CESPU
INSTITUTO UNIVERSITÁRIO
DE CIÊNCIAS DA SAÚDE

Calcium silicate-based cements and glass ionomer in permanent tooth external root resorption – a scoping review

Giulia Gardin

Dissertação conducente ao Grau de Mestre em Medicina Dentária (Ciclo Integrado)

Gandra, 18 de setembro de 2021

CESPU
INSTITUTO UNIVERSITÁRIO
DE CIÊNCIAS DA SAÚDE

Giulia Gardin

Dissertação conducente ao Grau de Mestre em Medicina Dentária (Ciclo Integrado)

Calcium silicate-based cements and glass ionomer in permanent tooth external root resorption – a scoping review

Trabalho realizado sob a Orientação de Professor Doutor Paulo Manuel Cruz Miller

CESPU
INSTITUTO UNIVERSITÁRIO
DE CIÊNCIAS DA SAÚDE

Declaração de Integridade

Eu, Giulia Gardin declaro ter atuado com absoluta integridade na elaboração deste trabalho, confirmo que em todo o trabalho conducente à sua elaboração não recorri a qualquer forma de falsificação de resultados ou à prática de plágio (ato pelo qual um indivíduo, mesmo por omissão, assume a autoria do trabalho intelectual pertencente a outrem, na sua totalidade ou em partes dele). Mais declaro que todas as frases que retirei de trabalhos anteriores pertencentes a outros autores foram referenciadas ou redigidas com novas palavras, tendo neste caso colocado a citação da fonte bibliográfica.

AGRADECIMENTOS

Os agradecimentos são a coisa mais difícil neste momento, tem medo de não encontrar as palavras certas ou de esquecer alguém.

Por isso, por ordem, devo agradecer aos meus companheiros de viagem que fizeram parte da minha família durante estes quatro anos, Silvia Bevilacqua, Sara Bertani, Elena Maronato, Giulio Righetti, Eleonora Coppola, Gianmarco Gronelli, Nicola Dabrazzi e Elena Zucchinelli, com quem tenho partilhado tantos, momentos de alegria, de tensão, por vezes difíceis e por vezes de grande satisfação. Estes quatro anos juntos consolidaram as bases para uma amizade que perdurará com o tempo. Em particular, gostaria de agradecer a Marco Manente, o meu amigo fraterno de confiança que sempre esteve perto de mim e sempre me apoiou e suportou em todos os momentos que passámos juntos na Cespu, e Valeria Mancini que desempenhou um papel fundamental nesta experiência, sempre me estimulou, sempre encontrou as palavras certas para me motivar, valorizar-me, ajudar-me a acreditar em mim mesmo e tornar-me consciente das minhas capacidades. Ela nunca hesitou em ajudar-me, mesmo na realização deste trabalho, e embora vivamos distantes, ela será sempre para mim um ponto de referência próximo.

Devo também agradecer o meu binomio Fernanda Pereira, que desempenhou o papel de irmã maior e professora, ensinando-me muito, tanto profissionalmente como pessoalmente, e juntos fizemos um grande trabalho. A sinergia criada durante a nossa colaboração na clínica trouxe-me ao fim de uma viagem cheio de satisfação e gratidão, e embora vivamos em dois países diferentes, ela terá sempre um lugar no meu coração.

Gostaria de agradecer à minha família, Papa Gilberto, Mamma Giovanna e Giovanni, que em 4 anos sempre tiveram fé em mim e me ajudaram a tornar-me na pessoa que sou hoje. Os seus sacrifícios para me ajudar, especialmente neste último ano, nunca poderão ser totalmente reembolsados, mas consciente do que fizeram e farão sempre, esforçar-me-ei todos os dias para que se orgulhem de mim; quando crescer quero ser dentista, mas acima de tudo quero ser como vós.

Agradeço a todos os meus amigos, que sempre aliviaram as dificuldades durante esto longo viagem, dando-me sempre belos momentos.

Gostaria de agradecer à tia Giuliana Gasparini e Giovanni Ballin que, em resposta ao meu pedido de ajuda, deram um forte contributo para a elaboração desta tese.

Gostaria de agradecer ao Studio Crepaldi, Studio Fossani e Studio Stocco que, nos últimos quatro anos, sempre facilitaram o meu trabalho e a minha carreira universitária como estudante pendular sem nunca me colocarem sob pressão, ajudando-me a melhorar sempre como profissional.

Um agradecimento especial vai para Nicola, o meu parceiro e melhor amigo, a quem devo o mérito de ter sido um ponto de força, especialmente durante os 10 meses que estive fora. Ele sempre me fez sentir a sua proximidade, sempre me encorajou em tudo, mesmo nas coisas mais pequenas, e nunca me fez sentir sozinha. Enfrentámos um desafio difícil, tendo estado afastados um do outro durante 10 meses; a vida certamente nos trará outras dificuldades, mas juntos, estando sempre presentes um para o outro, seremos sempre vencedores.

Os meus agradecimentos também ao Dr. Rostand Momo, a vida deu-me a oportunidade de o conhecer e apreciar a ele e a toda a sua família, o seu importante compromisso diário na sala de operações e na vida serão sempre uma fonte de grande exemplo e inspiração para mim.

Gostaria também de agradecer ao Prof. Paulo Miller, meu orientador, pela sua ajuda na redacção desta tese, a sua confiança em mim e o seu encorajamento foram fundamentais para a conclusão deste trabalho.

Gostaria também de agradecer a Vítor Freitas, que contribuiu para aumentar os meus conhecimentos ao longo dos últimos 4 anos, e ao Prof. Pedro Carvalho, que tive o prazer de conhecer este ano no hospital de Penafiel, os vossos ensinamentos ficarão sempre impressos na minha prática profissional diária.

Espero não ter esquecido ninguém, e gostaria de concluir agradecendo mais uma vez a todas as pessoas que me têm estado próximas ao longo destes 4 anos.

Obrigada pela atenção, até já!!!!

RESUMO

Introdução: A Reabsorção radicular externa, é um tipo de reabsorção associada a processos fisiológicos e patológicos; a condição patológica resulta na perda de tecidos como a dentina, cemento, ligamento periodontal e osso alveolar.

Objectivo: O objectivo do nosso estudo é identificar qual dos cimentos Biodentine (Septodont, Saint Maur des Fosses, França), Endosequence Root Repair Material (Brasseler USA, Savannah, GA, USA) ou cimento de ionómero de vidro é o material mais adequado para o tratamento da reabsorção radicular externa.

Materiais e Métodos: Foi realizada uma pesquisa bibliográfica utilizando quatro motores de busca diferentes (PubMed, EBSOC, The Cochrane Library e Onlinelibrary), utilizando as seguintes palavras-chave: "external root resorption" "root resorption" "treatment" "Biodentine" "glass ionomer" "calcium silicate-based cements".

Resultados: Ainda, não existe um " tratamento gold standard " para a gestão da reabsorção radicular externa. O Biodentine^{R} em comparação com o cimento Endosequence Root Repair Material e cimento de ionómero de vidro, obtiveram os melhores resultados.

