SCIENTIFIC FOUNDATIONS AND CLINICAL DIRECTIONS IN DENTISTRY: REMINERALIZATION, RADIATION AND RESTORATION

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PREFACE

Advancements in dental science and technology continue to reshape clinical practices and treatment protocols. This book aims to provide an up-to-date and evidence-based resource for both students and clinicians by addressing three critical areas in contemporary dentistry.

The first chapter explores remineralization agents, emphasizing their mechanisms of action, clinical applications, and current findings in the scientific literature. The second chapter focuses on the role of radiation in dental procedures, detailing its biological effects and presenting methods of protection to minimize exposure risks. The third chapter discusses material selection and adhesive cementation in indirect restorations, highlighting the importance of appropriate protocols in achieving long-term clinical success.

Each chapter has been prepared with attention to both academic rigor and practical relevance, aiming to support informed decision-making in clinical settings. It is our hope that this work will contribute meaningfully to the ongoing development of dental science and practice.

16.06.2025

Assoc. Prof. Dr. Nazan KOÇAK TOPBAŞ

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CHAPTER 1

REMINERALIZATION AGENTS

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INTRODUCTION

The pathophysiology of dental caries is characterised not only by cumulative loss of minerals from the tooth, but also by successive cycles of demineralisation and remineralisation. Progression or reversal of the lesion is achieved by a balance between pathological factors that promote demineralisation and factors that promote remineralisation. Remineralisation is a state in which calcium $(Ca)^{+2}$, phosphate $(PO)_4^{(-3)}$ ıons in plaque and saliva accumulate in the crystalline spaces of demineralised tooth structure, resulting in mineral gain. Free fluoride $(F)^{(-)}$ ıons allow $(Ca)^{+2}$ and $(PO)_4^{-3}$ to be incorporated into the crystal structure, resulting in the formation of fluorapatite mineral, making the enamel significantly more resistant to the acid threat.[1]

Dental caries, which occurs as a result of localised dissolution of dental hard tissues, is one of the chronic diseases seen in the society.[2] Demineralisation begins when the pH on the hard tissues of the teeth falls below the critical level. In this process, acids produced by plaque bacteria are neutralised by buffering with saliva and the pH increases. With the plaque pH level exceeding the critical pH, minerals begin to precipitate, thus remineralisation occurs.[3] The cavities formed as a result of mineral dissolution during the demineralisation process are filled with minerals during the remineralisation process, thus compensating for the lost minerals. As a result, the permeability of the enamel decreases and it becomes more resistant to acid attacks.[4, 5] To date, thanks to the understanding of the conditions affecting demineralisation and remineralisation in dental hard tissues, many applications and materials have emerged, especially within the scope of preventive dentistry. The aim of these preventive applications is basically to prevent demineralisation and to provide remineralisation in existing demineralised/hypomineralised areas.

Although fluoride applications have been accepted as the gold standard for the prevention of demineralisation and remineralisation until today, the use of different agents has become increasingly widespread, especially in recent years, as the effects of calcium and phosphate-containing agents have become more understood.

Initial Enamel Lesions

In initial enamel caries, it is possible to stop and treat the carious lesion. Initial caries lesions are limited to enamel. These lesions are also called "white spot" or "white spot lesions". Caries occurring on the smooth enamel surface first manifests itself as white spot lesions. These white spots can only be seen when the tooth surface is dried. These opaque surfaces are chalky white in colour and this colour is caused by the loss of translucency due to the expansion of the porosity of the subsurface area as a result of demineralisation. However, these areas need to be differentiated from hypocalcified areas. In the differential diagnosis of these lesions, drying of the lesion with air spray, visual and probe examination are important. Opaque lesions appear translucent when the surface is moist, while opaque white colour is observed when dried with air spray. Hypocalcified defects, on the other hand, are not affected by whether the environment is moist or dry and are opaque white in colour when the surface is moist. Although the surface of both lesions is non-cavitated, the surface of the initial caries lesions is softer and porous. Dental plaque accumulation is usually visible on the surfaces of the initial caries lesions, whereas no plaque accumulation is observed on the surfaces of hypocalcified defects.

DEMINERALISING AND REMINERALISING AGENTS

According to the production method or the type of active ingredient, it is possible to classify demineralisation inhibitors and remineralisation agents in 5 main groups:

1- Mineral and ion technologies
2- Sugar alcohols
3- Products of vegetable origin
4- Bioactive materials and nanotechnological products
5- Other calcium and phosphate derived products

1. Mineral and Ion Technologies

A) Fluorine Ion

Fluorine, which is the most widely used material to prevent dental caries today, shows its caries preventive effect on tooth enamel in many ways that prevent demineralisation and increase remineralisation. Prevention of pellicle and plaque formation, formation of fluorohydroxyapatite and bactericidal properties explain the caries preventive and remineralising effect of fluorine.[6, 7] Fluorine is very common in tea, tobacco and fish.[8] Fluorine can be applied systemically or topically. Topical fluorine applications can be made with varnishes, gels, solutions, pastes, mouthwashes and fluorine release devices. Today, it is accepted that topically applied fluorine preparations are more effective.[7] Therefore, the presence of fluorine ions in saliva and dental plaque is necessary for the prevention of demineralisation and remineralisation. With the proof of the caries preventive effect of fluorine, detailed studies have been carried out on fluorine alone or many products combined with fluorine. Nalbantgil et al.[9] evaluated the effect of NaF-containing fluorine varnishes around orthodontic brackets and found that the varnishes are very effective materials in both protection from demineralisation and reversal of demineralisation. Alsaffar et al.[10] , in their study evaluating the changes caused by fluorine-containing fissure sealants and conventional fluorine-free fissure sealants on the adjacent enamel tissue, reported that fluorine-containing fissure sealants were significantly successful in preventing demineralisation. Rodriques et al.[11] evaluated the effects of fluorine-releasing glass ionomers on demineralised tooth hard tissues and reported that high fluorine-releasing restorative materials gave more successful results in remineralisation. In another study, Chu et al.[12] examined the effects of sodium fluoride and silver diamine fluoride gels applied regularly for 12 months to the anterior teeth of children aged 5-7 years with initial caries lesions and concluded that demineralisation was significantly inhibited and remineralisation was achieved at the end of 12 months. Calvo et al.[13] stated that topical application of 1.23% acidul phosphate gel to the demineralised tooth surface is a highly effective method in reversing demineralisation. When the results of the studies are reviewed, fluorine and fluorine compounds are considered as useful materials that are widely preferred in caries prevention programmes due to inhibition of demineralisation, remineralisation, antibacterial effect and easy accessibility. They stated that it is a highly effective method in reversing demineralisation.

B) Silver Ion

Silver ion, which is used as an anti-caries agent, cavity disinfectant and desensitiser in permanent teeth, has been used since 1840s.[14] Silver ion, when used in different compounds, reduces the solubility of tooth structures in acidic environments and helps remineralisation. Silver ion has been the subject of studies because it provides remineralisation of demineralised tissues.[14-16] Zhi et al.[15] evaluated the effects of topical application of silver and fluorine ions on demineralised tooth surfaces and reported that both ions provided mineral deposition on the surface, but when applied together, they had no significant effect on remineralisation. Mei et al.[16] reported that 38% silver diamine fluoride solution prevents demineralisation and has bactericidal properties. In studies evaluating the antibacterial activity of silver ion-containing primers, it was reported that silver content contributed to antibacterial properties compared to silver ion-free control groups.[17, 18] These studies have shown that silver ion is preferable among caries prevention and remineralisation materials due to its positive properties such as antibacterial, prevention of demineralisation and remineralisation. However, its ability to cause discolouration on teeth stands out as a factor limiting its use.

C) Iron Ion

Iron ion is known to have caries preventive effect when used alone or in combination with ions such as fluorine. It provides this effect by reducing enamel solubility in acidic environments, showing bactericidal and bacteriostatic effect on cariogenic Streptococcus mutans and reducing the glycosyltransferase enzyme activity of these bacteria. On the other hand, iron ion, which has caries preventive and demineralisation reducing activity, has no remineralising property.[19]

In addition, undesirable effects such as toxicity, discolouration and taste disorders may be observed. There are studies on the caries preventive properties of iron added to foods for the treatment of iron deficiency anaemia alone or in combination with ions such as fluorine and copper. Pecharki et al. reported the inhibitory activity of iron ion in demineralisation caused by sucrose and that this effect was mediated by suppression of oral streptococcus formation.[20] In addition, some studies have shown that treatment of the tooth surface with ferric sulphate inhibits the glycosyltransferase enzyme of bacteria and reduces the loss of minerals from the surface.[21, 22] Alves et al.

reported that solutions containing 18 mg Fe/ml were the most successful concentration in preventing demineralisation [19].

2. Sugar Alcohols

A) Xylitol

Xylitol, which is a 5-carbon sugar alcohol, obtained from various cellulose products and cannot be metabolised by bacteria in the oral flora; It has been included in products such as toothpaste, medicine, gel or chewing gum. In many studies, it has been observed to reduce salivary S.Mutans levels. It is known to increase saliva flow rate and saliva buffering capacity. The hydroxyl ions in the structure of xylitol bind with Ca and P in the salivary fluid, thus ensuring that the Ca level in saliva and oral environment remains at a certain level. The fact that it cannot be fermented by bacteria suppresses the acid production of acid-forming microorganisms and thus prevents the pH value of the oral environment from decreasing.[23] Xylitol reduces the amount of extracellular polysaccharide and prevents acidogenic bacteria from adhering to the tooth surface.[24] There are many studies on the remineralisation capacity and caries preventive effect of xylitol. In one study, higher remineralisation was observed in the middle and deep layers of enamel samples immersed in 20% xylitol solution compared to the control group. [25] Studies show that the frequency of xylitol use is more important than the amount of use in preventing dental caries. [26] It has been observed in studies that it has a caries preventive effect by reducing the transmission of mutans streptococci from mother to child. [27] In the 6-year clinical follow-up study of Söderling et al., when the oral flora of the children of mothers chewing xylitol chewing gum was examined, a significant decrease was observed in mutans streptococci colonisation and caries prevalence at the end of the 5-year observation period. The results of the study showed that xylitol inhibited bacterial transfer and colonisation.[27] In the light of these studies, xylitol is a proven material that has taken its place in many products today as an anticaries agent due to its antibacterial activity, positive effects on saliva buffering capacity and its usability in many products.

B) Isomalt

Isomalt, which is widely used in confectionery, is thought to increase remineralisation with its calcium binding property.[28] Takatsuka et al. evaluated the effects of isomalt-containing toothpaste and mouth rinse solutions on enamel remineralisation and demineralisation in-situ and in-vitro and reported that isomalt had a positive effect on the remineralisation process and was more effective when used with fluorine. Therefore, they suggested that isomalt can be used in fluorine-containing products.[29] Recent studies have shown that the concentration of isomalt required for minimum biofilm eradication is higher than xylitol. This means that the amount of isomalt required for biofilm removal is higher than xylitol, which indicates that it is a more unsuccessful product than xylitol.[28]

C) Sorbitol

Sorbitol, a non-cariogenic sugar, can be fermented by mutans streptococci. [30] It is a type of sweetener used in many products. Studies show that sorbitol is a caries preventive agent, but this effect is less than xylitol.[31] Gonçalves et al. observed that mouth rinsing agents using fluoride, xylitol and sorbitol together reduced demineralisation, but did not find a significant difference between the efficacy of agents using fluoride alone or fluoride, xylitol and sorbitol together.[31] Splieth et al. also showed that xylitol decreased plaque pH significantly more than sorbitol in their study in which they examined the effect of xylitol and sorbitol.[32] In the light of these studies, it is seen that sorbitol can be used as a caries preventive material, but this effect is less compared to xylitol.

3. Products of Vegetable Origin

A) Chitosan

Chitosan is an amino polysaccharide with antibacterial and antifungal effects. It has bacteriostatic and bactericidal properties and can buffer the effects of organic acids that lower the pH values in the oral cavity.[33] It is obtained by deacetylation of chitin. In recent years, it has been stated that its use with amelogenin is also a good alternative.[34] Studies have proved that chewing gum with chitosan inhibits the growth of cariogenic bacteria in the oral flora and even shows bactericidal and bacteriostatic effect on these bacteria. In addition to stimulating salivary flow, it was also found to reduce enamel decalcification. [35-38] Fujiwara et al. examined the effects of solutions containing different concentrations of chitosan and showed that 2% chitosan solution provided the most ideal inhibition on mutans streptococci. [39] When the results obtained from these studies were evaluated, it was seen that chitosan was effective in preventing demineralisation, while there was insufficient data on remineralisation. Bactericidal and bacteriostatic effect of chitosan has been shown in many studies. Therefore, it is recommended to be used as an antibacterial caries preventive agent.

B) Galla Chinensis

Galla Chinensis, which is a traditional Chinese herb and defines the extract obtained from this plant; It exhibits antibacterial, antiviral, antioxidant, hepato-protective, antidiabetic, antithrombin, anti-inflammatory and antitumour activity and also shows detoxification properties when combined with various metallic ions, non-alcoholic substances or glycosides.[40] Various researches have been conducted on its use in dentistry. Galla Chinensis has been shown to have an inhibitory effect on S.mutans growth, glucan synthesis and aggregation and can be used as an anticariogenic agent.[40] In their study, Zou et al. showed that G. chinensis extract has the potential to inhibit demineralisation under dynamic pH cycling conditions.[41] Cheng et al. reported that gallic acid contained in G. chinensis extract provided remineralisation in artificial early enamel caries.[42] Chu et al. evaluated the effects of G. chinensis on early caries and reported that it inhibited demineralisation and increased remineralisation of enamel.[43] Xie et al. emphasised that G. Chinensis, unlike the remineralisation effect caused by fluorine, slows down the remineralisation of the outermost surface of the lesion and thus allows ion transport to the lesion body. Therefore, G. Chinensis has different remineralisation effect than fluorine.[44] These studies show that G. Chinensis can be used both as an anti-caries agent and as a remineralisation agent. In addition, its mechanism, which is different from the remineralisation mechanism of fluorine, suggests that it can be used as a successful material for the remineralisation of subsurface lesions.

C) Grape Seed Extract (Polyphenols)

Proanthocyanide, one of the polyphenols, is obtained in large amounts from grape seed extract. Proanthocyanide has the effect of inhibiting amylase and glycosyl transferase enzymes. Inhibition of the glycosyl transferase enzyme means that mutans streptococci cannot synthesise glucan and thus cannot attach to the tooth surface and accumulate, which is the caries inhibiting property of proanthocyanide.[45] It has anti-inflammatory and antioxidant properties. The study of Mirkarimi et al. on the effects of grape seed extract applied to demineralised deciduous teeth shows that grape seed extract significantly increased the microhardness of the enamel. Jawale et al. investigated the remineralising effect of grape seed extract, CPP-ACP and calcium glycerophosphate on experimental root caries and found that grape seed extract significantly increased the mineral content compared to the other two products.[46] Tang et al. reported that the optimum concentration of grape seed extract for remineralisation of demineralised dentin surface was 15%.[47] Grape seed extract has been proven to provide mineral accumulation and support remineralisation in various studies.[48]

D) Theobromine

It is a white crystalline powder, insoluble in water, obtained from Theobroma cacao tree, containing theophylline and caffeine-like compounds. It is also present in foods such as chocolate and tea. It increases the hardness of tooth enamel.[49] Amaechi et al. found that theobromine has a remineralisation-enhancing effect thanks to its ability to provide apatite formation and concluded that this effect is comparable to fluorine.[50] Kargül et al. observed that theobromine was effective in protecting the enamel surface.[51] Studies show that theobromine has remineralising and demineralising effects. It seems that it can be used for remineralisation of dental hard tissues. Although theobromine, which is widely used in toothpastes worldwide, is a nontoxic compound recommended as an alternative to fluoride, more studies are needed to evaluate its effectiveness. Although not many studies have been conducted on its effects on dental tissues, studies have proved its remineralising and demineralising efficacy.

