpotomy is evaluated by pulp sensibility testing and radiographs at 6 and 12 months postoperatively, followed by subsequent yearly intervals. The patient should react positively to sensibility tests without exaggeration and not be in pain. Clinical and radiological absence of pulp necrosis, internal root resorption and apical periodontitis is indicative of success. Pulp sclerosis, natural defensive pulp response, after pulpotomy complicates re-entry, if required, but does not mark failure [61].

Clinical and radiographic follow-up at 6 months and yearly for up to 5 years of teeth treated with pulpotomy is required according to the ESE. The outcome is identified as success when the following aspects are fulfilled [28]:

- Partial pulpotomy: positive response to cold and EPT tests
- Full pulpotomy: non-responsive to pulp testing
- Absence of signs and symptoms indicative of reversible or irreversible pulpitis
- No swelling or sinus tract
- No abnormal tooth mobility
- No radiographic signs of internal or external root resorption
- Absence of new periapical pathosis
- Healing of periapical pathosis, if preoperatively present

A systematic review by Martínez-Salas et al. (2024) analyzed the effectiveness of root canal treatment and vital pulp therapy taking eight studies into account of which three studies focused on comparison of pulpotomy and RCT. Results were reported after 1 year by Koli et al. (2021), 1,5 year by Galani et al. (2017) and 5 years by Asgary et al. (2014), presenting clinical success of pulpotomy (93,3%, 85%, and 78%) and of root canal treatment (90%, 87,5%, and 75%) [82].

Only Asgary et al. (2015) presented results according to groups ranged by age, but the patients' age did not affect the outcomes. Aging affects the potential of pulp regeneration responding to stressors by reducing size of pulp chamber, vascular supply, and cell density. In the elderly odontoblasts showed lower autophagic activity leading to functionality loss [83].

Success rate and postoperative pain following pulpotomy and root canal therapy in cariously exposed mature permanent molars with no signs of apical periodontitis were evaluated in a randomized control trial by Galani et al. (2017). A nonsignificant difference in success between the pulpotomy (85%) and RCT (87,5%) groups was found. Signs of preoperative pain predict postoperative pain. While preoperative pain ranged between 0 and 6 on a 10-cm visual analogue scale without a statistically significant difference between both groups, postoperative pain was statistically significantly less in the pulpotomy group. Therefore, pulpotomy can serve as an alternative treatment for symptomatic teeth with deep caries lesions, especially for emergency relief of pain [84].

Martínez-Salas et al. (2024) concluded that pulpotomy is a valid alternative to root canal treatment, but further research with longer follow-up periods and consideration of influence variables is needed. No comparative studies evaluating the outcomes of direct pulp capping and root canal treatment were found; thus, the lack of evidence prohibits a statement on the effectiveness of both approaches [82].

Eghbal et al. (2020) studied the effect of pain relief after full pulpotomy using MTA (PMTA group) or calcium-enriched mixture (PCEM group) and root canal treatment using rotary instruments in symptomatic or asymptomatic mature molars with cariously exposed pulps. Preoperative pain incidences amounted to in RCT arm (56,5%), PMTA (55,7%), PCEM (56,7%) which decreased after 24 hours (13, 1%, 10,6% and 12,9%). It should be noted that the time span of all endodontic therapies was statistically different. Patients with preoperative pain of greater intensity, symptomatic apical periodontitis or widening of periodontal ligament experienced more pain. Overall, the effectiveness of pain relief was comparable in all three groups [85]. In 2022, Asgary et al. investigated the outcome of PMTA and PCEM compared to RCT in mature permanent teeth with carious pulp exposure with and without signs of irreversible pulpitis, concluding no significant difference in high success rates, which makes pulpotomy an advantageous alternative to RCT [86].

Taha et al. (2023) investigated outcome, quality of life and patient's satisfaction following full pulpotomy and RCT in irreversible pulpitis. The success rate of both groups was comparable (93%). However, mean age was significantly different among groups, thus might have influenced results, although no association between age and success rate were found in available literature [61]. Levels of pain were significantly lower in the pulpotomy group (3,03) than in the RCT group (4,90). A significantly lower number of patients had to take analgesics after pulpotomy (20%) than after RCT (46,7%). Pulpotomy entails pain relief in a shorter period of time, which is related to a reduction in local tissue pressure and concentrations of inflammatory mediators and severance of nociceptive sensory neurons [76]. This is in concurrence with the findings of Galani et al. (2017), who demonstrated pain relief in a shorter time after pulpotomy compared to RCT [84]. On the other hand, pain following RCT may originate from instrumentation leading to acute periapical inflammatory response resulting from injury to tissues of mechanical, chemical or microbial origin. Inflammation may occur due to extrusion of dentinal debris, pulp tissue, microorganisms and irrigants to periapical tissues. No significant differences in patients' quality of life between both groups was found. Patients were more satisfied with pulpotomy than RCT regarding intraoperative pain, pleasantness, and cost. Based on the patient- and clinician-centered outcomes pulpotomy can be used alternatively to treat mature teeth with carious pulp exposure and clinical symptoms indicative of irreversible pulpitis [76].

4. Summary and outlook

A shift in management preferences in endodontics from an invasive to a conservative approach was achieved by the emergence of hydraulic calcium silicate-based cements and an understanding of the pulp's healing capabilities, thus broadening indications for vital pulp therapy. Avoidance of root canal treatment is highly important due to its negative aspects, including alteration of hard dental tissue composition and physical features, physico-chemical properties of dentin, biomechanics, and resistance to fracture. It is essential to maintain tooth structure to ensure biomechanical properties and fracture resistance of the tooth, taking an increased rate of mechanical failure following endodontic treatment into account.

Selection of treatment of pulpal diseases relies on accurate diagnosis which is difficult to obtain using available pulp sensibility and vitality testing methods. The most reliable way of determining the inflammatory status of the pulp is an assessment of pulpal haemorrhage. In addition, a new classification was proposed by Wolters (2017) to prevent overtreatment in teeth with irreversible pulpitis, which might have reparative potential after excision of inflamed tissues [21].

Methods of vital pulp therapy comprise indirect and direct pulp capping, as well as partial and full pulpotomy. Indirect pulp capping has several variations which share the same goal of caries excavation up to the greatest extent without pulp exposure. An enhanced treatment protocol of direct pulp capping is recommended for exposed pulps due to carious lesions and yielded a more favourable outcome than traditional direct pulp capping. Pulpotomy, both partial and coronal, entails benefits compared to root canal treatment, which includes maintaining tooth vitality, intra-radicular tooth structure, neurosensory performance, proprioceptive characteristics, cost-effectiveness in comparison with root canal treatment, minimally invasive and less-technique sensitive approach.

Hydraulic calcium silicate-based cements are the most promising pulp capping materials due to their composition and positive characteristics, such as early odontoblastic differentiation, pulp protection, biological activity, biocompatibility, and release of dentin matrix proteins.

The outcome of vital pulp therapy techniques is influenced by various patient, intra- and postoperative factors. However, many prognostic factors belonging to these three groups require further investigations targeted towards their association with the clinical outcome of vital pulp therapy.

Included studies presented higher or comparable success rates of vital pulp therapy compared to root canal treatment, suggesting it as an advantageous alternative.

In clinical practice, dentists are confronted with various cases and the choice of their appropriate therapy. It is of utmost importance to primarily employ vital pulp therapy. However, insusceptibility of the pulp implies root canal treatment which is inevitable to save the tooth.

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