Discussão: Para que um material endodôntico seja definido como eficaz, deve possuir certas características: ser não tóxico, ser insolúvel, ser dimensionalmente estável, ser antibacteriano, ser condutor de tecidos duros, ser biocompatível, ser radiopaco e ser fácil de manusear. O Biodentine^{R} cumpre os requisitos acima mencionados seguidos pela Endosequence^{R}, que também apresenta bons resultados, mas inferiores ao Biodentine^{R}. Os cimentos de ionómero de vidro relatam resultados mais fracos em comparativamente com o Biodentine^{R} e com o Endosequence^{R}.

Conclusão: Ambos os cimentos de silicato de cálcio são capazes de promover a cura dos tecidos envolvidos na reabsorção externa da raiz, em contraste com os cimentos de ionómero de vidro, que foram considerados menos eficazes.

ABSTRACT

Introduction: External root resorption is a type of resorption associated with both physiological and pathological processes; the pathological condition results in the loss of tissues such as dentin, cementum, periodontal ligament and alveolar bone.

Objective: The aim of our study is to identify which of Biodentine (Septodont, Saint Maur des Fosses, France), Endosequence Root Repair Material (Brasseler USA, Savannah, GA, USA) and Glass ionomer cements is the most suitable material for the treatment of external root resorption.

Materials and Methods: A literature search was performed using four different search engines (PubMed, EBSOC, The Cochrane Library and Online library), using the following keywords: "external root resorption" "root resorption" "treatment" "Biodentine" "glass ionomer" "calcium silicate-based cements".

Results: To date, there is no "gold standard treatment" for the management of external root resorption. Biodentine compared with Endosequence Root Repair Material and Glass ionomer cements reported the best results.

Discussion: For an endodontic material to be defined as effective it must possess certain characteristics: non-toxic, insoluble, dimensionally stable, antibacterial, hard tissue conductive, biocompatible, radiopaque and easy to handle. Biodentine meets the above requirements followed by Endosequence which shows effective results, but with lower performance than Biodentine. Glass ionomer cements reported weaker results in comparison to Biodentine and Endosequence.

Conclusion: Both calcium silicate cements are able to promote healing of tissues involved in external root resorption, in contrast to glass ionomer cements, which were found to be unsuitable.

GENERAL INDEX

TABLE INDEX

INDEX OF FIGURES

LIST OF ABBREVIATIONS AND ACRONYMS

BAG: Bioactive Glass

BD: Biodentine

CBCT: Cone Beam Computed Tomography

CH: Calcium Hydroxide

DSPP: Dentin Sialophosphoprotein

ERRM: Endosequence Root Repair Material

ERR: External Root Resorptions

GIC: Glass Ionomer Cements

HAp: Hydroxyapatite

IERR: Inflammatory External Root Resorption

IRR: Internal Root Resorptions

M-CFS: Macrophage Colony Stimulating Factor

OPG: Osteoprotegerin

PDL: Periodontal Ligament

SCAP: Apical Papilla Stem Cells

CESPU
INSTITUTO UNIVERSITÁRIO
DE CIÊNCIAS DA SAÚDE

1. INTRODUCTION

External root resorption (ERR) is defined as one of the main concerns of endodontists.[1] It can be defined as a multifactorial pathology, the main causes are trauma, orthodontic movements, pressure (adjacent cyst, granuloma, neoplasia, juxtaposed roots, impacted tooth), dento-alveolar surgery, periodontal inflammation, periodontal treatment, chemical irritation (hydrogen peroxide), idiopathic factors and systemic and endocrine diseases (Paget's disease). [2-7] It's a type of resorption associated both physiological and pathological processes; the pathological condition results in the loss of tissues such as dentin, cementum, PDL and alveolar bone. [4,9,10,11] Different from bone, which undergoes continuous physiological remodelling, ERR in the permanent dentition are the result of an inflammatory response that if left untreated would lead to premature loss of the teeth. [5]

ERR tends to occur more frequently in people aged between 21 and 30 years (28.40%) and is more common in females (59.04%) than males. [8] The early stage of ERR is usually asymptomatic and is normally detected by routine radiographs and clinical examinations. [4,12]

An appropriate method for classifying ERR has not yet been found and to date the literature still shows uncertainties. [8] Over the years, various classification methods have been proposed and used:

Andersen in 1985, classifies ERR into three subgroups. The classification is carried out following traumatic lesions:

- Superficial root resorption
- External inflammatory resorption
- Replacement resorption (ankylosis). [4,8,13]

In 1999, Ne classified them according to clinical and histological appearance:

- External superficial resorption
- External inflammatory root resorption
- Replacement resorption
- Ankylosis. [8,14]

In 2003, Fuss implemented a classification based on the triggers for ERR, this method is very effective in helping diagnosis and treatment:

- Pulpal infection root resorption
- Periodontal infection root resorption
- Orthodontic pression root resorption
- Impacted tooth or tumour pressure root resorption
- Ankylotic root resorption. [8]

Heithersay in 2007, classifies resorptions into three groups:

- Trauma-induced
- Infection-induced
- Invasive hyperplasic. [13]

Finally, Heithersay classifies as idiopathic those 'rare' resorptions of unknown aetiology.(8) This idiopathic resorption can occur spontaneously, without any determined risk factor. This idiopathic cause is still unknown, but it is hypothesised that a genetic alteration in the Interleukin 1B allele could be a trigger. (6)

In 2009, Hulsmann describes three types of ERR:

- Progressive inflammatory
- Cervical
- Replacement resorption. [4]

In addition to classifications based on aetiological effects or stimulating factors, it is usual to describe ERR according to anatomical location in relation to the root surface:(15)

- Cervical
- Middle
- Apex. [14]

2. OBJECTIVE

The aim of our study is to fully understand the external root resorption process of permanent tooth, and to identify which of Biodentine (BD), Endosequence Root Repair Material (ERRM) and glass ionomer cements (GIC) is the most suitable material for the treatment of ERR.

3. MATERIALS AND METHODS

3.1 STUDY DESIGN

Before starting the literature search, a research strategy according to the "PICOS" method was established with the aim of structuring efficient research that could provide concrete answers to our study. (Tab. 1)

PICOS	
Population, Intervention, Comparation, Outcome, Study design	
POPULATION	Target population: patients with external root resorptions in permanent teeth
INTERVENTION	Intervention: endodontic treatment
COMPARATION	Comparison: Biodentines, Errm-putty, glass ionomer cements
OUTCOME	Biodentine is the most suitable endodontic material for treating external root resorptions.
STUDY DESIGN	Scooping review

Tab. 1 PICOS.

3.2 KEYWORDS CONSULTED AND CRITERIA FOR INCLUSION AND EXLUSION

Publications were searched in PubMed, EBSCO, the Cochrane Library and Onlinelibrary. The search phrases included" (((((((external root resorption) AND (root resorption)) AND (treatment)) OR (Biodentina)) OR (glass ionomer)) OR (calcium silicate-based cements)) NOT (deciduous teeth)) NOT (capping pulp)) NOT (caries).

3.2.1 *Inclusion criteria*

- Type of articles: review, systematic review, case report, study in vitro.
- Articles published in the last 10 years.
- Included arguments: resorption of the external root in permanent teeth, causes, classification, plans of treatment, diagnostic techniques, "err" from the molecular point of view, chemical, mechanical, physical, and antimicrobial properties of materials and use on dentistry.
- Articles written in English.