4. Bioactive Materials and Nanotechnological Products

A) Calcium Sodium Phosphosilicate (Novamin/Bioactive Glass)

Bioactive glasses, which release sodium, phosphorus and calcium by rapidly releasing ions by rapidly releasing the nano-sized particles it contains as a result of contact with saliva, have started to find an area of use in dentistry due to their biocompatible materials. As a result of its ion release, it forms a hydroxycarbon apatite structure similar to the hydroxyapatite structure in the enamel. Bioactive glasses are used in dentistry in many areas such as removal of dentin sensitivity, vital treatments, bone regeneration, remineralisation of dental hard tissues, antibacterial treatments.[52] Particle sizes of bioactive glasses are at nano levels. Due to this feature, it can release ions faster and its bioactive properties are more pronounced. In a study comparing a commercial toothpaste containing fluorine with a fluorine and calcium sodium phosphosilicate product, it was concluded that the calcium sodium phosphosilicate tooth cleaning agent provided a higher degree of remineralisation in early caries lesions.[53] In the study of Diamanti et al. in which fluoride and bioactive glasses were compared, it was stated that bioactive glasses may be an alternative remineralisation agent group to fluoride.[54] When the microbial effects were examined, it was observed that Novamin had antimicrobial effects on oral streptococci and helped to increase oral pH.[55] In a study by Job et al., the effects of toothpastes containing Novamin and toothpastes containing CPP-ACP and NaF were compared, and it was reported that Novamin-containing toothpastes provided more remineralisation. [56] In the study of Jagga et al., the remineralisation effect of Novamine and tricalcium phosphate on experimental caries was examined and it was shown that Novamine caused significantly more remineralisation.[57] In a study evaluating the efficacy of different pastes in the treatment of demineralised areas around orthodontic brackets, it was reported that Novamine-containing toothpastes had more remineralisation potential than fluoride and probiotic-containing pastes.[58] These studies have shown that calcium sodium phosphosilicate is a caries preventive agent and remineralisation agent that can be used as an alternative to fluoride.

B) Tricalcium Silicate

Tricalcium silicate, which is the subject of studies on the prevention of demineralisation and remineralisation due to its apatite formation feature on hard tissues, is a bioactive material. It shows mineral precipitation, high bioactivity and remineralising effect on the enamel surface. In a study examining the effects of 2 different products containing 1000 ppm F and tricalcium silicate on demineralisation, it was stated that tricalcium silicate is an effective agent in preventing demineralisation and providing remineralisation because it shows similar effects to fluoride.[59] In another study by Dong et al., it was shown that tricalcium silicate stimulates apatite formation by providing calcium-phosphate precipitation on the enamel surface and that this agent is a product that can be used in the protection and renewal of enamel. The same study states that the product is also effective in the elimination of dentin sensitivity.[60] Today, tricalcium silicate, which is also included in the structure of products used in regenerative endodontics in dentistry, is a highly biocompatible material that can be used with its effect of supporting remineralisation by creating apatite formation on the enamel surface.

C) Nanohydroxyapatite

Hydroxyapatite, a calcium phosphate compound, has the molecular formula $Ca_{10}(PO_4)_6(OH)_2$. It reaches a certain level of activity with particles between 1 and 100 nm in size. Although enamel tissue shows a complex structure, it is mainly composed of hydroxyapatite crystals of 20-40 nm in size. These crystals are called nanoparticles. The first artificially produced materials for enamel development are microhydroxyapatite. However, since these are less soluble, nanohydroxyapatites were developed in order to increase the rate of Ca and P ions released by increasing this solubility . Today, it is included in toothpastes. In a study comparing the remineralising efficacy of toothpastes containing nano-HAP and amine fluoride, nano-HAP was shown to provide a higher level of remineralisation than amine fluoride.[61] Nano-hydroxyapatite is a biocompatible material that has multiple uses due to its similarity to inorganic bone structure; it is a calcium phosphate compound used in implantology, surgery, periodontology, aesthetic and preventive dentistry. In aesthetic and preventive dentistry, it is used in the treatment of dentine sensitivity, remineralisation and as a bleaching auxiliary agent. It is the most studied biomaterial in medicine. In the study of Haghgoo et al. comparing the remineralisation effects of Novamin and nano-HAP, it was observed that both products provided remineralisation in deciduous teeth with no significant difference between them.[62] The study by Daas et al. shows that nano-HAP-containing pastes have a long-term protective effect in terms of superficial mineral deposits in initial enamel lesions and a smoother surface is obtained compared to fluoride varnishes.[63] According to the results of the study by Reis et al., nano-HAP is a product that prevents demineralisation and provides remineralisation.[64] Today, nano-hydroxyapatites have been incorporated into oral care products to reduce or eliminate tooth sensitivity or to increase the remineralisation of enamel by blocking open dentinal tubules.

D) Casein Phosphopeptide Amorphous Calcium Phosphate (CPP-ACP):

CPP-ACP containing 18% calcium and 30% phosphate by weight was first used as a remineralisation agent in 1998. Casein, a 30-300 nm wide, particulate protein that constitutes 78% of the proteins contained in cow's milk, is found in foods such as milk, yoghurt and cheese.[65] Casein protein has $\alpha s1$, $\alpha s2$ and β subtypes. [66] It has a significant ability to stabilise ACP. It binds ACP in small clusters by means of phosphoseryl extensions and prevents them from reaching the size required for their precipitation into the solution and thus the CPP-ACP complex is formed.[67] CCP-ACP exerts its caries preventive effect by preventing bacterial colonisation, increasing the Ca and P levels of dental plaque and binding free Ca and P.[68, 69] Today, CCP-ACP is used in products such as solution, sugar-free chewing gum, mouthwash and toothpaste. In a study evaluating mouth rinses containing CPP-ACP, it provided a high rate of remineralisation in initial caries lesions.[69] There are three mechanisms of the caries inhibitory effect of the CPP-ACP complex. Firstly, as the desired and ideal mechanism for the prevention of demineralisation, the complex penetrates into the dental plaque and increases the calcium and phosphate levels of the plaque. In subsurface lesions, demineralisation is prevented and remineralisation is achieved by high calcium and phosphate concentrations.[70] It has been found to increase the Ca-P level in plaque up to 5 times. Secondly, the complex deposited on the tooth surface binds the free calcium and phosphate in the plaque and saturates the tooth surface.[71] The peptides in CPP-ACP bind to the tooth surface and allow minerals to precipitate, thus blocking the tubules.[72] CPP-ACP acts by preventing demineralisation and remineralisation of initial caries and this effect is due to the ability of CPP to stabilise Ca and P on the tooth surface. Ca and P ions in the CPP-ACP agent precipitate to the surface after application and cause an increase in microhardness.[73] Finally, the CPP-ACP complex is known to prevent the accumulation of mutans streptococci on the tooth by binding to the cell surfaces.[66] The inverse relationship between plaque Ca and P levels and caries formation indicates that this mechanism of CPP-ACP is an ideal mechanism to prevent demineralisation.[68] Casein phosphopeptide also has the ability to reduce the number of S.mutans by integrating into the pellicle.[70] CPP-ACP has been shown to have anticariogenic potential.[74] Zhou et al. 500 ppm NaF and CPP-ACP showed that CPP-ACP provided more remineralisation.[75] Reynolds et al. reported that chewing gums containing CPP-ACP were highly effective in the remineralisation of initial caries by finding CPP-ACP in the plaque even 3 hours after chewing gum use.[76] In a systematic review evaluating the effect of CPP-ACP containing products on white spot lesions around orthodontic brackets, it was emphasised that CPP-ACP is a highly effective remineralisation agent in these cases.[77] Job et al. compared the effects of toothpastes with 3 different ingredients on the enamel surface and observed that toothpaste containing CPP-ACP caused more phosphate ion accumulation on the enamel surface than toothpastes containing Novamin and NaF.[56] In parallel with the results of these studies, Rai et al. demonstrated that daily drinks containing CPP-ACP have remineralising effects on deciduous and permanent dentition.[78] It is also known that CPP-ACP prevents dental erosion, is used in whitening treatments and is incorporated into various glass ionomer-containing base and restoration materials to prevent caries and remineralise, in addition to providing healthy protection of enamel, preventing demineralisation and increasing remineralisation and inhibiting bacterial adhesion.[66, 79]

E) Casein Phosphopeptide Amorphous Calcium Fluoride Phosphate (CPP-ACFP):

Studies on CPP-ACP show that the best and maximum effect of the product is seen when used in combination with fluoride. On the other hand, in addition to the remineralisation effect of fluoride, which has been known for years, it is also stated that CPP-ACP alone has sufficient remineralisation capacity. Since studies suggest that the use of CPP-ACP in combination with fluoride will produce a higher remineralisation effect, Reynolds used 1% CPP solution with a pH of 7 in combination with a solution containing 500 ppm F in his study and showed that about half of the fluoride was bound with CPP-ACP. With the incorporation of fluoride into its structure, it has a higher remineralisation capacity than CPP-ACP.[80] It can release calcium, phosphate and fluoride and maintain the saturation of the tooth surface. Thus, it can suppress demineralisation and increase remineralisation.[81] In initial enamel lesions, CPP-ACFP application for 4 min daily for 4 weeks has been shown to play an effective role in remineralisation by significantly reducing laser fluorescence measurement values.[82] Llena et al. evaluated CPP-ACP, CPP-ACFP and fluoride varnishes on early caries lesions and showed that CPP-ACFP provided significantly more remineralisation at the end of 4 weeks.[83] It is known that the synergistic effect of CPP-ACP and fluoride will create more remineralisation when used as CPP-ACFP rather than when used separately. For this reason, studies on CPP-ACFP have gained momentum and the use of products with this content has become widespread.

F) Tricalcium Phosphate

There are two forms of tricalcium phosphate, alpha and beta, with the chemical formula Ca_3PO_4. Beta form is less soluble and therefore alpha form is widely preferred in studies since it has more solubility. Alpha tricalcium phosphate is thought to provide remineralisation by increasing free Ca and P levels.[84, 85] Jagga et al. investigated the efficacy of Novamin and TCP on experimental caries and showed that both products were successful in remineralisation.[57] In a systematic review, TCP was reported to have remineralising efficacy, but ACP and TCP were less effective than remineralising agents containing CPP-ACP.[86] Vogel et al. reported that chewing gums with 2.5% alpha tricalcium phosphate produced a small increase in Ca and P levels in plaque fluid and saliva.[87] More information and studies are needed for the use of tricalcium phosphate as a remineralisation agent.

G) Self-assembling Peptides

Anionic peptides are used in remineralisation studies. Unlike traditional remineralisation agents, they form a skeleton that allows ions to precipitate in the tooth and mineral deposition is achieved through this skeleton.[88] Alkilzy et al, Alkilzy et al. stated that the use of self-assembling peptides such as p11-4 in combination with fluoride may be preferred more in enamel remineralisation in the future as a low-cost, easy-to-apply and protective approach.[89] In a study on p11-4, it was stated that this peptide may be preferred in subsurface enamel remineralisation, especially because it forms an enamel close to the natural structure.[90] Other studies show that p11-4 peptide may be an effective remineralisation agent in early enamel lesions and initial interface caries.[91, 92] In the study of Üstün and Aktören evaluating the effect of p11-4 peptide, CPP-ACFP and NaF on enamel remineralisation, the highest remineralisation ability was found in p11-4 self-assembling peptide. The reduction in lesion depth was found to be statistically significantly greater in the p11-4 and CPP-ACFP groups than in the NaF and control groups.[93] Self-associating peptides used for biomimetic remineralisation in dentistry are also used in other medical fields. In a study conducted in our country, it was stated that they have a high regenerative capacity when used as tissue scaffolds in the regeneration of tissues or organs. In the treatment of initial caries lesions, the use of p11-4 self-associating peptide and fluoride together is quite simple and effective in terms of remineralisation. [89] On the other hand, more research is needed for the widespread use of this agent.

5. Other Calcium and Phosphate Source Products

A) Dicalcium Phosphate Dihydrate (DCPD)

Dicalcium phosphate dihydrate (DCPD) is used in fluoride-containing toothpastes to increase the remineralisation property of the fluorine component. In the in-vivo results of Sullivan et al. to evaluate the effects of the use of toothpaste containing DCPD on the Ca level in the oral environment and Ca activity in the plaque fluid, it was stated that toothpastes with DCPD release Ca ions into the oral environment and that this Ca released can provide remineralisation for the initial lesions that have started to form in the enamel. When the effect on plaque fluid was evaluated, it was reported that it increased the ratio of free calcium and phosphate in plaque fluid. This study shows that the addition of Ca and P in the form of DCPD to toothpastes has a caries preventive effect.[94] In the combined use of DCPD and fluorine in toothpaste, it was observed that there was a positive interaction between fluorine and DCPD and fluorapatite formation developed more with combined use, while remineralisation was faster.[95] There are studies suggesting that fluorapatite formation and therefore remineralisation occurs faster when included in fluoride-containing pastes. It has been reported that the caries preventive effect of toothpastes containing DCPD together with NaF is more effective than the separate use of both.[96] Studies show that the synergistic effect of DCPD with fluoride has a positive effect on remineralisation. For this reason, it is a material that can be used as an additive in toothpastes containing fluoride.

B) Calcium Phosphoryl Oligosaccharides

The Ca contained in calcium phosphoryl oligosaccharides (POs-Ca) formed by enzymatic hydrolysis of potato starch can be used as an additive in various products since it is available. Therefore, it is used as an in sugar-free chewing gums. Tanaka et al. investigated the concentration of POs-Ca that provides the optimal Ca/P ratio required for the remineralisation of subsurface enamel lesions and concluded that POs-Ca of 1.67 in combination with hydroxyapatite provides optimal remineralisation.[97] In the study of To-o et al. on the effects of chewing gums containing POs-Ca on remineralisation, it was observed that these chewing gums increased the free Ca ratio in the oral environment and provided remineralisation in subsurface enamel lesions.[98] In a study conducted by Kitasako et al. , it was reported that chewing gums containing POs-Ca provided significant remineralisation in subsurface enamel lesions.[99] Despite all these findings, the number of studies on POs-Ca is quite low today. More research is needed for its widespread use.

C) Calcium Carbonate

Calcium carbonate ($CaCO_3$) is an alkaline and buffering agent with abrasive properties in toothpastes. Calcium carbonate toothpastes have very low solubility at neutral pH. Thus, the effect of $CaCO_3$ on the acidogenicity of dental plaque is limited, but according to Duke, its small particles are stored in dental plaque even hours after brushing with calcium carbonate toothpastes. In an acidic environment, the solubility of these stored particles increases and plays a role in reducing plaque cariogenicity and potentialising the effect of fluorine.[100] In another study comparing calcium carbonate toothpastes with silica-based toothpastes, it was reported that calcium carbonate toothpaste was more effective in preventing demineralisation and increasing remineralisation.[100] In a study by Cury et al. comparing CPP-ACP and CaCO3-containing pastes, it was shown that both pastes had a remineralising effect, but CPP-ACP-containing pastes had significantly more remineralising effect.[101] It shows that more studies should be done in order to compare with newly developed remineralisation agents.

D) Sodium Trimetaphosphate (sTMP):

The addition of phosphate salts to the toothpaste content has been used for many years to increase the effectiveness of fluoridated toothpastes. Sodium trimetaphosphate is one of the most preferred ions to increase the effectiveness of fluorine-containing toothpastes with the help of sodium and phosphate ions. Many studies show that the addition of sTMP prevents demineralisation.[102, 103] In the study of Danelon et al. comparing the effects of sTMP-added low fluorine-containing preparations on the remineralisation of initial enamel lesions with high fluorine-containing preparations, it was stated that the addition of sTMP made low fluorine-containing preparations as successful as high fluorine-containing preparations.[103] Gonçalves et al. stated that 1.5% STMP solution inhibits matrix metalloproteinases by acting antiproteolytic and thus provides dentin remineralisation.[104] As a result, sTMP stands out as an agent that prevents demineralisation and increases remineralisation.