3.2.2. Exclusion criteria

- Articles published over 10 years
- Excluded arguments: physiological rizolysis, deciduous teeth, internal reabsorption, pulp vitality treatments.
- Articles not written in English

3.3 FLOWCHART

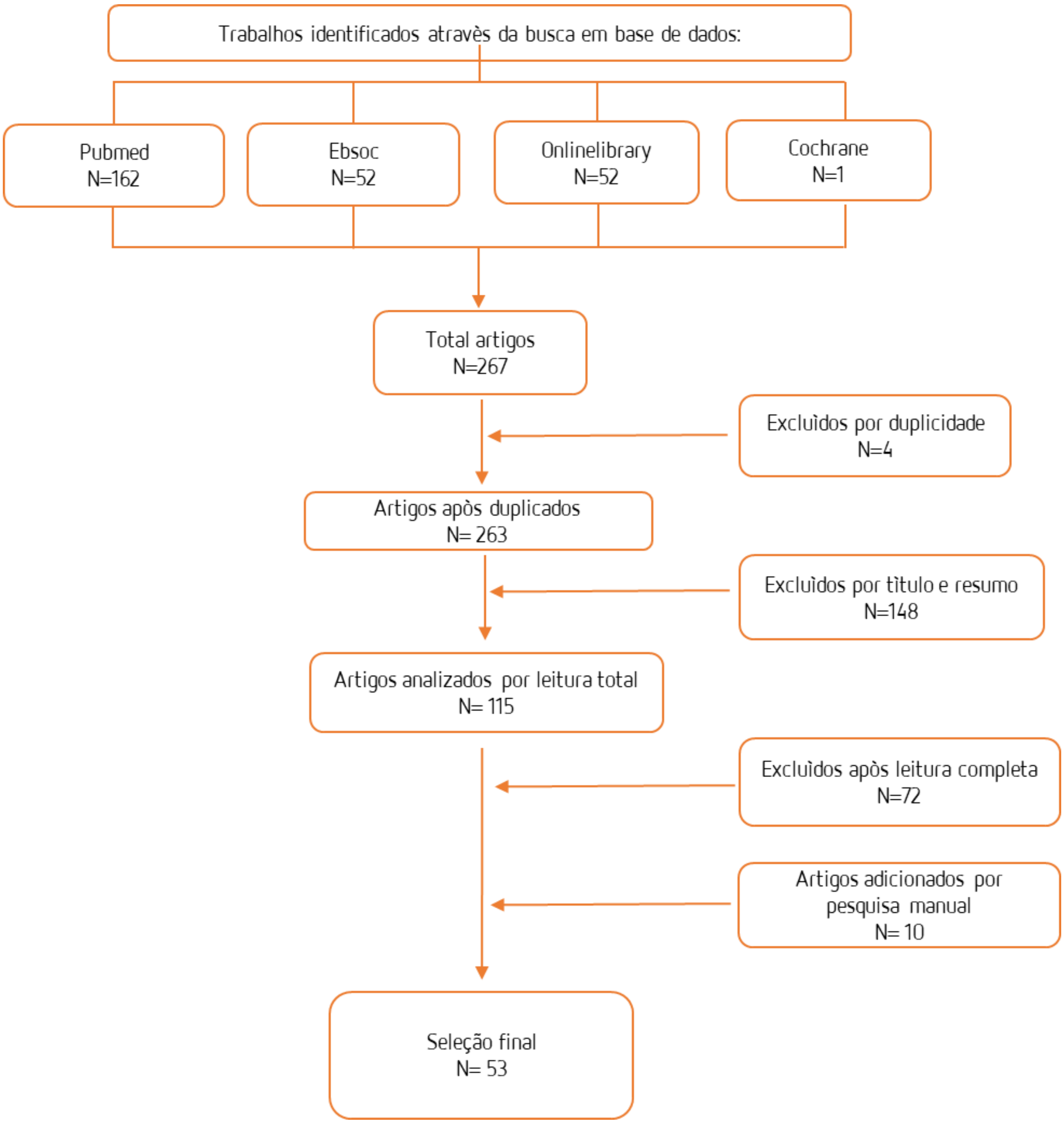


Fig. 1 Flowchart.

4. RESULTS

4.1. TYPE OF EXTERNAL ROOT RESORPTION

Due to the many variations of ERR, it's possible to describe each external resorption type.

4.1.1 SURFACE ROOT RESORPTION

Surface root resorption is defined as self-limiting and is followed by spontaneous repair. [1,10,6] Mineralized or denuded areas of the root surface will lead on hard tissue resorption cells that colonize the damaged areas of the root. However, resorbing cells require continuous stimulation during phagocytosis and stimulation from a denuded dentin or cementum surface appears to be insufficient to sustain the resorption process for more than 2-3 weeks. [1] After a few weeks, these resorbed cavities are repaired by new cement and Sharpey fibres, no treatment is necessary. [6,10]

4.1.2 PRESSURE ROOT RESORPTION

Root resorption depends on the pressure exerted on the root by erupting teeth, impacted teeth, excessive orthodontic movements, or occlusal trauma. This resorption process is interrupted when the pressure stimulus is removed. [10] Pressure root resorption from impacted teeth, frequently develop from the eruption of maxillary canines affecting lateral incisors or mandibular third molars affecting second molars. Surgery in these cases is mandatory to remove the pressure stimulus. [4]

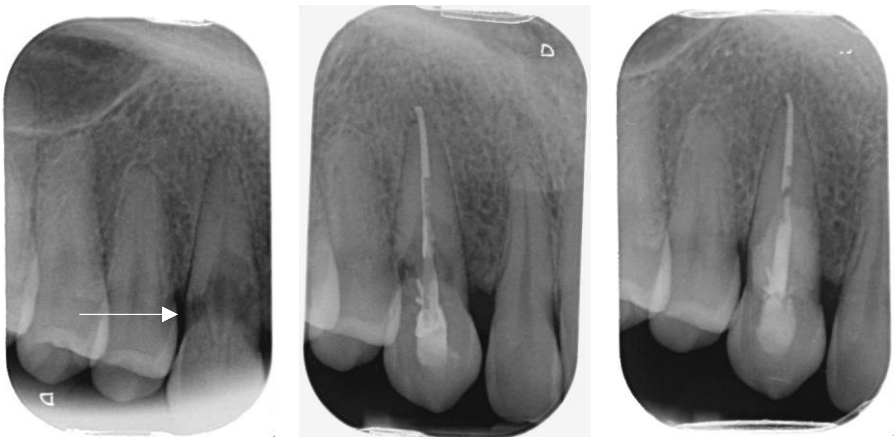
4.1.3 INVASIVE CERVICAL RESORPTION

Different from the other types of ERR, which can be in all parts of the root, this one is located in its cervical part. [10,12] This type of resorption is defined as aggressive, invasive, and progressive. [4,6,10] Case reports of external cervical resorptions associated with histories of virus exposure have been reported.[6] This variant is characterised by its subepithelial location at the gingival attachment; sometimes this lesion is characterised by giving the crown of the tooth a pink hue.[6,12] When more than three teeth are spontaneously involved, the term "multiple idiopathic cervical resorption" is used. [6] Radiographically, these lesions appear as gaps in the cervical area of the tooth. (Fig. 2)

Following an injury, the damaged area of the root surface is colonised by cells that absorb the hard tissues of the tooth and most of the time the cervical resorption is transient/superficial, therefore, cement repair takes place in 2-3 weeks without the need for treatment.

In cases where treatment is necessary, the gaps will be exposed through orthodontic treatment or surgery, the granulation tissue will be removed, and the defect will then be filled with biocompatible material. [1,4,10]

A differential diagnosis with these lesions can be made with internal resorption and subgingival caries. [4]



a b c

Fig.2 *image a)* The arrow indicates invasive cervical resorption of tooth 13. It is hypothesised that the cause is due to extrusion of the tooth through orthodontic treatment.
image b) control X-ray during treatment
image c) follow-up after one year
Clinical case kindly granted by Drs. Alberto e Francesco Fossani.

4.1.4 EXTERNAL REPLACEMENT RESORPTION (ANKYLOSIS)

External replacement resorption is a condition in which the root of the tooth is replaced by bone tissue. [12] Loss of protective barrier exposes the tooth which becomes part of the bone remodelling process leading the element into ankylosis. [15]

Replacement resorption occurs after a trauma which leads areas of necrosis of periodontal ligament, osteoclasts are in direct contact with the exposed root surface and bone replaces dentin.[4] In this case, when the surface involved is greater than 20% the self-repair with new layer cement would be impossible, and bone apposition will be observed to replace dentin. Radiography of a tooth with ankylosis show, the absence of tooth structure, replaced by bone, in the resorption site the margins are irregular, but the canal maintains its original shape. Clinically the element presents a reduced mobility and a "dull" sound to percussion. [1,4,6,10,15,16] The prognosis for replacement resorption is poor. [10]

4.1.5 INFLAMMATORY EXTERNAL ROOT RESORPTION

IERR is one of the complications most frequently associated with inflammation of periradicular tissues resulting from intracanal infections induced by microorganisms leading to progressive damage of the root structure. [3,13,16,17]

IERR requires the following two things to occur:

- The root canal system is infected or contaminated with bacteria.
- The cementum layer may be damaged by trauma or may be lost after external surface resorption and thus the dentinal tubules are exposed to the periodontal ligament and surrounding bone. [16]

Microorganisms reach the root canal through the exposed dentinal tubules and inflammation will set in after 2 to 3 weeks. The lack of protective tissues such as cementum and periodontal ligament will contribute to the establishment of resorption, the exposed dentinal tubules will act as a bridge for bacterial products from the infected root canal to reach the area being resorbed. [1] The end result leads to an exacerbation of the inflammation, with involvement of the PDL and bone which will trigger activation of the clastic cells. [16] Resorption can occur immediately after a traumatic accident or after some time. Once the process is activated, a progressive resorption of the root canal occurs and, if left untreated, the tooth will undergo complete root resorption.

Radiographically it presents with a loss of the root structure together with a radiolucency involving the periodontal ligament and bone.

IERR can occur anywhere on the root, but in most cases, they occur laterally or apically.

Biological factors are very important and mainly influence the development of the post-traumatic lesion.

These factors are the development of the root, its location, whether the pulp is involved, the degree of displacement of the tooth and the presence of simultaneous lesions. If the root is not fully developed, revascularisation of the pulp will be more likely, so with continuous root development there is a greater possibility that inflammatory resorption will not develop; therefore, it is very important that pulpal viability is maintained in the event of trauma.

The presence of certain inflammatory mediators present in the crevicular fluid, such as IL-1α, IL-1ß and TNF α.was found to be increased in traumatised teeth and in particular IL-1α was identified as a biomarker for early diagnosis of IERR. [(16) (15)]

The most common treatment in cases of IERR is endodontic treatment. [(3)]

4.1.6 ORTHODONTICALLY INDUCED ROOT RESORPTION (OIRR)

Orthodontic induced root resorption (OIRR) is a common and undesirable effect related to orthodontic treatment. [(18)] It appears that ERR affects more than 31% of all patients during active orthodontic treatment, with a mean reduction in root length of 2.5mm. [(6)] Although resorption is thought to be localised only at the apical level, OIRR appears to affect the entire root extension. [(18)] The literature suggests a complex aetiology and several variable and non-modifiable risk factors related to the patient, such as genetic predisposition, systemic condition, gender, age, tooth type, root morphology and history of previous trauma or root resorption. On the other hand, treatment-related risk factors depend on the type of appliance, duration of treatment, amount of force applied and type of tooth movement. The diagnosis of OIRR is made in most cases by radiographic examinations because the lesion does not present any symptoms. [(18) (19)]

4.2 BIOLOGICAL PATWAY

Bone resorption and ERR follow a very similar process and cells involved are very similar to each other.

Odontoclasts are multinucleated cells that reabsorb tooth hard tissue, they look like osteoclasts and originate from the same progenitor cells. There is still no agreement in the literature on the equality among odontoclast and osteoclast, but odontoclasts nevertheless have the same ultrastructural and histochemical properties, use the same mechanisms in tissue resorption, they use the same key enzymes and form Howship gaps.

The few differences with osteoclasts are fewer cell nuclei and smaller sealing areas. However, odontoclasts have the ability to simultaneously absorb both root tissue and bone tissue, and osteoclasts can also resorb dentin. [15,20]

The RANKL/RANK/OPG receptor ligand system plays a key role, these TNF family proteins are key molecules that regulate physiological and pathological resorption of mineralised tissues. They control all aspects of osteoclast functions, and they regulate the communication between bone cells, vascular cells, and immune cells. Osteoclastogenesis is mediated through osteoblasts, which through the expression of the stimulating factor M-CFS, promotes osteoclast differentiation and activation of the nuclear factor kappa-B (NF-κB) receptor by the membrane protein RANKL, which is expressed at the osteoblast membrane. By binding RANK, expressed by osteoclasts and dendritic cells, to the respective RANKL receptor, a cell-cell interaction occurs and, due to the presence of M-CFS, osteoclast differentiation is activated.

The mature osteoclast also expresses the RANK/RANKL system as a means of survival of clastic cells by stimulating resorption activity. This self-protective action is triggered to counteract OPG, defined as a RANKL decoy receptor. OPG is a soluble receptor, produced by osteoblasts as an inhibitor of osteoclasts and the RANK/RANKL system. [15,21,22,23] Experimental studies carried out on mice reported that in the presence of a deficiency in the RANK/RANKL system and consequent inhibition of osteoclasts, the mice showed osteopetrosis, whereas in the opposite case, with an increase in OPG, they showed severe osteoporosis. [21] At the periodontal level, RANKL/RANK/OPG is a determining factor that balances and regulates alveolar bone resorption as well as ERR.