E) Calcium Glycerophosphate

Calcium glycerophosphate (CaGP) is an organic phosphate and the calcium salt of glycerophosphoric acid. Although its mechanism of action is not fully understood, CaGP reduces the solubility of enamel and hydroxyapatite by direct contact with the outer layers of hydroxyapatite. CaGP is a source of calcium and phosphate. The fact that it has a pH buffering effect suggests that it has anti-cariogenic effects by reducing the amount of plaque. Although these events explain the efficacy of CaGP, there is no evidence that it provides remineralisation.[105] In general, it is known that fluoride-containing agents, when in contact with tooth enamel, form a calcium fluoride-like layer that acts as a reservoir of calcium and fluoride. During acid attacks by cariogenic bacteria, calcium and fluorine ions released from this layer play a protective role by increasing the tooth's resistance to these attacks.[106] Agents containing calcium glycerophosphate have also been proven to increase the resistance of hydroxyapatite. It is thought that their use in combination with fluoride has a cumulative effect and increases the caries preventive efficacy even more.[107] Carvalho et al. In a study comparing fluoride varnishes with and without CaGP, it was reported that experimental fluoride varnishes containing CaGP released more fluorine, but did not increase the preventive effect on enamel demineralisation.[108] In a study by Rezende et al. in which the effects of agents containing different levels of fluoride and additionally containing and not containing CaGP in preventing mineralisation and providing remineralisation of deciduous teeth were examined, it was shown that the presence of CaGP was effective in preventing demineralisation and providing remineralisation at a significant level, although no significant difference was found between the effects of different fluoride concentrations on demineralisation. In the same study, it was reported that 500 ppm F content with 0.13% CaGP was the most effective combination in preventing enamel demineralisation. [109] Sezer et . evaluated a remineralisation gel containing CaGP and xylitol applied to incisors with bicuspid-incisor hypomineralisation and reported that this product provided remineralisation in incisors with this finding in a 3-month period. [110] Nowadays, it is thought that CaGP can be an effective agent in providing remineralisation by adding it into various products.

CONCLUSION

Remineralisation agents have an important place in preventive dentistry. Although fluoride applications are mostly used to prevent demineralisation of hard tissues and to remineralise existing demineralised areas, many new materials and methods have been developed today. In recent years, nanotechnology produced and bioactive remineralisation agents and caries prevention agents that are available for individual and professional use are promising for the future.

REFERENCES

1. Ustaoglu, S. and N. Akal, Current Approaches in Remineralisation Agents. Selcuk Dental Journal, 2023. 10(1).
2. Sicca, C., et al., *Prevention of dental caries: A review of effective treatments.* Journal of clinical and experimental dentistry, 2016. **8**(5): p. e604.
3. Vieira, A.E.d.M., et al., *In vitro effect of amorphous calcium phosphate paste applied for extended periods of time on enamel remineralisation.* Journal of Applied Oral Science, 2017.**25** (6): p. 596-603.
4. Hemagaran, G. and P. Neelakantan, *Remineralisation of the tooth structure-the future of dentistry.* International Journal of PharmTech Research, 2014.
5. Abou Neel, E.A., et al., *Demineralisation-remineralisation dynamics in teeth and bone.* International journal of nanomedicine, 2016: p. 4743-4763.
6. Moi, G.P., L.M.A. Tenuta, and J.A. Cury, *Anticaries potential of a fluoride mouthrinse evaluated in vitro by validated protocols.* Brazilian dental journal, 2008.**19** : p. 91-96.
7. Groeneveld, A., A. Van Eck, and O.B. Dirks, *Fluoride in caries prevention: is the effect pre- or post-eruptive?* Journal of dental research, 1990.**69** (2_suppl): p. 751-755.
8. Everett, E., *Fluoride's effects on the formation of teeth and bones, and the influence of genetics.* Journal of dental research, 2011. **90**(5): p. 552-560.
9. Nalbantgil, D., et al., *Prevention of demineralisation around orthodontic brackets using two different fluoride varnishes.* European journal of dentistry, 2013. **7**(01): p. 041-047.
10. Alsaffar, A., et al., *Protective effect of pit and fissure sealants on demineralisation of adjacent enamel.* Paediatric dentistry, 2011. **33**(7): p. 491-495.
11. Rodrigues, E., et al., *Enamel remineralisation by fluoride-releasing materials: proposal of a pH-cycling model.* Brazilian dental journal, 2010.**21** : p. 446-451.
12. Chu, C. and E.C. Lo, *Microhardness of dentine in primary teeth after topical fluoride applications.* Journal of Dentistry, 2008.**36** (6): p. 387-391.

13. Calvo, A., et al., *Effect of acidulated phosphate fluoride gel application time on enamel demineralisation of deciduous and permanent teeth.* Caries Research, 2012.**46** (1): p. 31-37.
14. Peng, J.-Y., M. Botelho, and J. Matinlinna, *Silver compounds used in dentistry for caries management: a review.* Journal of dentistry, 2012.**40** (7): p. 531-541.
15. Zhi, Q., E. Lo, and A. Kwok, *An in vitro study of silver and fluoride ions on remineralisation of demineralised enamel and dentine.* Australian dental journal, 2013. **58**(1): p. 50-56.
16. Mei, M.L., et al., *Antibacterial effects of silver diamine fluoride on multi-species cariogenic biofilm on caries.* Annals of clinical microbiology and antimicrobials, 2013.**12** : p. 1-7.
17. Cheng, L., et al., *Effects of antibacterial primers with quaternary ammonium and nano-silver on Streptococcus mutans impregnated in human dentin blocks.* Dental Materials, 2013. **29**(4): p. 462-472.
18. Zhang, K., et al., *Dual antibacterial agents of nano-silver and 12-methacryloyloxydodecylpyridinium bromide in dental adhesive to inhibit caries.* Journal of Biomedical Materials Research Part B: Applied Biomaterials, 2013. **101**(6): p. 929-938.
19. Alves, K.M.R.P., et al., *Effect of iron on enamel demineralisation and remineralisation in vitro.* Archives of oral biology, 2011. **56**(11): p. 1192-1198.
20. Pecharki, G., et al., *Effect of sucrose containing iron (II) on dental biofilm and enamel demineralisation in situ.* Caries research, 2005. **39**(2): p. 123-129.
21. Devulapalle, K. and G. Mooser, *Glucosyltransferase inactivation reduces dental caries.* Journal of dental research, 2001.**80** (2): p. 466-469.
22. Martinhon, C.C.R., et al., *Effect of iron on bovine enamel and on the composition of the dental biofilm formed "in situ".* Archives of oral biology, 2006. **51**(6): p. 471-475.
23. Mäkinen, K., et al., *Similarity of the effects oferythritol and xylitol on somerisk factors of dental caries.* Caries Research, 2005. **39**(3): p. 207-215.
24. Balakrishnan, M., R.S. Simmonds, and J.R. Tagg, *Dental caries is a preventable infectious disease.* Australian dental journal, 2000.**45** (4): p. 235-245.

25. Miake, Y., et al., *Remineralisation effects of xylitol on demineralised enamel.* Journal of electron microscopy, 2003. **52**(5): p. 471-476.
26. Honkala, E., et al., *Field trial on caries prevention with xylitol candies among disabled school students.* Caries research, 2006. **40**(6): p. 508-513.
27. Soderling, E., et al., *Influence of maternal xylitol consumption on acquisition of mutans streptococci by infants.* Journal of Dental Research, 2000.**79** (3): p. 882-887.
28. Featherstone, J., B. Rodgers, and M. Smith, *Physicochemical requirements for rapid remineralisation of early carious lesions.* Caries research, 1981.**15** (3): p. 221-235.
29. Takatsuka, T., R.A. Exterkate, and J.M. ten Cate, *Effects of Isomalt on enamel de-and remineralisation, a combined in vitro pH-cycling model and in situ study.* Clinical Oral Investigations, 2008.**12** : p. 173-177.
30. Birkhed, D., et al., *Cariogenicity of sorbitol.* Swedish dental journal, 1984.**8** (3): p. 147-154.
31. Gonçalves, N., et al., *Effect of xylitol: sorbitol on fluoride enamel demineralisation reduction in situ.* Journal of dentistry, 2006. **34**(9): p. 662-667.
32. Alkilzy, M., et al., *Effect of xylitol and sorbitol on plaque acidogenesis.* Quintessence Int, 2009.**40** : p. 279-285.
33. Shibasaki, K., et al., *Effects of low molecular chitosan on pH changes in human dental plaque.* The Bulletin of Tokyo Dental College, 1994.**35** (1): p. 33-39.
34. Mukherjee, K., et al., *Repairing human tooth enamel with leucine-rich amelogenin peptide-chitosan hydrogel.* Journal of Materials Research, 2016. **31**(5): p. 556-563.
35. Muzzarelli, R., et al., *Antimicrobial properties of N-carboxybutyl chitosan.* Antimicrobial agents and chemotherapy, 1990.**34** (10): p. 2019-2023.
36. Hayashi, Y., et al., *Chewing chitosan-containing gum effectively inhibits the growth of cariogenic bacteria.* Archives of oral biology, 2007.**52** (3): p. 290-294.
37. Arnaud, T.M.S., B. de Barros Neto, and F.B. Diniz, *Chitosan effect on dental enamel de-remineralisation: an in vitro evaluation.* Journal of dentistry, 2010.**38** (11): p. 848-852.

38. Uysal, T., et al., *Does a chitosan-containing dentifrice prevent demineralisation around orthodontic brackets?* The Angle Orthodontist, 2011. **81**(2): p. 319-325.
39. Fujiwara, M., Y. Hayashi, and N. Ohara, *Inhibitory effect of water-soluble chitosan on growth of Streptococcus mutans.* The new microbiologica, 2004.**27** (1): p. 83-86.
40. Zhang, T., J. Chu, and X. Zhou, *Anti-carious effects of Galla chinensis: A systematic review.* Phytotherapy Research, 2015. **29**(12): p. 1837-1842.
41. Zou, L., et al., *Effect of Galla chinensis extract and chemical fractions on demineralisation of bovine enamel in vitro.* Journal of dentistry, 2008.**36** (12): p. 999-1004.
42. Cheng, L., et al., *Effect of Galla chinensis on enhancing remineralisation of enamel crystals.* Biomedical Materials, 2009.**4** (3): p. 034103.
43. Chu, J., et al., *Effect of compounds of Galla chinensis on remineralisation of initial enamel carious lesions in vitro.* Journal of Dentistry, 2007.**35** (5): p. 383-387.
44. Xie, Q., et al., *The effect of galla chinensis on the growth of cariogenic bacteria in vitro.* Hua xi kou qiang yi xue za zhi= Huaxi kouqiang yixue zazhi= West China journal of stomatology, 2005. **23**(1): p. 82-84.
45. Christine, D.W., *Grape products and oral health.* The Journal of nutrition, 2009.**139** (9): p. 1818S-1823S.
46. Jawale, K.D., et al., *Grape seed extract: An innovation in remineralisation.* Journal of Conservative Dentistry and Endodontics, 2017.**20** (6): p. 415-418.
47. Tang, C.-f., et al., *The role of grape seed extract in the remineralisation of demineralised dentine: micromorphological and physical analyses.* Archives of oral biology, 2013. **58**(12): p. 1769-1776.
48. Benjamin, S., S.S. Thomas, and M.T. Nainan, *Grape seed extract as a potential remineralising agent: a comparative in vitro study.* The journal of contemporary dental practice, 2012.**13** (4): p. 425-430.
49. George, D., S.S. Bhat, and B. Antony, *Comparative evaluation of the antimicrobial efficacy of aloe vera tooth gel and two popular commercial toothpastes: an in vitro study.* General dentistry, 2009.**57** (3): p. 238-241.

50. Amaechi, B., et al., *Remineralisation of artificial enamel lesions by theobromine.* Caries research, 2013. **47**(5): p. 399-405.
51. Kargul, B., et al., *Evaluation of human enamel surfaces treated with theobromine: a pilot study.* Oral Health and Preventive Dentistry, 2012.**10** (3): p. 275.
52. Ceyhan, T., et al., *Production and characterisation of a glass-ceramic biomaterial and in vitro and in vivo evaluation of its biological effects.* Acta orthopaedica et traumatologica turcica, 2007.**41** (4): p. 307-313.
53. Golpayegani, M.V., et al., *Remineralisation effect of topical NovaMin versus sodium fluoride (1.1%) on caries-like lesions in permanent teeth.* Journal of dentistry (Tehran, Iran), 2012.**9** (1): p. 68.
54. Diamanti, I., et al., *In vitro evaluation of fluoride and calcium sodium phosphosilicate toothpastes, on root dentine caries lesions.* Journal of dentistry, 2011. **39**(9): p. 619-628.
55. Prabhakar, A.R. and V. Arali, *Comparison of the remineralising effects of sodium fluoride and bioactive glass using bioerodible gel systems.* Journal of dental research, dental clinics, dental prospects, 2017.**3** (4): p. 117-121.
56. Job, T., et al., *Remineralisation potential of three different dentifrices using Raman spectroscopy and confocal laser scanning microscope.* 2018.
57. Jagga, U., et al., *Comparative Evaluation of Remineralising Effect of Novamin and Tricalcium Phosphate on Artificial Caries: An in vitro Study.* The journal of contemporary dental practice, 2018.**19** (1): p. 109-112.
58. Gokce, G., et al., *Effects of toothpastes on white spot lesions around orthodontic brackets using quantitative light-induced fluorescence (QLF).* Journal of Orofacial Orthopedics/Fortschritte der Kieferorthopadie, 2017. **78**(6).
59. Wang, Y., et al., *Effect of tricalcium silicate (Ca3SiO5) bioactive material on reducing enamel demineralisation: An in vitro pH-cycling study.* Journal of dentistry, 2012.**40** (12): p. 1119-1126.
60. Dong, Z., et al., *Tricalcium silicate induced mineralisation for occlusion of dentinal tubules.* Australian dental journal, 2011. **56**(2): p. 175-180.

61. Tschoppe, P., et al., *Enamel and dentine remineralisation by nano-hydroxyapatite toothpastes.* Journal of dentistry, 2011. **39**(6): p. 430-437.
62. Haghgoo, R., M. Ahmadvand, and S. Moshaverinia, *Remineralising Effect of Topical NovaMin and Nano-hydroxyapatite on caries-like Lesions in Primary teeth.* The Journal of Contemporary Dental Practice, 2016. **17**(8): p. 645-649.
63. Daas, I., S. Badr, and E. Osman, *Comparison between fluoride and nano-hydroxyapatite in remineralising initial enamel lesion: an in vitro study.* J Contemp Dent Pract, 2018.**19** (3): p. 306-312.
64. Reis, P.Q., et al., *Effect of a dentifrice containing nanohydroxyapatite on the roughness, colour, lightness, and brightness of dental enamel subjected to a demineralisation challenge.* General Dentistry, 2018.**66** (4): p. 66-70.
65. Deglaire, A., et al., *Impact of human milk pasteurisation on the kinetics of peptide release during in vitro dynamic digestion at the preterm newborn stage.* Food chemistry, 2019.**281** : p. 294-303.
66. Salman, N.R., et al., *Comparison of remineralisation by fluoride varnishes with and without casein phosphopeptide amorphous calcium phosphate in primary teeth.* Acta Odontologica Scandinavica, 2019.**77** (1): p. 9-14.
67. Reynolds, E.C., *Anticariogenic complexes of amorphous calcium phosphate stabilised by casein phosphopeptides: a review.* Special Care in Dentistry, 1998.**18** (1): p. 8-16.
68. Reynolds, E., et al., *Retention in plaque and remineralisation of enamel lesions by various forms of calcium in a mouthrinse or sugar-free chewing gum.* Journal of dental research, 2003. **82**(3): p. 206-211.
69. Celik, E.U. and G. Katirci, *Treatment of Initial Caries Lesions.* Journal of Atatürk University Faculty of Dentistry, 2011. **2011**(1): p. 48-56.
70. Farooq, I., et al., *A review of novel dental caries preventive material: Casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) complex.* King Saud University Journal of Dental Sciences, 2013. **4**(2): p. 47-51.

71. Sezer, B. and B. Kargül, *Current Remineralisation Agents in Caries Management.* Turkey Clinics Journal of Dental Sciences, 2020. **26**(3).
72. Bartold, P., *Dentinal hypersensitivity: a review.* Australian dental journal, 2006. **51**(3): p. 212-218.
73. Taştan, E., E. Güler, and F. AYTAÇ BAL, *In-Vitro Investigation of the Effect of Combined Use of Different Remineralisation Agents with Laser and Ozone Therapy on Initial Caries.* Turkiye Klinikleri Journal of Dental Sciences, 2021. **27**(2).
74. Manton, D.J., et al., *Remineralisation of enamel subsurface lesions in situ by the use of three commercially available sugar-free gums.* International Journal of Paediatric Dentistry, 2008.**18** (4): p. 284-290.
75. Zhou, C., et al., *Casein phosphopeptide-amorphous calcium phosphate remineralisation of primary teeth early enamel lesions.* Journal of dentistry, 2014. **42**(1): p. 21-29.
76. Reynolds, E., et al., *Fluoride and casein phosphopeptide-amorphous calcium phosphate.* Journal of Dental Research, 2008.**87** (4): p. 344-348.
77. Pithon, M.M., et al., *Effectiveness of casein phosphopeptide-amorphous calcium phosphate-containing products in the prevention and treatment of white spot lesions in orthodontic patients: A systematic review.* Journal of investigative and clinical dentistry, 2019.**10** (2): p. e12391.
78. Rai, N., et al., *Evaluation of remineralisation potential of beverages modified with casein phosphopeptide-amorphous calcium phosphate on primary and permanent enamel: a laser profiler study.* International Journal of Clinical Paediatric Dentistry, 2018.**11** (1): p. 7.
79. Bullappa, D., M.P. Puranik, and S. Uma, *Casein phosphopeptide-Amorphous calcium phosphate: A review.* Int. J. Dent. Health Sci, 2015. **2**: p. 116-125.
80. Reynolds, E., *Remineralisation of enamel subsurface lesions by casein phosphopeptide-stabilised calcium phosphate solutions.* Journal of dental research, 1997. **76**(9): p. 1587-1595.

81. Walsh, L.J., *Evidence that demands a verdict: latest developments in remineralisation therapies.* Aust Dent Prac, 2009: p. 48-59.
82. Yazicioglu, O., et al., *Quantitative evaluation of the enamel caries which were treated with casein phosphopeptide-amorphous calcium fluoride phosphate.* Nigerian journal of clinical practice, 2017.**20** (6): p. 686-692.
83. Llena, C., A. Leyda, and L. Forner, *CPP-ACP and CPP-ACFP versus fluoride varnish in remineralisation of early caries lesions. A prospective study.* Eur J Paediatr Dent, 2015. **16**(3): p. 181-6.
84. Cochrane, N., et al., *Enamel subsurface lesion remineralisation with casein phosphopeptide stabilised solutions of calcium, phosphate and fluoride.* Caries research, 2008.**42** (2): p. 88-97.
85. Karlinsey, R.L., *Materials and methods for manufacturing amorphous tricalcium phosphate and metal oxide alloys of amorphous tricalcium phosphate and methods of using the same*. 2007, Google Patents.
86. Ekambaram, M., S. Mohd Said, and C.K. Yiu, *A review of enamel remineralisation potential of calcium-and phosphate-based remineralisation systems.* Oral Health Prev Dent, 2017.**15** (5): p. 415-420.
87. Karlinsey, R.L. and A.C. Mackey, *Solid-state preparation and dental application of an organically modified calcium phosphate.* Journal of materials science, 2009.**44** (1): p. 346-349.
88. Vogel, G., et al., *Composition of plaque and saliva following a sucrose challenge and use of an a-tricalcium-phosphate-containing chewing gum.* Journal of dental research, 1998.**77** (3): p. 518-524.
89. Alkilzy, M., et al., *Treatment of carious lesions using self-assembling peptides.* Advances in dental research, 2018.**29** (1): p. 42-47.
90. Kind, L., et al., *Biomimetic remineralisation of carious lesions by self-assembling peptide.* Journal of dental research, 2017.**96** (7): p. 790-797.
91. Silvertown, J.D., et al., *Remineralisation of natural early caries lesions in vitro by P11-4 monitored with photothermal*

radiometry and luminescence. Journal of investigative and clinical dentistry, 2017.**8** (4): p. e12257.

92. Schlee, M., et al., *Clinical performance of self-assembling peptide P11-4 in the treatment of initial proximal carious lesions: A practice-based case series.* Journal of investigative and clinical dentistry, 2018.**9** (1): p. e12286.
93. Üstün, N. and O. Aktören, *Analysis of efficacy of the self-assembling peptide-based remineralisation agent on artificial enamel lesions.* Microscopy research and technique, 2019.**82** (7): p. 1065-1072.
94. Sullivan, R., et al., *In vivo detection of calcium from dicalcium phosphate dihydrate dentifrices in demineralised human enamel and plaque.* Advances in dental research, 1997. **11**(4): p. 380-387.
95. Wefel, J. and J. Harless, *The use of saturated DCPD in remineralisation of artificial caries lesions in vitro.* Journal of Dental Research, 1987.**66** (11): p. 1640-1643.
96. Sullivan, R., et al., *Development of an enhanced anticaries efficacy dual component dentifrice containing sodium fluoride and dicalcium phosphate dihydrate.* American journal of dentistry, 2001.**14** : p. 3A-11A.
97. Tanaka, T., et al., *Optimisation of calcium concentration of saliva with phosphoryl oligosaccharides of calcium (POs-Ca) for enamel remineralisation in vitro.* Archives of oral biology, 2013. **58**(2): p. 174-180.
98. To-o, K., et al., *Absorbability of calcium from calcium-bound phosphoryl oligosaccharides in comparison with that from various calcium compounds in the rat ligated jejunum loop.* Bioscience, biotechnology, and biochemistry, 2003. **67**(8): p. 1713-1718.
99. Kitasako, Y., et al., *Effects of a chewing gum containing phosphoryl oligosaccharides of calcium (POs-Ca) and fluoride on remineralisation and crystallisation of enamel subsurface lesions in situ.* Journal of dentistry, 2011. **39**(11): p. 771-779.
100. Duke, S., *Effect induced by a chalk-based toothpaste on the pH changes of plaque challenged by a high sugar diet over an 8-hour period.* 1986.

101. Cury, J., et al., *Effect of a calcium carbonate-based dentifrice on in situ enamel remineralisation.* Caries research, 2005. **39**(3): p. 255-257.
102. Cury, J., et al., *Effect of a calcium carbonate-based dentifrice on enamel demineralisation in situ.* Caries research, 2003. **37**(3): p. 194-199.
103. Danelon, M., et al., *In situ evaluation of a low fluoride concentration gel with sodium trimetaphosphate in enamel remineralisation.* Am J Dent, 2013. **26**(1): p. 15-20.
104. Gonçalves, R.S., et al., *Use of sodium trimetaphosphate in the inhibition of dentin matrix metalloproteinases and as a remineralising agent.* Journal of Dentistry, 2018.**68** : p. 34-40.
105. Lynch, R. and J. Ten Cate, *Effect of calcium glycerophosphate on demineralisation in an in vitro biofilm model.* Caries research, 2006. **40**(2): p. 142-147.
106. Buzalaf, M.A.R., et al., *Mechanisms of action of fluoride for caries control.* Fluoride and the oral environment, 2011.**22** : p. 97-114.
107. Grenby, T., *Trials of three organic phosphorus-containing compounds as protective agents against dental caries in rats.* Journal of Dental Research, 1973.**52** (3): p. 454-461.
108. Carvalho, T.S., et al., *Fluoride varnishes with calcium glycerophosphate: fluoride release and effect on in vitro enamel demineralisation.* Brazilian oral research, 2015. **29**: p. 1-6.
109. Rezende, K.M., et al., *Can babies oral wipes with fluoride and/or calcium glycerophosphate prevent cariogenic demineralisation? An in-vitro study.* Minerva stomatologica, 2017.**66** (5): p. 226-231.
110. Sezer, B., et al. *Efficacy of mineral containing gel for remineralisation in MIH-affected incisors: a 3-months clinical study*. in *64th ORCA Congress. Caries Res*. 2017.

CHAPTER 2

THE ROLE OF RADIATION IN DENTISTRY AND METHODS OF PROTECTION AGAINST ITS HARMFUL EFFECTS

Dr. Aslıhan ŞAHAN KESKİN

INTRODUCTION

Radiation is the transmission of energy through particles or electromagnetic waves without the need for a physical medium (Bushong, 1988). Electromagnetic radiation includes various types such as visible light, infrared rays, ultraviolet rays, X-rays, and gamma rays, while particulate radiation consists of subatomic particles such as electrons, positrons, protons, and neutrons (Dance, Christofides, Maidment, McLean, & Ng, 2014).

Radiation constitutes a fundamental component of dental imaging Technologies (White & Pharoah, 2014). Today, radiation-based imaging modalities are frequently utilized in dentistry for diagnostic purposes and treatment planning. However, both ionizing and non-ionizing forms of radiation may pose adverse effects on human health (Harorlı et al., 2014). Therefore, implementing effective radiation protection strategies is of great importance in dental practice. This chapter will discuss the types of radiation, its applications in dentistry, potential hazards, and protective measures.

1. TYPES AND DEFINITIONS OF RADIATION

Radiation is broadly classified into two main categories based on its origin: natural and artificial. Natural sources of radiation include cosmic rays, radon gas, gamma radiation, and internal exposure resulting from the ingestion or inhalation of environmental radioisotopes. This form of radiation exists inherently in nature and affects all living organisms (Harorlı et al., 2014). In contrast, artificial radiation sources arise from human activities and are associated with the release of radioactive materials into the environment (Coşkun, 2011). Examples of artificial radiation include medical imaging procedures (e.g., radiography), nuclear medicine applications, nuclear power plants, aviation exposure, and occupational radiation exposure (White & Pharoah, 2014). While people were predominantly exposed to natural sources of radiation in the past, exposure to artificial radiation has increased significantly in recent years. This shift is largely attributed to technological advancements in medicine. Particularly, the use of techniques such as computed tomography (CT), interventional radiology, and nuclear medicine has become more prevalent in the diagnosis and treatment of conditions such as cancer and cardiovascular diseases (White & Pharoah, 2014).

Radiation is also defined as energy transmitted in the form of electromagnetic waves or particles (Harorlı et al., 2014). Depending on their ability to ionize matter, both particulate and electromagnetic radiations are categorized into two groups: ionizing and non-ionizing radiation. Ionization refers to the process of removing an electron from an atom, and radiation capable of initiating this process is termed "*ionizing radiation"*. X-rays, gamma rays, and cosmic rays are examples of ionizing electromagnetic radiation. In addition, certain types of particulate radiation with high kinetic energy can also trigger ionization. Examples of such ionizing particulate radiation include beta particles, alpha particles, and neutrons (Daşdağ, 2010; Gökoğlan, Ekinci, Özgenç, İlem-özdemir, & Aşıkoğlu, 2020). Non-ionizing electromagnetic radiation includes radio waves, microwaves, infrared rays, visible light (red, orange, yellow, green, blue, violet), and ultraviolet rays (Gökoğlan et al., 2020). The type of radiation used in dentistry typically falls under the category of ionizing radiation, with X-rays being the most commonly utilized form. Ionizing radiation has the capacity to displace electrons from atoms, resulting in ion formation, which can lead to alterations in living tissues. This characteristic, while essential for imaging purposes in dentistry, represents a critical consideration in terms of radiation safety (Harorlı et al., 2014; White & Pharoah, 2014).

1.1. Radiation Units

Ionizing radiation is a measurable quantity within specific parameters. To define and quantify the various physical and biological effects associated with radiation, a range of measurement units has been developed. These units have been standardized by the International Commission on Radiation Units and Measurements (ICRU) (https://www.icru.org/) and over time, traditional units have largely been replaced by those of the International System of Units (SI). The main types of measurements used to assess radiation intensity, its biological effects, and associated risks are summarized below:

Radioactivity

Radioactivity refers to the number of nuclear disintegrations occurring per unit time within a given sample of material. This parameter is used to determine the activity level of radioactive sources (https://www.icrp.org/).

- *Curie (Ci):* Corresponds to 3.7×10^{10} nuclear disintegrations per second (https://www.icrp.org/).
- *Becquerel (Bq):* The SI unit, defined as one disintegration per second (https://www.icrp.org/).
- $1\ Ci = 3.7 \times 10^{10}\ Bq$ (https://www.icrp.org/)

Exposure

Exposure refers to the amount of ionization produced by ionizing radiation in air and is primarily used for X-rays and gamma rays (https://www.icrp.org/).

- *Roentgen (R):* The amount of X-ray or gamma radiation that generates an electric charge of 2.58×10^{-4} coulombs in 1 kg of dry air (https://www.icrp.org/).
- *Coulomb per kilogram (C/kg):* The SI unit, providing a direct measure of ionization capacity (https://www.icrp.org/).
- $1\ R = 2.58 \times 10^{-4}\ C/kg$ (https://www.icrp.org/)

Absorbed Dose

This type of dose refers to the amount of energy absorbed per unit mass of a given material or tissue (Allisy-Roberts & Williams, 2007).

- *Rad:* Represents an energy absorption of 0.01 joules per kilogram of material (Allisy-Roberts & Williams, 2007).
- *Gray (Gy):* The SI unit, defined as the absorption of 1 joule of energy per kilogram of tissue (Allisy-Roberts & Williams, 2007).
- *1 Gy = 100 rad* (Allisy-Roberts & Williams, 2007).

Equivalent Dose

Equivalent dose is used to compare the biological effects of different types of radiation. This calculation considers the radiation-specific quality factor (Allisy-Roberts & Williams, 2007).

- *Rem (Roentgen Equivalent in Man):* A conventional unit calculated using the formula: Rad × Quality Factor. In diagnostic radiology, the quality factor is typically assumed to be 1. (1 Rad ≈ 1 Rem)(Allisy-Roberts & Williams, 2007).
- *Sievert (Sv):* The SI unit, representing a biological effect equivalent to an energy absorption of 1 joule per kilogram of tissue.
- *1 Sv = 100 rem = 1,000 mSv = 1,000,000 µSv* (Allisy-Roberts & Williams, 2007).

Effective Dose

The effective dose allows for an assessment of the total body risk by accounting for the varying sensitivity of different tissues to radiation (Martin, 2020).

- Calculation formula: $E = H \times W$ (where H = equivalent dose, and W = tissue weighting factor).
- The unit of effective dose is the sievert (Sv).
- The average annual effective dose from natural sources is approximately 2.4 mSv.

Table 1 summarizes the units of radiation measurement.