The RANKL factor is expressed by:

- Osteoblasts
- Odontoblasts
- Dental pulp fibres
- PDL fibres

- Cementoblasts
- Active T cells
- Deciduous teeth in resorption phase
- Ameloblasts

The OPG factor is expressed by:

- Odontoblasts / osteoblasts
- Osteocytes
- osteoclasts
- Ameloblasts
- Dental pulp fibroblasts
- PDL fibroblasts
- PDL cells of deciduous teeth in non-resorption phase
- PDL cells of permanent teeth. (15,22,23)

The ERR action occurs at the level of the mineralised tissues, after partial removal of the cement layer.[24] The development of ERR requires a persistent stimulus that causes an initial injury to the PDL . [15] Osteoclasts, once activated, bind to the mineral matrix, adopt a polarised shape forming sealed zones and then assuming a ruffled border begin with the secretion of proteases to promote resorption. [15,20] This attack occurs in a specific area of the periodontal ligament called the hyalinised area. Three stages of development of the hyalinised area are described, degeneration, tissue elimination and repair.

Degeneration occurs when a pressure stimulus affects the structure of the PDL; then the ligament membrane begins to shrink and the bone is eliminated by clastic cells to reduce the pressure and to allow revascularisation, and then cellular activity is detected in the hard tissues to allow repair. If the hyalinised area continues to persist or increase in size, odontoblastic activity is initiated with the aim of decompressing the affected area leading to the destruction of the tooth tissue. [24] If the persistent stimulus causes damage to the dental pulp, leading to necrosis of the element, the inflammatory response triggers activation of clastic cells. T-cells found in periapical lesions express the receptor activator of nuclear factor kappa B (RANKL) and consequently with the expression of RANK by clastic progenitor cells a direct RANKL/RANK interaction and activation of clastic cells will occur. (25) Damage to these structures leads to dentinal exposure, giving odontoclasts the opportunity to bind to the damaged area. The adhesion process of the clastic cells has a great relevance for their activation and fusion through the binding of the dentin sialoprotein to the RGD-motif via the integrin receptor and to E-cadherin causing a reorganisation of the cytoskeleton and the stimulation of resorption. [15,20,24] E-cadherin and integrin are also responsible for cell motility, signal transmission and induction of resorption. [15,23] At the level of the mineral matrix, after the binding to the odontoclast, the V-ATPase pump transports protons produced by carbonic anhydrase, generating an acidic microenvironment with a pH of 4.5, which is then completed by the transport of chloride, breaking down the hydroxyapatite crystals. Subsequently, the TRAP enzyme will be responsible for the elimination of the endocytosed material. Finally, the resorption process ends with the degradation of the organic component through the action of cathepsins B, E, K, L, S and MMPs. [15,20,23] Attracted by chemotactic signals, monocytes migrate to resorption zones and mutate into macrophages.

Two main phenotypes are described: M1 the 'killer' macrophages and M2 'healing' macrophages, which manage to predominate over each other through polarisation steps, depending on the different microenvironmental conditions. Macrophages M 1, are promoters of inflammation, secreting pro-inflammatory cytokines such as TNF-α, IL-1ß, but also calcitriol, PGE2, dexamentasone and an over-regulation of nitric oxide. These products lead to stimulation of RANKL expression in PDL fibroblasts and T cells. As an opposite function M2 macrophages promote an inhibitory effect on inflammation, mediated by IL-10 and arginase I. IL-1ß, IL- 6 and TNFα are also described as products of osteoclasts due to traumatic impact or orthodontic forces. TNFα in the presence of RANKL can influence osteoclast differentiation and induce bone resorption; this is identified as one of the direct causes of the inflammatory reaction leading to ERR. [12,15,20,23] The adhesion of clastic cells is greater in dentin than in bone, the sealed zone shows a longer half-life and Howship gaps develop faster. The substrate of dentin shows a greater potential than bone to induce the genesis and maturation of new clastic cells, which may be since dentin contains more extracellular matrix proteins of non-collagenous origin such as osteopontin. [15,20]

Osteopontin is a protein that allows odontoclast adhesion to the tooth root and an increase in IL-1 levels, is produced at the level of the PDL as a means of defence when it is subjected to mechanical stress, such as orthodontic treatment, and if it is not secreted there is a suppression of ERR. [20] As an osteopontin inhibitor, we find calcitonin, an intercellular protein produced by the C cells of the thyroid gland. In the presence of this protein, osteoclasts respond rapidly by assuming a flat shape and losing their adhesion to the mineralised surface. [20,23]

Another essential protein in the development of ERR is ameloblastin, it has been shown that in vivo upregulation of this protein induced severe ERR in transgenic mice and in vitro, clastic cells treated with ameloblastin, produced increased diffusion and formation of podosomes and actin rings favouring adhesion. [20] The outer surface of dentin is protected by newly formed enamel, outer epithelium, stellate reticulum, intermediate layer, ameloblasts, root epithelial sheath, intermediate cementum, cementum, and cementum blasts; the inner surface is protected by the layer of odontoblasts, juxtaposed with each other. Growth factors such as TGF-B, TGF-I and BMP-2, after complete mineralisation of dentin, also remain trapped within it and their presence potentially reduces the resorption activity of clastic cells by increasing OPG levels and regulating the RANKL system. [15,20,24]

During tooth formation, the root dentin is covered by Hertwig's sheath and remains protected by it throughout the development of the tooth. As dentin continues to form, Hertwig's sheath disintegrates through apoptosis; however, prior to fragmentation, the cells in the sheath synthesise a tissue called the intermediate cementum or Hopewell-smith layer, which acts as a protector against the pathological destruction of the cementum. [15,24] Hopewell-smith membrane cells, through the production of specific matrix proteins including osteopontine, ameloblastine and morphogenic proteins (BMPs) play a strategic role in cement repair after resorption. [5,15] Some authors have shown that the expression of amelogenins by Malassez remnants in the periodontal region between bone and cementum can protect against pathological cementum destruction by reducing resorptive activity. [12,15,20]

4.3 SIGNS AND SYMTOMS

To date, the literature reports the inexistence of pathognomonic signs and symptoms in ERR. (11)

The table below (Tab. 2) lists 11 case reports from the 46 articles analysed in which the signs and symptoms and the pulpal and periodontal diagnostics of each case are described. (2,3,9,13,14,17,25,27,28,29)

SOURCE OF RESEARCH	ARTICLE NAME	AUTHOR	YEAR	MAGAZINE	PATIENT	SIGNS and SYMPTOMS	PULP / PERIODONTAL DIAGNOSTICS	CAUSES
EBSCO	Accessory branch of canalis sinuosus mimicking external root resorption: A diagnostic dilemma	Shah P. *et al*	2018	Journal of Conservative Dentistry	Male 60-year-old	Pain Intermittent episodes of swelling.	pulp necrosis	Trauma 21 years before
EBSOC	Extraoral Retrograde Root Canal Filling of an Orthodontic Induced External Root Resorption Using CEM Cement	Kheirieh S. *et al*	2014	Iranian Endodontic Journal	Female 22-year-old	Swelling Class II tooth mobility Severe tenderness to percussion and palpation	pulp necrosis and acute apical abscess	Intensive orthodontic forces
EBSCO	Clinical Management of Severe External Root Resorption and Immature Open Apex with MTA and Calcium Hydroxide	Rangwala A.	2014	Clinical Dentistry	25-year-old	Discoloration Buccal sinus	Chronic apical periodontitis	Trauma 10/11 years before