Table 1. Radiation Units

Quantity Measured	Definition	Conventional Unit	SI Unit	Conversion
Radioactivity	Number of nuclear disintegrations per unit time	Curie (Ci)	Becquerel (Bq)	1 Ci = 3.7×10^{10} Bq
Exposure	Ionization capacity in air (X-rays/gamma rays)	Roentgen (R)	Coulomb/kg (C/kg)	1 R = 2.58×10^{-4} C/kg
Absorbed Dose	Radiation energy absorbed per kilogram of material	Rad	Gray (Gy)	1 Gy = 100 rad
Equivalent Dose	Biological effect of radiation (weighted by quality factor)	Rem	Sievert (Sv)	1 Sv = 100 Rem

Effective Dose	Risk assessment based on tissue-specific weighting factors	-	Sievert (Sv)	1 Sv = 1 Joule/kg

Maximum Permissible Doses

According to the recommendations of the International Commission on Radiological Protection (ICRP) (https://www.icrp.org/):

- **For radiation workers:**
  - 5-year average: **20 mSv/year**
  - Maximum in a single year: **50 mSv/year**
  - Lifetime dose limit: **5 × (N − 18) rem** (N = age in years)
- **For members of the general public:**
  - 5-year average: **1 mSv/year**
  - Maximum in a single year: **5 mSv**

2. RADIATION USAGE AREAS IN DENTISTRY

Dental radiology is primarily used in dentistry for diagnostic purposes and treatment planning. The most commonly employed radiographic imaging techniques include intraoral radiographs (periapical, bitewing, and occlusal radiographs), extraoral radiographs (panoramic radiography, posteroanterior and lateral cephalometric radiographs, submentovertex and Waters' projection, etc.), and cone-beam computed tomography (CBCT) (Shah, Bansal, & Logani, 2014). These modalities play a critical role in the detection of dental caries, diagnosis of periodontal diseases, planning of dental implants and orthodontic treatments, as well as in the identification of various cysts and tumors in the jaws (Harorlı et al., 2014; Shah et al., 2014; White & Pharoah, 2014).

3. EFFECTS OF RADIATION ON HUMAN HEALTH

Radiobiology is the scientific discipline that studies the effects of radiation on living organisms (Harorlı et al., 2014). It aims to understand how radiation induces cellular damage, its impact on DNA, and the mechanisms involved in the repair of such damage. Through radiobiology, the safe limits of beneficial applications such as medical imaging and radiotherapy are established, and protective strategies are developed by anticipating the potential risks associated with radiation exposure (Hall & Giaccia, 2006). Ionizing radiation, due to its high energy, can ionize atoms by displacing electrons. This ionization process can lead to both direct and indirect effects on cellular biomolecules, particularly DNA (Hall & Giaccia, 2006; Harorlı et al., 2014; White & Pharoah, 2014). The biological effects of radiation occur through two main mechanisms:

- **Direct Effects:** Radiation can directly strike the DNA molecule within the cell, causing double-strand breaks. If unrepaired, these breaks may result in mutations or cell death (Harorlı et al., 2014).

- **Indirect Effects:** Radiation interacts with water molecules to produce free radicals. These radicals can react with intracellular biomolecules and damage DNA. Indirect effects occur more frequently than direct ones, as the human body is predominantly composed of water (Harorlı et al., 2014).

The biological effects of radiation vary depending on the dose and duration of exposure. Although the doses used in dentistry are generally low, ionizing radiation may still have several harmful effects on biological tissues, including the following (White & Pharoah, 2014):

- **DNA Damage:** Radiation can induce DNA damage in cells through both direct and indirect mechanisms. Such damage may result in cell death, mutations, or the development of cancer (Harorlı et al., 2014).
- **Somatic Effects:** These effects occur in the irradiated individual during their lifetime and are caused by damage to somatic (non-reproductive) cells. Common somatic effects include radiation-induced burns and the development of malignancies. At higher doses, radiation can cause serious harm to the bone marrow, gastrointestinal system, and nervous system. While dental radiation typically involves low doses that are not considered to cause significant somatic effects, the cumulative impact of repeated exposures should not be overlooked (Harorlı et al., 2014).

- **Genetic Effects:** Genetic effects refer to the heritable consequences of DNA damage in the reproductive cells (sperm or oocytes) of individuals exposed to radiation. Ionizing radiation may induce mutations in these cells, which can be transmitted to future generations. Although such effects are rare at the low radiation doses used in dentistry, they may pose long-term risks, particularly for children and individuals of reproductive age (Harorlı et al., 2014).

- **Tissue Sensitivity:** Tissues with rapidly dividing cells are more sensitive to radiation. Therefore, the adverse effects of radiation tend to be more pronounced in children and young individuals (Brenner, Elliston, Hall, & Berdon, 2001; Choudhary, 2018).

These considerations are particularly important for radiology technicians and patients who are frequently exposed to ionizing radiation. Special precautions should be taken with vulnerable populations such as children and pregnant women (White & Pharoah, 2014).

3.1. Cellular-Level Effects of Radiation

Ionizing radiation can trigger a range of biological responses at the cellular level. These responses vary depending on the radiation dose, the duration of exposure, and the biological characteristics of the target tissue. The cellular responses to radiation are generally classified into three main categories based on the severity of the damage and the cell's repair capacity (Harorlı et al., 2014):

- ***Sublethal Damage***

This type of damage occurs in cells exposed to low doses of radiation and does not result in cell death. Given sufficient time, the cellular repair mechanisms can restore the affected structures (Harorlı et al., 2014).

- ***Potentially Lethal Damage***

This form of damage occurs just before cell division. If the cell enters mitosis shortly after the damage, it may become lethal. However, if mitosis is delayed, repair mechanisms may intervene and reverse the damage. Therefore, the outcome depends on the timing of the mitotic process (Harorlı et al., 2014).

- ***Lethal Damage***

This occurs when radiation induces irreversible structural and functional damage in the cell. Such damage cannot be repaired and ultimately results in cell death (Harorlı et al., 2014).

Latent Period, Damage, and Repair Processes

Following radiation exposure, it is typical for cellular effects not to be immediately observable. This delayed phase is referred to as the "*latent period*", which encompasses the time between irradiation and the emergence of detectable biological responses. The duration of the latent period depends on several factors, including the radiation dose, dose rate, and tissue sensitivity. Exposure to high doses over a short period tends to shorten the latent phase (Kumaş, 2009).

The *damage phase* follows the latent period and is characterized by structural and functional alterations such as disruptions in cellular function, chromosomal breaks, and either inhibition or stimulation of mitotic activity. During this phase, cell death may also occur (Kumaş, 2009).

The final phase of this process is the *repair period*, during which cellular damage is either reversed or becomes permanent. Cells possess a significant capacity to repair radiation-induced damage, particularly following low-dose exposures.

However, if repair mechanisms are incomplete or faulty, permanent DNA mutations may result. In such cases, the affected cell may continue functioning with impaired metabolic activity or undergo apoptosis. Incorrectly repaired DNA may encode erroneous genetic information, potentially leading to genetic disorders or cellular transformation in the long term (Kumaş, 2009).

Acute and Chronic Effects of Radiation

The biological effects of radiation on the human body are generally classified as either *acute* (short-term) or *chronic* (long-term):

- **Acute Effects:**

  These effects result from the absorption of a high dose of radiation over a short period. Acute effects manifest as erythema, hair loss, gastrointestinal disturbances, fatigue, and, in severe cases, multi-organ failure—primarily due to rapid cell death. Such effects are typically observed in scenarios involving radiotherapy or nuclear accidents. In contrast, the low doses used in diagnostic imaging are not associated with these outcomes (Harorlı et al., 2014; White & Pharoah, 2014).

- **Chronic Effects:**

  Prolonged exposure to low-dose radiation may lead to the accumulation of DNA damage, increasing the risk of genetic mutations and, consequently, malignancies. The literature reports strong correlations between ionizing radiation and various cancers, including leukemia, thyroid, breast, and skin cancers. Chronic effects typically have a long latent period and may take years to manifest clinically. Additionally, cataracts, cardiovascular disorders, and adverse reproductive outcomes are also considered part of chronic radiation effects (Harorlı et al., 2014; White & Pharoah, 2014).

The cumulative nature of radiation's biological effects is particularly significant in the context of repeated low-dose exposures. Therefore, adherence to the principle of dose minimization in medical applications involving radiation is crucial to preventing both acute and chronic effects.

3.2. Radiation Sensitivity and Influencing Factors

Certain tissues and organs are more sensitive to radiation than others. This sensitivity depends on factors such as cellular proliferation rate, cell cycle phase, and tissue type. The hypothesis formulated by Bergonié and Tribondeau in 1906, which has become known as the "***Fundamental Law of Radiobiology***", states that *"The biological effects observed in irradiated organisms are directly proportional to the proliferative capacity of irradiated cells and inversely proportional to their degree of differentiation"* (Bergonié & Tribondeau, 2003).

Radiosensitive Critical Organs and Tissues in Dentistry

From a radiobiological perspective, certain tissues and organs exhibit higher radiosensitivity due to their structural and cellular characteristics. This sensitivity is influenced by factors such as mitotic activity, the specific phase of the cell cycle, and the tissue's regenerative capacity. Tissues composed of rapidly dividing cells are especially susceptible to the effects of ionizing radiation (Haring & Jansen, 2000).

During dental radiographic procedures, some organs and tissues in the head and neck region are considered critical despite exposure to relatively low radiation doses. A *critical organ* is defined as one whose radiation-induced impairment may significantly affect the individual’s quality of life. In dental practice, the critical organs and tissues include the following (Haring & Jansen, 2000):

- **Skin:** Moderately sensitive to ionizing radiation. One of the early deterministic effects of radiation on the skin, erythema, may occur if a threshold dose of approximately 2.5 Gray (250 rad) is received within 14 days. Reaching this dose would require about 500 periapical exposures using E-speed film—an impractical scenario in dental settings (Haring & Jansen, 2000).
- **Thyroid Gland:** Although not typically exposed to the primary beam during head and neck radiographic procedures, the thyroid gland can be affected by scattered radiation. The estimated threshold dose for radiation-induced thyroid cancer is approximately 0.06 Gray (6 rad). In comparison, the dose absorbed by the thyroid from 20 periapical exposures using D-speed film and long-cone technique is only 0.00006 Gray—roughly 1,000 times lower. In panoramic imaging, the thyroid receives only about 1% of the dose absorbed during cervical spine radiography. Nonetheless, due to the stochastic nature of radiation effects, the routine use of thyroid collars is recommended for every radiographic procedure (Haring & Jansen, 2000).
- **Bone Marrow:** The maxilla and mandible, which are irradiated during dental procedures, contain only a small portion of the body’s total active bone marrow. The average bone

marrow dose refers to the total amount of radiation absorbed by all active marrow in the body. In a full-mouth radiographic series with 20 films using a cylindrical collimator, the dose is approximately 0.142 mSv, whereas for panoramic radiography, it is about 0.01 mSv. Therefore, the risk of leukemia from dental radiographic exposure is considered extremely low (Haring & Jansen, 2000).

- **Eye Lenses:** Cataract formation is a deterministic effect and is associated with doses exceeding 2 Gray. Since the radiation dose in dental radiographic applications is far below this threshold, the risk of cataract development is negligible (Haring & Jansen, 2000).
- **Gonads (Reproductive Organs):** Due to their anatomical distance from the head and neck region, the gonads receive negligible doses during dental radiographic procedures—approximately 1 µGy. This corresponds to only about 0.003% of the average annual natural background radiation. However, in pediatric patients with shorter necks, relatively higher gonadal exposure may occur and should be considered (Haring & Jansen, 2000).

In conclusion, although dental radiography is classified as a low-dose imaging modality, protecting radiation-sensitive critical organs in the head and neck region remains essential for ensuring patient safety.

3.3. Biological Effects of Radiation

The biological effects of ionizing radiation can manifest as either *deterministic* or *stochastic* effects, depending on the dose and nature of exposure (Choudhary, 2018).

Deterministic effects occur only when a certain threshold dose is exceeded, and once this threshold is surpassed, the likelihood of the effect occurring approaches 100%. These effects arise when the radiation-induced damage to cellular structures exceeds the organism's repair capacity. Clinically observed deterministic effects include skin erythema, epilation, cataract formation, and acute radiation syndrome resulting from high-dose exposure. These effects are generally associated with short-term, high-dose radiation exposure and are typically observed in unusual circumstances such as medical or industrial accidents (Choudhary, 2018).

Stochastic effects, on the other hand, are random biological effects that can occur regardless of the radiation dose magnitude. These effects do not have a threshold dose requirement. While higher doses increase the probability of occurrence, they do not affect the *severity* of the effect. Thus, stochastic effects are purely probabilistic in nature (Choudhary, 2018). Stochastic effects are primarily associated with radiation-induced mutations in DNA and can lead to clinical manifestations after long latent periods. Among these, carcinogenesis (radiation-induced cancer) is the most prominent, with strong associations to malignancies such as leukemia, thyroid cancer, breast cancer, and lung cancer. Additionally, hereditary disorders resulting from genetic mutations in germ cells are also classified as stochastic effects (Choudhary, 2018).

Radiation-induced biological effects can be categorized into three groups based on the type of target cell (Harorlı et al., 2014; White & Pharoah, 2014):

I. *Somatic effects*: These are effects that directly impact the individual's health and may present as either short- or long-term consequences of radiation exposure.
II. *Hereditary effects*: These effects result from radiation-induced damage to germ cells, potentially leading to genetic mutations that can be transmitted to future generations.
III. *Teratogenic effects*: These occur when radiation exposure during pregnancy affects the embryo or fetus, potentially resulting in structural or functional abnormalities (Harorlı et al., 2014; White & Pharoah, 2014).

Factors Determining Radiation-Induced Damage

- *Total dose*: The total amount of absorbed radiation is the primary determinant of biological damage. As the dose increases, the severity of the damage also rises (Harorlı et al., 2014; White & Pharoah, 2014).

• *Dose rate:* This refers to the rate at which radiation is delivered over time. At high dose rates, cells have less opportunity for repair, leading to greater damage (Harorlı et al., 2014; White & Pharoah, 2014).

• *Irradiated tissue volume*: As the area exposed to radiation increases, systemic effects become more pronounced. Radiation affecting large volumes, such as the hematopoietic system, may lead to widespread physiological disruptions (Harorlı et al., 2014; White & Pharoah, 2014).

• *Degree of cell differentiation*: Cells with low levels of differentiation—i.e., less specialized cells—are more sensitive to radiation (Bergonié & Tribondeau, 2003).

• *Metabolic activity*: Cells with high metabolic rates are more susceptible to radiation-induced damage (Harorlı et al., 2014).

• *Mitotic activity*: Rapidly dividing cells are more vulnerable to radiation. For instance, tissues such as bone marrow, which exhibit high mitotic activity, may sustain damage even at moderate doses. In contrast, tissues composed of rarely dividing cells, such as muscle, are more resistant (White & Pharoah, 2014).

• *Oxygen presence*: The presence of oxygen at the cellular level enhances the formation of free radicals, thereby intensifying radiation-induced damage. Hypoxic cells are generally more resistant to radiation (Harorlı et al., 2014).

• *<u>Age:</u>* Developing organisms, particularly children, are more sensitive to radiation and may exhibit more pronounced biological effects at the same dose (Hall & Giaccia, 2006).

• *<u>Chemical agents</u>*: Substances that increase cellular radiosensitivity are known as *radiosensitizers*, while those that reduce sensitivity are termed *radioprotectors*. Oxygen and halogenated pyrimidines are among the most common radiosensitizers, whereas compounds containing sulfhydryl (-SH) groups are recognized for their radioprotective effects (Harorlı et al., 2014).

4. RADIATION PROTECTION METHODS AND FUTURE PERSPECTIVES

4.1. The ALARA Principle (As Low As Reasonably Achievable)

The fundamental principle of radiation protection in dentistry is the ALARA concept—*keeping radiation exposure As Low As Reasonably Achievable* (Bilge H & N, 2017; Yeung, 2019). This principle aims to minimize radiation exposure for both patients and healthcare personnel (https://www.icrp.org/). The following methods can be implemented to support this goal:

• **Dose Limitation**: Unnecessary radiographic examinations should be avoided. The radiographic needs of each patient must be individually assessed, and imaging should be performed only when clinically justified.

- **Use of Digital Radiography**: Digital radiographic systems allow for diagnostic imaging with significantly lower radiation doses compared to conventional film-based techniques. This method not only reduces radiation exposure but also delivers faster results.

- **Lead Aprons and Thyroid Shields**: Patients should be provided with lead aprons and thyroid collars during radiographic procedures. This is particularly important for vulnerable groups such as children and pregnant women.

- **Distance from the Radiation Source**: Increasing the distance between the X-ray tube and the patient reduces the radiation dose received. Therefore, maintaining an appropriate distance during imaging is crucial.

4.2. Protection of Dental Personnel and the Environment

Dentists and radiology technicians are required to implement appropriate protective measures against radiation exposure. The following strategies may be employed in this context:

- **Radiation Shielding**: The use of lead shields and physical barriers can effectively limit the dispersion of radiation.
- **Use of Personal Dosimeters**: Dental personnel should regularly monitor their exposure levels by wearing personal dosimeters.
- **Regular Training and Inspections**: Dentists and radiology technicians must receive continuous education on radiation

safety, and facilities should be subject to periodic inspections to ensure compliance with radiation protection standards.

In the context of radiation safety, precautions to protect the patient exposed to radiation also apply to the practitioner. The dentist or technician must avoid standing within the primary beam. Preferably, they should remain behind a protective lead barrier or exit the room during exposure. If neither is feasible, the *position and distance rule* should be applied: the operator should stand at an angle of 90–135° to the central X-ray beam and maintain a minimum distance of 180 cm from the source. This position corresponds to the area where scatter radiation is at its lowest (White & Pharoah, 2014).

From an environmental safety perspective, X-ray rooms should have a single entry door, and the primary beam must not be directed toward it. The ventilation system should be designed with an exhaust at floor level and an inlet at the ceiling to prevent accumulation of toxic gases (e.g., ozone) resulting from ionized air. Walls and doors should be lined with at least 1–2 mm of lead, and the structural elements of the room must ensure radiation containment—for example, 20 cm of concrete or 30 cm of solid brickwork (https://www.icrp.org/; White & Pharoah, 2014).

4.3. Protection of Pediatric and Pregnant Patients

Children and pregnant women are more vulnerable to the potential risks associated with radiation exposure. Therefore, specific protective measures must be implemented for these patient groups:

- **Assessment of Imaging Necessity**: Radiographic examinations should be performed in children and pregnant women only when absolutely necessary. As children are more radiosensitive, imaging procedures must be conducted using the lowest possible radiation dose. For instance, pediatric patients should be imaged using lower energy settings tailored to their anatomical characteristics.
- **Radiation-Free Alternatives**: When radiographic imaging is essential for pregnant women, non-ionizing alternatives should be considered first. Although their use in dentistry is limited, imaging modalities such as magnetic resonance imaging (MRI) and ultrasonography may be appropriate in certain cases. MRI, in particular, is effective for soft tissue evaluation and is considered safe for use during pregnancy.

In female patients of reproductive age, the first 10 days from the onset of menstruation are generally considered the period of lowest likelihood of pregnancy. Accordingly, this interval is regarded as the safest time for procedures involving ionizing radiation. This protocol is widely known as the “10-day rule” in the literature. For any female patient in whom pregnancy cannot be definitively ruled out, a cautious approach should be adopted, assuming the possibility of pregnancy as a matter of patient safety (Carmichael & Warrick, 1978).

4.4. Head and Neck Radiotherapy and Oral Complications

Radiotherapy applied to the head and neck region can lead to a range of acute and chronic oral complications. Depending on the intensity of radiation, the skin may exhibit erythema, epilation, dryness, and cracking. The oral mucosa is particularly radiosensitive, and by the second week of treatment, radiation mucositis characterized by hyperemia, edema, and ulceration in advanced stages may develop. This condition often results in painful swallowing and difficulty in eating. Although mucosal healing is generally completed within two months after treatment, residual atrophy, reduced vascularity, and scarring may compromise the use of dental prostheses (Yalçın, 2019).

Salivary glands undergo radiation-induced atrophy, leading to decreased salivary flow, increased viscosity, and reduced pH. This condition, known as xerostomia, can cause mucosal atrophy and ulceration, and negatively impact essential functions such as mastication, speech, and swallowing. If xerostomia becomes chronic, the likelihood of full recovery diminishes. Management options include artificial saliva, mouth rinses (e.g., bicarbonate or chlorhexidine), chewing gum, and systemic antifungal agents (Jensen, Vissink, Limesand, & Reyland, 2019).

Developing dental and jaw tissues are more sensitive to radiation. Adverse effects include delayed tooth eruption, root development anomalies, hypodontia, enamel hypoplasia, and intrinsic discoloration. At high doses, dental germ development may be completely arrested. In fully developed teeth, radiation may cause caries, dentin hypersensitivity, discoloration, cementum and root anomalies (Harorlı et al., 2014).

Although adult jawbones are relatively more resistant, serious complications such as osteoradionecrosis (ORN) can occur. ORN typically affects the mandible and is often triggered by infection or trauma. Due to poor vascularization of necrotic bone, the effectiveness of antibiotics is limited; treatment may require hyperbaric oxygen therapy and, if necessary, surgical debridement (Thorn, Hansen, Specht, & Bastholt, 2000).

Prior to radiotherapy, dentists and radiation oncologists should collaborate to perform comprehensive oral evaluations using panoramic and periapical radiographs. Infected teeth should be extracted, periodontal diseases treated, and optimal oral hygiene established. During radiotherapy, chlorhexidine mouth rinses may be used to facilitate oral care. If removable prostheses are required, they should ideally be fabricated after complete mucosal healing, preferably one year post-treatment. Pressure-free impression techniques, soft acrylic materials, and meticulous adaptation are recommended (Yalçın, 2019).

4.5. The Contribution of Artificial Intelligence and Automation to Radiology and Future Perspectives

Advancements in technology have facilitated the development of novel imaging techniques that reduce radiation exposure (Guckenberger et al., 2024; Zhou, 2023). Digital radiography requires significantly lower radiation doses compared to film-based methods, while three-dimensional imaging systems enhance diagnostic accuracy (Zhou, Tan, & Davidson, 2020).

Artificial intelligence (AI) holds great potential in the diagnostic processes of dental radiology. Automated image analysis systems allow for faster and more precise interpretation of radiographic images. These technologies can contribute to the more efficient use of radiation by enabling accurate diagnoses and optimized treatment planning.

5. CONCLUSION

Although radiation is an indispensable diagnostic tool in the field of dentistry, its potential hazards necessitate cautious and responsible use. In line with the ALARA principle, appropriate protective measures—such as the use of lead shields, digital radiographic systems, and maintaining adequate distance from the radiation source—can help minimize exposure and protect both patients and dental personnel from harmful effects. With ongoing technological advancements, it is anticipated that safer and more efficient imaging modalities will become increasingly widespread in the future. Enhancing the awareness of dental professionals and healthcare personnel regarding radiation safety will yield significant benefits for public health in the long term.

REFERENCES

Allisy-Roberts, P. J., & Williams, J. (2007). *Farr's physics for medical imaging*: Elsevier Health Sciences.

Bergonié, J., & Tribondeau, L. (2003). Interpretation of some results from radiotherapy and an attempt to determine a rational treatment technique. 1906. *The Yale journal of biology medicine, 76*(4-6), 181.

Bilge H, & N, D. K. (2017). Radyasyondan korunma In İ. Özcan (Ed.), *Diş Hekimliğinde Radyolojinin Esasları: Konvansiyonelden Dijitale* (1 ed.). İstanbul: İstanbul Medikal Yayıncılık.

Brenner, D. J., Elliston, C. D., Hall, E. J., & Berdon, W. E. (2001). Estimated risks of radiation-induced fatal cancer from pediatric CT. *American Journal of Roentgenology, 176*(2), 289-296.

Bushong, S. C. (1988). Radiologic science for technologists.

Carmichael, J., & Warrick, C. (1978). The ten day rule—principles and practice. *The British Journal of Radiology, 51*(611), 843-846.

Choudhary, S. (2018). Deterministic and stochastic effects of radiation. *Cancer Therapy Oncology International Journal, 12*(2), 31-32.

Coşkun, Ö. (2011). İyonize radyasyonun biyolojik etkileri. *Teknik Bilimler Dergisi, 1*(2), 13-17.

Dance, D., Christofides, S., Maidment, A., McLean, I., & Ng, K. (2014). Diagnostic radiology physics. *International Atomic Energy Agency, 299*, 12-14.

Daşdağ, S. (2010). İyonlaştırıcı radyasyonlar ve kanser. *Dicle tıp dergisi, 37*(2).

Gökoğlan, E., Ekinci, M., Özgenç, E., İlem-özdemir, D., & Aşıkoğlu, M. (2020). Radyasyon ve insan sağlığı üzerindeki etkileri. *Anatolian Clinic the Journal of Medical Sciences, 25*(3), 289-294.

Guckenberger, M., Andratschke, N., Chung, C., Fuller, D., Tanadini-Lang, S., & Jaffray, D. A. (2024). *The future of MR-guided radiation therapy.* Paper presented at the Seminars in radiation oncology.

Hall, E. J., & Giaccia, A. J. (2006). Radiobiology for the Radiologist. *Int J Radiat Oncol Biol Phys, 66*(627), 10.1016.
Haring, J., & Jansen, L. (2000). *Dental radiography, Principles Techniques* (Vol. 3).
Harorlı, A., Akgül, H., Yılmaz, A., Bilge, O., Dağistan, S., Çakur, B., . . . Sümbüllü, M. (2014). *Ağız, diş ve çene radyolojisi* (A. Harorlı Ed. 1 ed.). İstanbul: Nobel Tıp Kitabevleri.
https://www.icru.org/. International Committee for Radiological Units (ICRU). Retrieved from https://www.icru.org/
Jensen, S. B., Vissink, A., Limesand, K. H., & Reyland, M. E. (2019). Salivary gland hypofunction and xerostomia in head and neck radiation patients. *JNCI Monographs, 2019*(53), lgz016.
Kumaş, A. (2009). *Radyasyon fiziği ve tıbbi uygulamaları* (2 ed.). Ankara: Palme.
Martin, C. (2020). Effective dose in medicine. *Annals of the ICRP, 49*(1_suppl), 126-140.
Protection, I. C. o. R. International Commission on Radiolgical Protection (ICRP). Retrieved from https://www.icrp.org/
Shah, N., Bansal, N., & Logani, A. (2014). Recent advances in imaging technologies in dentistry. *World journal of radiology, 6*(10), 794.
Thorn, J. J., Hansen, H. S., Specht, L., & Bastholt, L. (2000). Osteoradionecrosis of the jaws: clinical characteristics and relation to the field of irradiation. *Journal of oral maxillofacial surgery, 58*(10), 1088-1093.
White, S. C., & Pharoah, M. J. (2014). *Oral radiology-E-Book: Principles and interpretation* (7 ed.). New York, USA: Elsevier Health Sciences.
Yalçın, E. D. (2019). Radyoterapi ve kemoterapi öncesi ve sonrası dental yaklaşımlar. *Turkiye Klinikleri Oral Maxillofacial Radiology-Special Topics, 5*(3), 7-16.
Yeung, A. (2019). The'As Low as Reasonably Achievable'(ALARA) principle: a brief historical overview and a bibliometric analysis of the most cited publications. *Radioprotection*.
Zhou, A. (2023). Radiobiology and Radiation Protection. In *Computed Tomography: Advanced Clinical Applications* (pp. 3-18): Springer.
Zhou, A., Tan, Q., & Davidson, R. (2020). *Image enhancement using convolutional neural network*. Paper presented at the 2020

International Conference on Image, Video Processing and Artificial Intelligence.

CHAPTER 3

MATERIAL SELECTION AND ADHESIVE CEMENTATION IN INDIRECT RESTORATION APPLICATIONS

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INTRODUCTION

In recent years, the adoption of computer-aided design and manufacturing (CAD/CAM) technologies in dentistry has grown significantly. This advancement has positioned the development and investigation of materials compatible with CAD/CAM systems as one of the most dynamic and rapidly progressing fields in dental materials science. The ability of these systems to eliminate the need for conventional impressions and to deliver restorations with improved precision in a shorter timeframe plays a key role in their increasing popularity.

CAD/CAM technology has found widespread application across various areas of dentistry, including the fabrication of inlays, onlays, crowns, laminate veneers, complete dentures, frameworks for removable partial dentures, post-core restorations, and the design and manufacture of surgical guides used in implantology (Çömlekoğlu, 2018; Vichi et al., 2014). Understanding the general characteristics of aesthetic indirect restorative materials suitable for CAD/CAM processing is essential for identifying appropriate clinical indications.

These materials are generally categorized into two main groups: glass-ceramics/ceramics and composite resins. Glass-ceramic and ceramic materials are known for their high strength and hardness but are inherently brittle with low fracture toughness (Nguyen et al., 2012). Due to their superior optical characteristics—such as translucency, fluorescence, and opalescence—they are often preferred for cases where aesthetic outcomes are a priority, outperforming resin-based materials in this regard (Güth et al., 2013; Lim et al., 2010).

Composite resin materials, by contrast, are favored for their simpler fabrication processes and improved potential for intraoral repair. When repairing ceramic or glass-ceramic restorations, the surface must be etched with hydrofluoric acid—a substance that is both abrasive and toxic—before applying a composite resin that differs significantly in physical and optical behavior (Tsitrou et al., 2007). On the other hand, composite restorations can be more easily repaired by sandblasting the surface and applying a resin composite with matching material properties (Tsitrou et al., 2007).

1.Types of CAD/CAM Materials

1.1. Feldspathic Ceramic Blocks

Since the 1980s, advancements in CAD/CAM technology within dentistry have enabled the industrial fabrication of feldspathic ceramic blocks. Compared to traditional methods, these industrially manufactured blocks are reported to minimize internal porosity, enhancing structural consistency (Vita Zahnfabrik, 2012).

According to various studies, feldspathic ceramic blocks are considered suitable for a range of restorations, including inlays, onlays, veneers, partial crowns, and full-coverage crowns (Denry & Kelly, 2008). In a study conducted by Sağlam et al. (2020), which assessed the marginal fit and fracture resistance of feldspathic versus polymer-infiltrated ceramic CAD/CAM endocrowns used on maxillary premolars, both materials showed clinically acceptable marginal adaptation. However, the polymer-infiltrated ceramic endocrowns exhibited superior fracture resistance compared to their feldspathic counterparts.

1.2. Leucite-Reinforced (LS) Glass Ceramic Blocks

Leucite-reinforced (LS) blocks contain a leucite crystal phase that makes up around 30–40% of the glass matrix by volume (Liebermann et al., 2019). These materials exhibit translucency and wear characteristics that closely resemble those of natural enamel (Giordano, 1996). Avram et al. (2022) found that treating LS blocks with hydrofluoric acid for 90 seconds enhances their micro-shear bond strength. Similarly, a study by Gönüldaş et al. (2019), which explored the impact of various surface finishing techniques on both feldspathic and leucite-reinforced ceramics, reported that applying a glaze coating substantially improves the flexural strength of LS ceramics.

Current literature supports the use of LS blocks in the fabrication of partial and full crowns as well as laminate veneers (Fasbinder, 2002). Furthermore, due to their favorable stress distribution, LS materials have been proposed as a viable alternative to lithium disilicate ceramics in endocrown restorations (Tribst et al., 2018).

1.3. Lithium Disilicate-Reinforced (LDS) Glass Ceramic Blocks

Lithium disilicate (LDS) blocks are brittle ceramic materials composed of approximately 57–80% quartz, 11–19% lithium oxide, and up to 5% aluminum oxide, and they present some challenges in terms of machinability (Cengiz & Ordu, 2015). These blocks are typically supplied in a partially crystallized state and undergo a thermal treatment process at 850 °C, during which their crystalline phase transforms into lithium metasilicate, significantly enhancing their mechanical strength (Cengiz & Ordu, 2015). The flexural strength of LDS materials ranges from 320 to 450 MPa, while their elastic modulus lies between 90 and 95 GPa (Höland et al., 2007).