EBSCO	Clinical Management of Severe External Root Resorption and Immature Open Apex with MTA and Calcium Hydroxide	Rangwala A.	2014	Clinical Dentistry	25-year-old	Discoloration Buccal sinus	Chronic apical periodontitis	Trauma 10/11 years before
EBSOC	Nonsurgical management of a large periapical lesion associated with an immature tooth displaying external inflammatory resorption	Fernandes M. *et al*	2015	Journal of Conservative Dentistry	Female 21-years-old	Soft and fluctuant swelling in the labial sulcus between 11 and 12 Discoloration of crown	periapical lesion	Two episodes of trauma of the anterior teeth, in which the first we find avulsion of 21
EBSOC	Management of Internal and External Resorption with Open Apex	Sengar E. *et al*	2019	Journal of Interdisciplinary Dentistry	Female 26-years-old	Pain Discoloration Sinus Purulent material	Ellis class IV	Trauma
PUBMED	Combined surgical and endodontic therapy to repair the external root resorption defect using a condensable bioceramic material. a case report	Bahabri R.	2020	International Journal of Medical Dentistry	Male 19-years-old	Class II tooth mobility	pulp necrosis and symptomatic apical periodontitis	Trauma
EBSOC	Root resection under the surgical field employed for extraction of impacted tooth and management of external resorption	Vivekananda Pai A *et. all*	2012	Journal of Conservative Dentistry	Female 31-years-old	Pain Purulent material Swelling Sinus opening	Pulp necrosis	Impaction with tooth 18

PUBMED	Management of external perforating root resorption by intentional replantation followed by Biodentine restoration	Pruthi P. *et. Al*	2015	Dental Research Journal	Male 28-years-old	Spontaneus pain	previous treatment	Trauma
PUBMED	Endodontic management of a tooth with apical overfilling and perforating external root resorption: A case report	Sayyad Soufdoost R. *et. Al*	2020	WILE	Male 18-years-old	Pain Swelling Discoloration of the crown	previous treatment	Trauma
PUBMED	Regenerative Endodontic Procedures for traumatized immature permanent teeth with severe external root resorption and root perforation	Lu J *et. Al*	2020	American Association of Endodontists.	Female 9-years-old	Discoloration of crow Sinus tract Class II tooth mobility	necrotic pulp and symptomatic apical periodontitis	Trauma
PUBMED	Surgical repair of external inflammatory root resorption with resin-modified glass ionomer cement	Kim S-Y *et. Al*	2011	Oral Surg Oral Med Oral Pathol Oral Radiol Endod	Male 22-years-old	Sinus tract Discoloration of crown Periodontal probing: 10 mm	Data not found	Trauma

Tab. 2 List of relevant data from the consulted case reports

4.4 DIAGNOSTIC

Very often ERR are misdiagnosed and confused with caries or internal root resorptions (IRR) (Fig.3) [1]. Early diagnosis is an important factor in resolving lesions; early treatment will help to avoid serious consequences. Misdiagnosis or incorrect treatment plan will lead to treatment failure with a high probability of tooth loss. [8] As a first step in diagnosing ERR, it is important to establish the origin of the lesion by identifying it is located internally or externally to the root canal system. At the radiographic level, ERR shows a radiolucent irregularity at the periradicular level without changing the continuity of the canal, while an IRR will show the irregularity at the root canal level, altering its path along the root. [10] The diagnosis of ERR is very complicated, and the use of radiographs for imaging results poorly comprehensive and inaccurate. [11] Periapical radiography cannot identify lingual or buccal lesions equal to or better than 0.6mm in diameter, while lesions more than or equal to 1.8mm in diameter are identified in 74-78% of case. [12] To overcome these limitations, many authors encourage the use of the CBCT for its high specificity and sensitivity. CBCT gives a 3-D view of the anatomical parts which are analysed, allowing a more accurate study of the image by eliminating overlapping structures that could alter the view and the diagnosis. [11,13]

CBCT, which is used in the daily clinical practice of every dentist, ensures an excellent diagnostic efficiency, and permits to detect the unexpected. [26] Reza Sayyad Soufdoost at all, proposes a case report in which, after a diagnosis of IRR, the lesion is simply treated with traditional endodontic therapy. The ineffectiveness of the treatment and the persistent symptoms forces the patient to seek further treatment and with the help of CBCT, a diagnosis of ERR is made. In this case, the use of CBCT was able to make a more extensive and detailed analysis of the situation, giving the clinician the possibility to draw up a suitable treatment plan. [28]

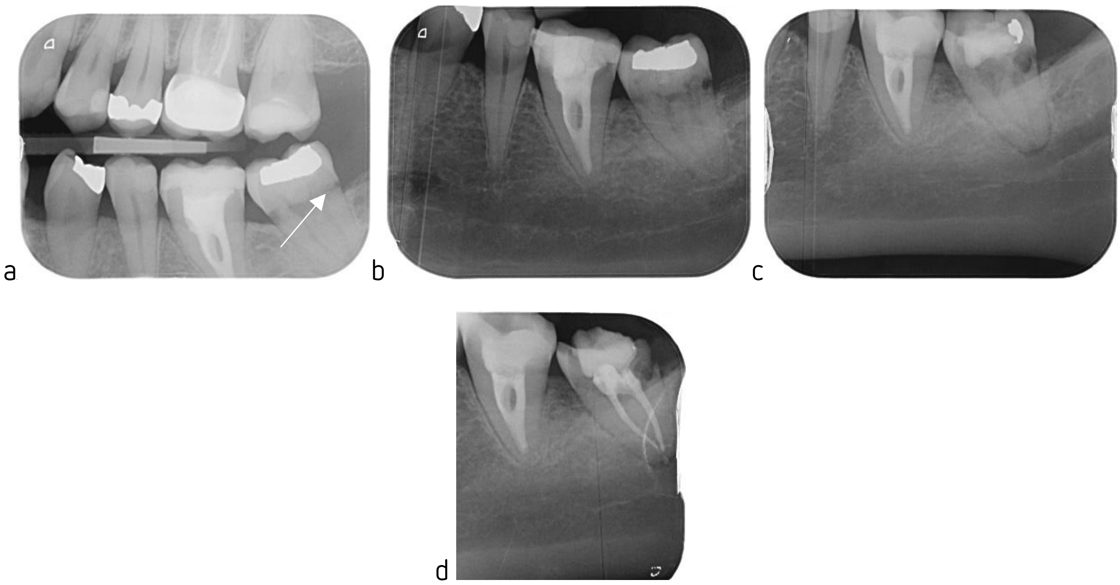


Fig.3 *image a)* routine bitewing, arrow indicates external root resorption, diagnosed as carious lesion of tooth 37
image b) c) progression of external root resorption
image d) endodontic treatment of tooth 37 and progression of external root resorption. The tooth was subsequently extracted.
Clinical case kindly granted by Drs. Alberto e Francesco Fossani.

4.5 TREATMENTS

After timely and accurate diagnosis, and a right classification of the ERR, is important to establish an appropriate treatment plan, which will depend on the extent of the pathology, the presence of certain symptoms, the stability of the tooth and the causes that induced it.[8,9,12] The treatment goal in the ERR is to remove or destroy bacteria to allow healing to take place in the periradicular space. [14]

Three lists are given where the treatments encountered in the literature and the various procedures are illustrated.

4.5.1 CONVENTIONAL ENDODONTIC TREATMENT

<u>First appointment:</u>

1. Intraoral examination
2. X-ray
3. Administration of anesthetic

4. Tooth isolation by rubber dam
5. Access cavity
6. Inspection of the anatomy of the canals
7. Determining the working length
8. Canal instrumentation
9. Irrigation
10. Canal drying
11. Calcium hydroxide placed into the canal
12. Applied temporary restoration

Second appointment

(after 1/2 weeks)

1. All temporary filling material is removed
2. Root canal is irrigated several times
3. The material is inserted into the canal to seal the root defect
4. Condensation of material
5. Root canal filling
6. Postoperative X-ray
7. Permanent restoration
8. Follow up. (9,13,14,17,25,27,28)

In situations where resorption is inaccessible or surgery risks damaging the tissue, conventional endodontic therapy will be considered.(6)

When ERR is a consequence of pulpal necrosis and periodontal injury, endodontic treatment can be performed with the aid of calcium hydroxide (CH) as a temporary medication. (14)

As described on the literature it is common, especially in the case of IERR, to perform chemo mechanical root canal disinfection using NaOCl and during appointments fill the canal with CH to provide an alkaline ph and ensure inactivation of odontoclasts, elimination of bacteria and neutralisation of their products, such as endotoxins. (3) (13) Since its introduction, CH has been widely used in endodontics; it is a strongly alkaline substance with a pH of approximately 11-13, it has excellent antimicrobial abilities, it dissolves tissue, inhibits resorption, and it induces repair through hard tissue formation. However, the use of CH is limited in the case of immature teeth with an open apex, as in the long term it would lead to the progressive weakening of the root; this does not seem to happen in mature teeth. (14)

The use of 2% chlorhexidine as an irrigant is recommended, by some authors, when treating teeth with an open apex, due to its relative non-toxicity and non-dissolution of tissues, as the use of NaOCl could damage periradicular structures, and it is also reported in the literature that, compared to NaOCL, chlorhexidine has a superior effect against E. Fecalis. (14)

In ERR, with abscess, it is necessary to drain the abscess through the access cavity.
Once the purulent material has been eliminated, we can proceed with irrigation and instrumentation of the root canal. If the infection persists, a triple antibiotic therapy based on ciprofloxacin 500mg, metronidazole 400mg, and monocyclines 100mg can be carried out, the antibiotic paste will be maintained into the canal for about a week. (25)
Thus, in the case of pulpal involvement, conventional endodontic therapy is required and may be followed by endodontic surgery to remove the granulation tissue and filling the root defect or root- end cavity by providing an apical seal to the root. (8)

In cases where conventional endodontic therapy fails, endodontic surgery is considered. The success of surgery is based on the regeneration of periodontal tissue including cement, PDL and alveolar bone. (30)

4.5.2 ENDODOTIC SURGERY

1. Intraoral examination
2. X-ray
3. Administration of anesthetic
4. Full thickness incision
5. Vertical releasing incision
6. Curettage
7. Osteotomy
8. Soft tissue removal (granulation tissue)
9. Amputation of the apex at 90 °
10. Staining of the remaining root
11. Identification of any fractures
12. Preparation of root-end cavity
13. Material compacted into the root-end cavity and resorptive defect (3-4mm)
14. Periapical radiograph
15. Check the quality of the root-end filling

16. Follow up (27)

As 98% of apical canal anomalies and 93% of lateral canal system occur in the 3 mm range, (it is essential that at least 3 mm), it is essential that at least 3 mm of the root tip is removed. It is advisable to perform root end resection perpendicular to the long axis to preserve more root structure and improve the crown/root ratio while achieving the goal of removing most of the apical ramifications. Thanks to advances in equipment for periradicular surgery it is possible to perform a more perpendicular root tip resection with less exposure of the dentinal tubules. [31]

In cases of endodontic surgery and subsequent root resection, it is necessary to assess the location of the lesion without damaging the remaining cortical bone and compromising tissue stability. Due to IERR, the anatomy of the root surface and canal may be irregular. [27]

Retrograde canal preparation is more effective with the use of ultrasonic techniques, because it allows better control during execution and greater ability to give centrality to the canal, reducing the risk of perforation. [32]

Endodontic surgery is a highly predictable procedure, with a success rate reported to be higher than 90%. [27]

4.5.3 INTENTIONAL REPLANTATION AND EXTRAORAL ENDODONTIC TREATMENT

1. Intraoral examination
2. X-ray
3. Administration of anesthetic
4. Atraumatic tooth extraction
5. Curettage
6. Root canal is retrogradely prepared
7. Saline irrigation
8. Material compacted into the root-end cavity (3-4mm)
9. Tooth is reimplanted into its socket
10. Splinting
11. X-ray to confirm the repositioning
12. Post-operative instruction
13. Follow up [3,13]

Intentional replantation is defined as the purposeful extraction of a tooth to repair a defect or the cause of treatment failure, and thereafter the return of the tooth to its original socket. [13] It is considered as a last option after failure of other endodontic procedures and should only be planned when no other treatment is feasible, as it is associated with risk of root fracture, replacement resorption and ankylosis. [3,13]

Extraoral endodontic treatment (EET) can be performed in a retrograde approach, including root canal cleaning/shaping and root-end filling with appropriate biomaterials. ETT, is also defined as an economical and conventional technique with shorter time and easy handling. The greatest difficulties occur at the PDL if the tooth remains in the extraoral environment for too long time . [3]

The periodontal ligament reaction to a replanted tooth can be:

- Surface resorption; a good indication of repair with cementum-like tissue.
- Replacement resorption can be detected radiographically, as early as two months.
- IERR can be detected as early as three months after replantation [27]

If an apical lesion is present, a histopathological examination of the removed tissue is carried out after extraction and curettage. [3,27] Although it is suggested only for limited cases, this procedure has been reported with a success rate of up to 95%, if done by following the guidelines. The best prognosis of a replanted tooth is indirectly related to the time that the tooth is maintained extra orally during the procedure. It has been stated that the potential for resorption in replanted teeth increases if they remain outside the mouth for more than 30 min. [13] AR Vivekananda Pai et al. describe a case report of a severe ERR of the distobuccal root of a 17, caused by the impact of an 18. After extraction of the 18, resection of the compromised root was sufficient, thus avoiding loss of the element. After tissue healing, endodontic therapy was performed; at follow-up after one year, the tooth was asymptomatic. With a diagnosis of replacement resorption (ankylosis), in most cases the prognosis is ominous. No 'gold standard' treatments have been introduced for replacement resorption, but therapeutic strategies to minimise the extent of damage are hypothesised. [6,15] If ERR is very extensive and also involves the cervical area of the tooth with numerous parts of the root, usually any treatment could be complicated, so extraction of the tooth is the only option.[8] To conclude Kerstin M.Galler et al. Through a scoping review, describes the use of denosumab, a human monoclonal antibody that mimics the effects of osteoprotegerin in bone metabolism, by inhibiting RANKL expression and considerably reducing resorption after 2 months, in rat teeth after extraction and remodelling in an extraoral time of 60 minutes. In addition, topical application of alendronate, an osteoclastic inhibitor used for osteoporosis, also demonstrated effects very similar to denosumab, and application of N-acetylcysteine as an intracanal drug, also used in an animal model, demonstrated a decrease in clastic cells and a reduction in the resorbed area. The results obtained highlight the potential of a drug therapy in resolving ERR. [15]