LDS ceramics offer a favorable combination of translucency and mechanical durability. Various studies have shown that LDS restorations outperform zirconia in certain clinical outcomes (Aziz et al., 2020). For instance, Moher et al. (2009) reported that LDS restorations exhibited three times the flexural strength of leucite-reinforced ceramics. Long-term clinical performance has also been promising: Cortellini and Canale (2012) documented a 10-year survival rate of 90%, whereas Garling et al. (2019) noted a reduced survival rate of 49% over a 15-year period. Notably, research by Hammoudi et al. (2020) showed a 6-year survival rate of 99.7% in patients with bruxism. Given that chronic bruxism is typically associated with higher failure rates in restorations (Minervini et al., 2022), these findings suggest that LDS ceramics may offer a reliable solution for patients exhibiting parafunctional habits.

According to the literature, lithium disilicate (LDS) blocks are widely recommended for a variety of restorative applications, including veneers, inlays, onlays, anterior and posterior crowns, three-unit bridges excluding molar involvement, as well as for hybrid abutments and abutment superstructures (Taskonak et al., 2005).

Tribst et al. (2019) reported that both LDS and leucite-reinforced (LS) ceramics show satisfactory fracture resistance and clinical performance in endocrown applications, provided that enamel bonding is achieved and a minimum material thickness of 1.5 mm is maintained.

In a recent investigation by Ellakany et al. (2023), which evaluated how various CAD/CAM ceramics and material thicknesses influence the mechanical properties of ceramic restorations, LDS blocks exhibited the highest microhardness and the lowest surface roughness among the materials tested. The study recommended an optimal thickness of 1.5 mm for full-ceramic restorations and 0.5 mm for ceramic veneers.

1.4. Zirconia-Reinforced Lithium Disilicate Ceramic Blocks (ZLS)

Zirconia-reinforced lithium silicate (ZLS) materials typically contain 8–12% zirconium dioxide (ZrO_2) and are available in both pre-crystallized and fully crystallized forms (Güth et al., 2013). Upon thermal processing, the pre-crystallized variants undergo transformation into their crystallized state, significantly enhancing their mechanical strength. The rising popularity of ZLS blocks in CAD/CAM dentistry is largely due to their combination of high mechanical durability—conferred by the zirconia content—and desirable esthetic qualities—attributed to the glass-ceramic matrix (Komar et al., 2021).

Unlike more opaque zirconia ceramics, ZLS materials exhibit greater translucency and are manufactured in both high-translucency (HT) and low-translucency (LT) options. The flexural strength of ZLS has been reported to range from 405 to 553 MPa, which is notably higher than the 300–441 MPa range typically observed in lithium disilicate (LDS) materials (Curran et al., 2017; Elsaka & Elnaghy, 2016).

ZLS blocks are recommended for various clinical applications, including crowns, veneers, inlays, onlays, and implant abutments (Vita Zahnfabrik, 2012). Furthermore, Darwich et al. (2023) proposed ZLS as a suitable option for endocrown restorations due to its favorable stress-distribution characteristics.

1.5. Hybrid Ceramic Blocks

Ceramic-based restorative materials, while known for their high hardness and superior wear resistance, tend to be more brittle and prone to fracture compared to composite resins. Their hardness, although advantageous in terms of durability, can contribute to increased wear of opposing dentition (Fron Chabouis et al., 2013; Solá-Ruíz et al., 2020). Hybrid materials, which integrate characteristics of both ceramics and composites, provide a more balanced performance. These materials typically exhibit an elastic modulus close to that of natural dentition and offer improved reparability, similar to composite resins (Amesti-Garaizabal et al., 2019).

One such material, *Vita Enamic*, is a polymer-infiltrated ceramic network (PICN) hybrid block that contains approximately 14% by weight and 25% by volume of urethane dimethacrylate (UDMA) and triethylene glycol dimethacrylate (TEGDMA) (Swain et al., 2016). With an elastic modulus in the range of 30–32 GPa, Vita Enamic closely replicates the biomechanical behavior of natural tooth structure (He & Swain, 2011). Its ability to resist crack initiation and propagation makes it especially effective under high occlusal loads, and its gentler interaction with antagonist teeth minimizes the risk of excessive wear (Coldea et al., 2015).

Hybrid ceramic blocks such as Vita Enamic are suggested in the literature for a variety of indications, including inlays, onlays, veneers, full crowns, restorations on molars subjected to high masticatory forces, and cases requiring conservative tooth preparation (Raigrodski, 2004).

1.6. Resin Nano-Ceramic (RNC) Blocks

Lava Ultimate (3M), one of the pioneering nano-ceramic materials on the market, incorporates silica particles approximately 20 nm in size and zirconia particles ranging from 4 to 11 nm. The ceramic content constitutes about 80% of the material's polymer matrix (Fasbinder, 2018). While the manufacturer reports a flexural strength of 200 MPa for Lava Ultimate—surpassing that of feldspathic and leucite-reinforced ceramics (Fasbinder, 2012)—independent laboratory studies have measured the flexural strength closer to 170 MPa (Albero et al., 2015; Awada & Nathanson, 2015).

Resin nanoceramic (RNC) blocks like Lava Ultimate are commonly recommended for applications including inlays, onlays, laminate veneers, crowns, and implant-supported crowns (GC America). Shembish et al. (2016) demonstrated that monolithic Lava Ultimate CAD/CAM crowns can endure significant fatigue stresses, fulfilling the mechanical demands of high-load posterior restorations, thus supporting their use in such clinical scenarios.

However, Liebermann et al. (2019) reported that Lava Ultimate showed a higher degree of color alteration when subjected to different storage media and temperature conditions, indicating potential limitations in color stability.

1.7. Composite Blocks

Composite CAD/CAM blocks incorporate zirconia-silica fillers roughly 0.6 μm in size, accounting for approximately 85% of the material's weight (Paradigm, 2006). These blocks offer excellent intraoral adaptability and can be conveniently repaired using conventional composite resin restorative materials. Clinically, they are indicated for a variety of restorations including inlays, onlays, veneers, and full crowns (Paradigm, 2006).

Beyond aesthetics, composite blocks are relatively cost-effective, cause less wear on opposing teeth, and align well with minimally invasive dentistry principles (Avram, 2022). Compared to ceramic alternatives, resin-based CAD/CAM materials demonstrate a more favorable elastic modulus, enhanced load-bearing capacity, and improved machinability (Awada & Nathanson, 2015; Rohr et al., 2015).

Long-term clinical data indicate somewhat higher survival rates for ceramic restorations. Mangani et al. (2015) reported survival rates of 94.9% for ceramic versus 91.1% for composite restorations. Similarly, Goujat et al. (2019) observed a 10-year success rate of 88.7% for ceramics compared to 84.78% for composites over a 5-year follow-up. However, a randomized clinical trial by Van Meerbeek et al. (2019) found no statistically significant difference in 3-year survival between composite and ceramic CAD/CAM restorations.

1.8. Zirconia Blocks

Zirconia is a heterogeneous polycrystalline ceramic known for its exceptional mechanical properties, exhibiting flexural strengths ranging from 500 to 1200 MPa and an elastic modulus of approximately 210 GPa (Denry & Kelly, 2008; Zarone et al., 2011). Both clinical and laboratory studies have demonstrated that zirconia surfaces accumulate less plaque compared to titanium and possess excellent biocompatibility (Nakashima et al., 2016).

While zirconia is generally more opaque than glass ceramics, newer formulations containing 30–35% cubic zirconia offer enhanced translucency. However, this increased translucency comes at the expense of mechanical strength, as the larger cubic grains yield lower flexural resistance values, typically between 500 and 900 MPa (Shahmiri et al., 2018).

Zirconia blocks are widely used for fabricating single crowns, implant abutments, and three-unit fixed dental prostheses, with a minimum recommended thickness of 0.5 mm for monolithic restorations (Sorrentino et al., 2016). The introduction of the first zirconia block, Cerec Zirconia by Dentsply Sirona in 2016, was accompanied by the development of the SpeedFire induction furnace, which significantly reduced sintering times to under 20 minutes, enabling same-day design, milling, and delivery of restorations (Marchesi et al., 2021).

Although zirconia restorations can be cemented using either conventional or adhesive techniques, current evidence does not definitively favor one method over the other in terms of retention strength.

2. Surface Preparation of CAD/CAM Materials Prior to Adhesive Cementation

Surface treatment of CAD/CAM restorative materials is essential for optimizing their bonding strength to dental tissues. A comprehensive understanding of the ceramic microstructure is critical to achieving effective surface conditioning. Treatments can be broadly classified into chemical and mechanical methods (Strasser et al., 2018).

Chemical surface treatment commonly involves the application of hydrofluoric acid at concentrations of 5% or 9% (Tian et al., 2014). This acid selectively etches the silica phase of the ceramic, resulting in the formation of hexafluorosilicic acid and creating micro-retentive sites that enhance the bonding surface for resin cements (Alex, 2008). Following etching, a silane coupling agent—such as Monobond—is applied to improve chemical adhesion. Silane molecules contain functional groups like phosphoric acid and sulfur methacrylate, which facilitate coupling between the ceramic surface and resin cement.

Mechanical surface preparation typically involves airborne-particle abrasion using aluminum oxide particles with sizes ranging from 25 to 50 µm. This method effectively roughens the surface, particularly impacting hybrid ceramic-resin and zirconia materials, thereby improving micromechanical retention (Alsaeed, 2022).

2.1. Adhesion in Restorations Containing Glass Matrix

Prior to cementation, the surfaces of feldspathic, leucite-reinforced, and lithium disilicate ceramics must be etched using hydrofluoric acid gel or phosphate fluoride. This acidic treatment selectively dissolves portions of the silica matrix, thereby exposing the glassy phase and enhancing the surface roughness. Such modification significantly improves the bonding efficacy of resin-based luting cements to the treated ceramic surface (Alsaeed, 2022).

Additionally, silane coupling agents facilitate adhesion by forming siloxane bonds that chemically link the inorganic ceramic substrate to the organic components of the bonding resin, thereby strengthening the interface (Matinlinna et al., 2006).

2.2. Adhesion in Polymer-Infiltrated Restorations

Polymer-infiltrated materials feature a microstructure composed predominantly of a ceramic matrix with a relatively lower polymer filler content. To optimize bonding with resin cement, these materials undergo acid etching, which selectively removes portions of the ceramic matrix and exposes the underlying resin network, thereby enhancing the interfacial adhesion (Hu et al., 2016).

2.3. Adhesion in Zirconia Restorations

With the growing availability of CAD/CAM technologies, zirconia has become one of the most commonly used restorative materials. Due to the absence of silica in zirconia, acid etching is ineffective for surface roughening. Consequently, bonding relies on the APC protocol, which consists of three key steps: airborne particle abrasion, application of a zirconia-specific primer, and the use of adhesive resin cement (Blatz et al., 2016).

2.4. Adhesion in Nanoceramic Indirect Restorations

New hybrid materials such as Lava Ultimate present several benefits compared to traditional composite resins, including a glossy finish, satisfactory compressive strength, and excellent machinability and reparability. These materials are composed of roughly 20% resin matrix by weight, reinforced with approximately 80% zirconia and silica filler particles (Fasbinder, 2012). Surface conditioning is typically achieved through airborne particle abrasion using 27 μm aluminum oxide particles at a pressure of 2 bar (Özcan & Volpato, 2016). This sandblasting procedure enhances surface roughness, facilitating both micromechanical interlocking and chemical adhesion of the resin-based adhesive cement (Blatz et al., 2003).

3. Adhesive Resin Cements for CAD/CAM Restorations

Resin cements are categorized according to their chemical bonding mechanisms with tooth structures into non-adhesive, chemically bonding, and micromechanically bonding types (Sillas Duarte Jr, 2011). Non-adhesive cements, which do not require any prior surface treatment of the tooth or restoration, are predominantly used for metal-supported porcelain or ceramic restorations with thicknesses ranging from 1.5 to 2 mm.

Etch-and-rinse adhesive cements, including products such as Variolink II (Ivoclar-Vivadent), RelyX ARC (3M ESPE), Variolink Veneer (Ivoclar-Vivadent), and RelyX Veneer Cement (3M ESPE), employ a protocol similar to that of conventional etch-and-rinse adhesive systems. Typically, the tooth surface is conditioned with 35% phosphoric acid to promote deeper penetration of the resin cement (Thompson et al., 2011).

Self-etch adhesive cements, exemplified by Clearfil Esthetic Cement, Panavia 21, and Panavia F 2.0 (all Kuraray Noritake Dental), eliminate the need for rinsing as their acidic monomers chemically modify the smear layer during application (Tay et al., 2000). The incorporation of 10-MDP monomer in these cements significantly improves bond strength (Van Meerbeek et al., 2011). These self-etch cements exhibit a range of acidic pH values: ultra-mild ($pH > 2.5$), mild ($pH \approx 2.0$), and strong ($pH \approx 1.0$) (Van Meerbeek et al., 2011), and do not require separate surface treatment.

Shear bond strength tends to be lowest with zinc phosphate and glass ionomer cements. Peutzfeldt et al. (2011) identified the highest bond strengths in cements such as Panavia F2.0, Multilink (Ivoclar-Vivadent), and RelyX Unicem (3M ESPE).

Self-etch cements generally achieve superior adhesion to dentin compared to self-adhesive variants (Alsaeed, 2022). Furthermore, dual-cure or light-cured self-etch cements demonstrate enhanced bonding performance on enamel surfaces (Alsaeed, 2022).

Conclusion

Recent advancements in digital impression-taking and manufacturing technologies have significantly increased their adoption in dental practices. Consequently, the research and development of materials compatible with CAD/CAM systems have become among the fastest evolving areas within dental material science. In a survey conducted by Nassabi et al., the majority of respondents (81%) expressed the opinion that chairside CAD/CAM restorations are of equal or superior quality compared to those fabricated by dental laboratory technicians (Van Meerbeek et al., 2019).

A 2021 survey investigating dentists' material preferences for single-unit posterior crowns revealed that 32% favored monolithic zirconia restorations, while 21% preferred lithium disilicate glass ceramics (Nassani et al., 2021).

While the success of CAD/CAM restorations largely hinges on the physicomechanical properties of the chosen material, factors such as proper case selection, accurate tooth preparation, and correct material application also play critical roles (Denry & Kelly, 2008).

For effective adhesion to ceramic substrates, micro-retentive surfaces are commonly achieved via sandblasting or hydrofluoric acid etching, followed by the application of a silane-based primer like Monobond to enhance chemical bonding.

Ultimately, the longevity and success of CAD/CAM restorations depend on selecting an appropriate material, ensuring optimal bonding procedures, and choosing the correct luting cement. Three-step adhesive systems are typically favored when enamel is present, whereas self-etch adhesive systems are preferred for dentin substrates.

MATERIAL	INDICATION	Example (Manufacturer)
Feldspathic Ceramic Blocks	Inlay, onlay, veneer, partial/full crown	VITABLOCKS Mark II (VITA, BadSäckingen, Germany), VITABLOCS TriLuxe (VITA, BadSäckingen, Germany)
Lithium Silicate (LS) Reinforced Glass Ceramic Blocks	Partial/full crown, laminate veneer	IPS Empress CAD (Ivoclar-Vivadent, Schaan, Liechtenstein)
Lithium Disilicate (LDS) Reinforced Glass Ceramic Blocks	Thin veneer (0.4 mm), veneer, inlay, onlay, crown, three-unit bridges excluding molars, hybrid abutments, and the superstructures of these abutments	IPS e.max CAD (Ivoclar-Vivadent, Schaan, Liechtenstein)
Zirconia-Reinforced Lithium Disilicate Ceramic Blocks (ZLS)	Crown, implant-supported crown, veneer, inlay, onlay	Vita Suprinity (VITA Zahnfabrik, Bad Säckingen, Germany), Celtra Duo (Dentsply, KT13 0NY, United Kingdom)
Hybrid Ceramic Blocks	Inlays, onlays, veneers, crowns, in large molars subjected to high occlusal forces, and in teeth with minimal preparation	Vita Enamic (VITA, Bad Säckingen, Germany), Block HC (Shofu Inc., Kyoto, Japan)

Resin Nanoceramics (RNS)	Inlays, onlays, laminate veneers, crowns, implant-supported crowns	Lava Ultimate (3M ESPE, Rüschlikon, Switzerland), Cerasmart blocks (GC Corp., Tokyo, Japan)
Composites	Inlay, onlay, veneer, crown	Paradigm MZ100 (3M ESPE, Rüschlikon, Switzerland)
Zirconia Blocks	Crown, implant abutments, three-unit bridges	CEREC Zirconia e.max (Dentsply Sirona, KT13 0NY, UK), ZirCAD (Ivoclar-Vivadent, Schaan, Liechtenstein)

Table 1: CAD/CAM Materials, Their Indications, and Examples of Available Products on the Market

REFERENCES

Alex, G. (2008). Preparing porcelain surfaces for optimal bonding. *Compendium of Continuing Education in Dentistry*, 29(6), 324–335.

Albero, A., Pascual, A., Camps, I., & Grau-Benitez, M. (2015). Comparative characterization of a novel CAD/CAM polymer-infiltrated-ceramic network. *Journal of Clinical and Experimental Dentistry*, 7(4), 495–500.

Alsaeed, A. Y. (2022). Bonding CAD/CAM materials with current adhesive systems: An overview. *Saudi Dental Journal*, 34, 259–269.

Amesti-Garaizabal, A., Agustín-Panadero, R., Verdejo-Solá, B., Fons-Font, A., Fernández-Estevan, L., Montiel-Company, J., & Solá-Ruíz, M. F. (2019). Fracture resistance of partial indirect restorations made with CAD/CAM technology: A systematic review and meta-analysis. *Journal of Clinical Medicine*, *8*, 1932–1943.

Avram, L. T., Galatanu, S. V., Opris, C., Pop, C., & Jivănescu, A. (2022). Effect of different etching times with hydrofluoric acid on the bond strength of CAD/CAM ceramic material. *Materials*, 15, 7071–7084.

Azeem, R. A., & Sureshbabu, N. M. (2018). Clinical performance of direct versus indirect composite restorations in posterior teeth: A systematic review. *Journal of Conservative Dentistry*, 21(1), 2–9.

Aziz, A., El-Mowafy, O., & Paredes, S. (2020). Clinical outcomes of lithium disilicate glass-ceramic crowns fabricated with CAD/CAM technology: A systematic review. *Dental and Medical Problems*, *57*, 197–206.

Awada, A., & Nathanson, D. (2015). Mechanical properties of resin-ceramic CAD/CAM restorative materials. *Journal of Prosthetic Dentistry*, 114(4), 587–593.

Blatz, M. B., Alvarez, M., Sawyer, K., & Brindis, M. (2016). How to bond zirconia: The APC concept. *Compendium of Continuing Education in Dentistry*, 37(9), 611–617.

Blatz, M. B., Sadan, A., & Kern, M. (2003). Resin-ceramic bonding: A review of the literature. *Journal of Prosthetic Dentistry*, 89(3), 268–274.

Cengiz, S., & Ordu, Ü. (2015). Klinikte kullanılan CAD/CAM sistemlerinin güncel materyalleri. *Journal of International Dental Sciences*, 1, 9–12.

Coldea, A., Fischer, J., Swain, M. V., & Thiel, N. (2015). Damage tolerance of indirect restorative materials (including PICN) after simulated bur adjustments. *Dental Materials*, 31(6), 684–696.

Cortellini, D., & Canale, A. (2012). Bonding lithium disilicate ceramic to feather-edge tooth preparations: A minimally invasive treatment concept. *Journal of Adhesive Dentistry*, 14, 7–10.

Curran, P., Cattani-Lorente, M., Wiskott, H. W. A., Durual, S., & Scherrer, S. S. (2017). Grinding damage assessment for CAD-CAM restorative materials. *Dental Materials, 33*, 294–308.

Çömlekoğlu, E. (2018). Klinik tipi CAD/CAM sistemlerinde kullanılan materyaller. *Protetik Diş Tedavisinde CAD/CAM Uygulamaları, Türkiye Klinikleri*, 1, 24–32.

Darwich, A., Aljareh, A., Alhouri, N., Szávai, S., Nazha, H., Duvigneau, F., Juhre, D. Biomechanical Assessment of Endodontically Treated Molars Restored by Endocrowns Made from Different CAD/CAM Materials. Materials, 16,764-781.

Denry, I., & Kelly, J. R. (2008). State of the art of zirconia for dental applications. *Dental Materials*, 24, 299–307.

Ellakany, P., Madi, M., Aly, N. M., Alshehri, T., Alameer, S. T., & Al-Harbi, F. A. (2023). Influences of different CAD/CAM ceramic compositions and thicknesses on the mechanical properties of ceramic restorations: An in vitro study. *Materials*, 16, 646–660.

Elsaka, S. E., & Elnaghy, A. M. (2016). Mechanical properties of zirconia reinforced lithium silicate glass-ceramic. *Dental Materials*, 32, 908–914.

Fasbinder, D. J. (2002). Restorative material options for CAD/CAM restorations. *Compendium of Continuing Education in Dentistry*, 23, 911–916.

Fasbinder, D. J. (2012). Chairside CAD/CAM: An overview of restorative material options. *Compendium of Continuing Education in Dentistry*, 33(1), 50–58.

Fasbinder, D. J. (2018). A review of chairside CAD/CAM restorative materials. *Journal of Cosmetic Dentistry*, 34(3), 64–75.

Fron Chabouis, H., Smail Faugeron, V., & Attal, J. P. (2013). Clinical efficacy of composite versus ceramic inlays and onlays: A systematic review. *Dental Materials*, 29, 1209–1218.

Garling, A., Sasse, M., Becker, M. E. E., & Kern, M. (2019). Fifteen-year outcome of three-unit fixed dental prostheses made from monolithic lithium disilicate ceramic. *Journal of Dentistry*, 89, 103178.

Giardano, R. A. (1996). Dental ceramic restorative systems. *Compendium of Continuing Education in Dentistry*, 17, 779–782.

Goujat, A., Abouelleil, H., Colon, P., Jeannin, C., Pradelle, N., Seux, D., & Grosgogeat, B. (2019). Marginal and internal fit of CAD-CAM inlay/onlay restorations: A systematic review of in vitro studies. *Journal of Prosthetic Dentistry*, 121, 590–597.

Gönüldaş, F., Öztürk, C., Atalay, P., & Öztaş D. (2019). Influence of different surface finishing techniques on machinable feldspathic and leucite-reinforced ceramics. Dental Materials Journal, 38: 317–322.

Güth, J. F., Zuch, T., Zwinge, S., Engels, J., Stimmelmayr, M., & Edelhoff, D. (2013). Optical properties of manually and CAD/CAM-fabricated polymers. *Dental Materials Journal*, 32, 865–871.

Hammoudi, W., Trulsson, M., Svensson, P., & Smedberg, J. I. (2020). Long-term results of a randomized clinical trial of 2 types of ceramic crowns in participants with extensive tooth wear. *Journal of Prosthetic Dentistry*, 127, 248–257.

He, L. H., & Swain, M. (2011). A novel polymer infiltrated ceramic dental material. *Dental Materials*, 27(6), 527–534.

Höland, W., Rheinberger, V., Apel, E., & van't Hoen, C. (2007). Principles and phenomena of bioengineering with glass-ceramics for dental restoration. *Journal of the European Ceramic Society*, 27(2-3), 1521–1526.

Hu, M., Weiger, R., & Fischer, J. (2016). Comparison of two test designs for evaluating the shear bond strength of resin composite cements. *Dental Materials*, 32(2), 223–232.

Kelly, J. R., Nishimura, I., & Campbell, S. D. (1996). Ceramics in dentistry: Historical roots and current perspectives. *Journal of Prosthetic Dentistry*, 75, 18–32.

Komar, D., Bago, I., Vranić, D. N., Kranjčić, J., Brkić, B., & Carek, A. (2021). Influence of different surface pretreatments of zirconium dioxide reinforced lithium disilicate ceramics on the shear bond strength of self-adhesive resin cement. *Acta Stomatologica Croatica*, 55(3), 264–279.

Liebermann, A., Vehling, D., Eichberger, M., & Stawarczyk, B. (2019). Impact of storage media and temperature on color stability of tooth-colored CAD/CAM materials for final restorations. *Journal of Applied Biomaterials*, 17(4), 1–7.

Lim, H. N., Yu, B., & Lee, Y. K. (2010). Spectroradiometric and spectrophotometric translucency of ceramic materials. *Journal of Prosthetic Dentistry*, 104, 239–246.

Makhija, S. K., Lawson, N. C., Gilbert, G. H., et al. (2016). Dentist material selection for single-unit crowns: Findings from the National Dental Practice-Based Research Network. *Journal of Dentistry*, 55, 40–47.

Mangani, F., Marini, S., Barabanti, N., Preti, A., & Cerutti, A. (2015). The success of indirect restorations in posterior teeth: A systematic review of the literature. *Minerva Stomatologica*, 64(5), 231–240.

Marchesi, G., Camurri Piloni, A., Nicolin, V., Turco, G., & Di Lenarda, R. (2021). Chairside CAD/CAM materials: Current trends of clinical uses. *Biology*, 10, 1170–1181.

Matinlinna, J. P., Heikkinen, T., Ozcan, M., Lassila, L. V., & Vallittu, P. K. (2006). Evaluation of resin adhesion to zirconia ceramic using some organosilanes. *Dental Materials*, 22(9), 824–832.

Miura, S., & Fujisawa, M. (2020). Current status and perspective of CAD/CAM-produced resin composite crowns: A review of clinical effectiveness. *Japanese Dental Science Review*, 56, 184–189.

Minervini, G., Fiorillo, L., Russo, D., Lanza, A., D'Amico, C., Cervino, G., Meto, A., & Di Francesco, F. (2022). Prosthodontic treatment in patients with temporomandibular disorders and orofacial pain and/or bruxism: A review of the literature. *Prosthesis*, 4, 253–262.

Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *Annals of Internal Medicine*, 151, 264–269.

Nakashima, J., Taira, Y., & Sawase, T. (2016). In vitro wear of four ceramic materials and human enamel on enamel antagonist. *European Journal of Oral Sciences*, 124, 295–300.

Nassani, M. Z., Ibraheem, S., Shamsy, E., Darwish, M., Faden, A., & Kujan, O. (2021). A survey of dentists' perception of chair-side CAD/CAM technology. *Healthcare*, 9, 68–77.

Nguyen, J. F., Migonney, V., Ruse, N. D., & Sadoun, M. (2012). Resin composite blocks via high-pressure high-temperature polymerization. *Dental Materials*, 28, 534–592.

Özcan, M., & Volpato, C. (2016). Surface conditioning and bonding protocol for nanocomposite indirect restorations: How and why? *Journal of Adhesive Dentistry*, 18(1), 82.

Paradigm C. (2006). Technical Product Profile. St. Paul, MN: 3M ESPE.

Peutzfeldt, A., Sahafi, A., & Flury, S. (2011). Bonding of restorative materials to dentin with various luting agents. *Operative Dentistry*, 36(3), 266–273.

Raigrodski, A. J. (2004). Contemporary all ceramic fixed partial dentures: A review. *Dental Clinics of North America*, 48, 531–544.

Rohr, N., Coldea, A., Zitzmann, N. U., & Fischer, J. (2015). Loading capacity of zirconia implant supported hybrid ceramic crowns. *Dental Materials*, 31, 279–287.

Sağlam, G., Cengiz, S., & Karacaer, O. (2020). Marginal adaptation and fracture resistance of feldspathic and polymer-infiltrated ceramic network CAD/CAM endocrowns for maxillary premolars. *Nigerian Journal of Clinical Practice*, 23(1), 1–6.

Shahmiri, R., Standard, O. C., Hart, J. N., & Sisters, C. C. (2018). Optical properties of zirconia ceramics for esthetic dental restorations: A systematic review. *Journal of Prosthetic Dentistry*, 119, 36–46.

Shembish, F. A., Tong, H., Kaizer, M., Janal, M. N., Thompson, V. P., Opdam, N. J., & Zhang, Y. (2016). Fatigue resistance of CAD/CAM resin composite molar crowns. *Dental Materials*, 32(4), 499–509.

Sillas Duarte Jr, N. S. (2011). Adhesive resin cements for bonding esthetic restorations: A review. *Quintessence Dental Technology*.

Solá-Ruíz, M. F., Baima-Moscardó, A., Selva-Otaolaurruchi, E., Montiel-Company, J. M., Agustín-Panadero, R., Fons-Badal, C., & Fernández-Estevan, L. (2020). Wear in antagonist teeth produced by monolithic zirconia crowns: A systematic review and meta-analysis. *Journal of Clinical Medicine*, 9(4), 997–1014.

Sorrentino, R., Triulzio, C., Tricarico, M. G., Bonadeo, G., Gherlone, E. F., & Ferrari, M. (2016). In vitro analysis of the fracture resistance of CAD-CAM monolithic zirconia molar crowns with different occlusal thickness. *Journal of the Mechanical Behavior of Biomedical Materials*, 199, 36–46.

Strasser, T., Preis, V., Behr, M., & Rosentritt, M. (2018). Roughness, surface energy, and superficial damages of CAD/CAM materials after surface treatment. *Clinical Oral Investigations*, 22(8), 2787–2797.

Swain, M. V., Coldea, A., Bilkhair, A., & Guess, P. C. (2016). Interpenetrating network ceramic-resin composite dental restorative materials. *Dental Materials*, 32(1), 34–42.

Taskonak, B., et al. (2005). Residual stresses in bilayer dental ceramics. *Biomaterials*, 26, 3235–3241.

Tay, F. R., Carvalho, R., Sano, H., & Pashley, D. H. (2000). Effect of smear layers on the bonding of a self-etching primer to dentin. *Journal of Adhesive Dentistry*, 2(2), 99–116.

Thompson, J. Y., Stoner, B. R., Piascik, J. R., & Smith, R. (2011). Adhesion/cementation to zirconia and other non-silicate ceramics: Where are we now? *Dental Materials*, 27(1), 71–82.

Tian, T., Tsoi, J. K. H., Matinlinna, J. P., & Burrow, M. F. (2014). Aspects of bonding between resin luting cements and glass ceramic materials. *Dental Materials*, 30(7), e147–e162.

Tribst, J. P. M., Dal Piva, A. M. O., Madruga, C. F. L., Valera, M. C., Borges, A. L. S., Bresciani, E., et al. (2018). Endocrown restorations: Influence of dental remnant and restorative material on stress distribution. *Dental Materials*. https://doi.org/10.1016/j.dental.2018.11.008

Tribst, J. P. M., Dal Piva, A. M. O., Madruga, C. F. L., Valera, M. C., Bresciani, E., Bottino, M. A., & Melo, R. M. (2019). The impact of restorative material and ceramic thickness on CAD/CAM endocrowns. *Journal of Clinical and Experimental Dentistry*, 11(11), 969–977.

Tsitrou, E. A., Northeast, S. E., & van Noort, R. (2007). Brittleness index of machinable dental materials and its relation to the marginal chipping factor. *Journal of Dentistry*, 35, 897–902.

Van Meerbeek, B., Yoshihara, K., Yoshida, Y., Mine, A., De Munck, J., & Van Landuyt, K. L. (2019). State of the art of self-etch adhesives. *Dental Materials*, 31(1), 13–25.

Van Meerbeek, B., Yoshihara, K., Yoshida, Y., Mine, A., De Munck, J., & Van Landuyt, K. L. (2011). State of the art of self-etch adhesives. *Dental Materials*, *27*(1), 17–28.

Vichi A, Carrabba M, Paravina R, Ferrari M. (2014), Translucency of ceramic materials for CEREC CAD/CAM system, *J Esthet Restor Dent*, 26(4), 224-231.

Vita Zahnfabrik. (2012). *VITABLOCS® working instructions 1769E (05)*. https://www.vita-zahnfabrik.com/.

Zarone, F., Russo, S., & Sorrentino, R. (2011). From porcelain-fused to metal to zirconia: Clinical and experimental considerations. *Dental Materials, 87*, 83–96.

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