4.6 MATERIALS

4.6.1 CALCIUM SILICATE CEMENTS

Calcium silicate cements (CSC) are self-setting hydraulic cements.[33] One of the best known is MTA, but despite its great success, the disadvantages of long setting time, discolouration, poor handling properties and high cost have led to the need for new materials. [32,34] These new calcium silicate materials have a similar composition to MTA but distinct properties.[35] Numerous products have entered the market: Biodentine (Septodont, Saint Maur des Fosses, France), Bioaggregate (Innovative Bioceramics, Vancouver, Canada), Endoseque root repair material (Brasseler USA, Savannah, GA, USA), Calcium-enriched mixture cement (CEM) (BioniqueDent, Tehran, Iran), and TheraCal (Bisco, Schamburg, IL, USA). (35) (33) These biomaterials are widely used in the endodontic field, in procedures such as pulp capping, pulpotomy, root canal filling, perforation treatment, apexification and root-end filling. [33,35,36] Their sealing ability results from the interaction of dentin through the formation of tag-like structures that extend into the dentinal tubules, expansion capacity and setting time. [33,35,37] These materials exhibit high compressive strength and physical characteristics like dentin. In vitro studies report antimicrobial activity of these materials, linked to the alkalinisation of the environment, made possible by the release and diffusion of hydroxyl ions through dentin. Cytotoxicity also performed well, with 91% greater cell viability observed when these materials were in contact with human fibroblasts.[35] Biocompatibility in dental materials is essential to avoid inflammatory reactions and to allow tissue repair. To be considered such a biocompatible material, should present a low toxicity, without triggering an inflammatory cascade.

It is defined as biocompatible when the inflammatory reaction is not significant or when it is mild or present for a limit period of 14 days. (30) Bioceramics are composed of alumina and zirconia, bioactive glass, glass ceramics, calcium silicates, hydroxyapatite and resorbable calcium phosphates, and radiotherapy glass. (36)

4.6.2 BIODENTINE

Biodentine (BD) is a calcium silicate material, which requires a low amount of water for its preparation. (38) BD contains tricalcium silicate, calcium carbonate, zirconium oxide, and a water-based liquid-containing calcium chloride. (37) It is sold as a powder in a capsule and the liquid is contained in a pipette.

Physical properties are improved by changes in powder composition and the addition of setting accelerators. (33) It is a fast-setting CSC, defined as a dentine substitute. (33,37,38,39) When used as a dentin substitute, placement of the composite restoration should be delayed by one to two weeks to allow adequate setting and curing of BD to withstand the shrinkage forces of the resin composite. (33,40) BD can be placed within the cavity without dentinal pre-treatment. (33) It is a biocompatible and easily manipulated material with a short setting time of 12 to 13 minutes and a lower cost than MTA. (28,32,387,38,39,41) The reduction in setting time seems to have been achieved by the dimensional increase in the specific surface area of the particles, the addition of $CaCl_2$ and the decrease in the liquid component. (33,37) The short setting-time of BD is a clinical advantage especially in situations requiring definitive treatment in one visit; e.g. paediatric dentistry. (33) In addition, the shorter setting time would prevent prolonged leakage, reducing bacterial contamination. (30) Literature reports different setting times, times vary from 6.5 min to 45 min, these differences may depend on different testing methods and environments. (35)

It has a high compressive strength, microhardness, flexural strength, push-out bond strength and a release of calcium ions which promote antimicrobial action. (30,33,37) It bonds chemo-mechanically to composites and teeth, giving them high flexural and compressive strength. (38) It is assumed that the resistance of BD depends on the small particle size, which gives the cement better penetration into the dentinal tubules. (30,40) The literature states that the push-out bond strength decreases significantly if the smear layer is removed, which would be detrimental to the bond between dentin and cement. [37] BD does not show a significant reduction in compressive strength when exposed to NaOCl, while a reduction is present when exposed to EDTA. [40] One of the limitations of BD is its susceptibility to abrasion. BD is considered a weak enamel substitute; it is most successful when used as a dentin substitute in permanent teeth under composite restorations and as a temporary restoration in posterior teeth for a time limit of 6 months. [33] In accordance with ISO standards, BD exhibits radiopacity greater than 3mm of aluminium thickness, making it a valuable product in providing guidance during endodontic procedures. [37] In contrast, another study states the radiopacity of BD a disadvantage in the long term, claiming poor radiopacity. [38] In terms of biocompatibility BD leads to induction of odontoblastic differentiation in different stem cells, with subsequent increase in mRNA levels of osteogenic genes, including ALP, osteocalcin and bone sialoprotein for 3 days. [33,37] BD can regress inflammation, reduce bone resorption and promote osteoclastic/odontoblastic differentiation, leading to the formation of collagen bundles of the PDL and bone matrix creating mineralised tissue. [38] Although BD may facilitate a remineralisation of dentin, a prolonged contact with it has shown an adverse effect on the integrity of the dentin collagen matrix. However, the authors suggest that the amount of altered dentinal collagen was limited to the contact surface with BD, and therefore did not affect its use in endodontic procedures. [37] Other studies report that BD demonstrated a potential for bioactivity by producing an interfacial layer of amorphous calcium phosphate (ACP) on root canal dentin in simulated body fluid. [40] BD has the ability to interact with dentin by forming a mineralised interfacial zone with tag-like structures that extend into the dentinal tubules. [30,33,40,41] Micromechanical anchoring is also partly determined by the increased release of calcium ions and hydroxyl ions, the latter being responsible for improved apatite formation. [40] After evaluation of various handling techniques, an increase in microleakage was evident when BD was handled manually compared to mechanical grinding. This could be explained by the homogeneity conferred by mechanical trituration. [38,40] The PH value of BD was reported to be 11.7 after 1 day of immersion in Hank's balanced salt solution, showing no significant changes after a period of 28 days. [37]

4.6.3 ENDOSEQUENCE ROOT REPAIR MATERIAL

The search for bioceramic materials with similar properties to MTA, but with better handling characteristics and shorter setting times, led to the development of EndoSequence Root

Repair Material (ERRM). [42] ERRM also known as iRoot BP Plus [5] is a fully synthetic calcium silicate cement with nanotechnology bioceramics.. [34] Both materials are composed mainly of calcium silicates, zirconium oxide, tantalum oxide and calcium phosphate monobasic [37] and filler agents. [43] It has a pre-mixed putty consistency to improve handling characteristics. [44] It is a radiopaque material with a setting time of 2 to 4 hours; (average 2.7h). [33] [37] It has a working time of about 30 minutes and requires a humid environment. [37] [42] ERRM is delivered as premixed mouldable putty or as a preloaded paste in a syringe with delivery tips for intracanal delivery. ERRM has a similar crystallographic surface structure to GMTA, with hexagonal crystals of varying sizes. [37] The setting time is reduced when the humidity of the environment increases but reduces the microhardness of ERRM. [33] Recent studies have reported that ERRM greatly reduces microhardness values in acidic environments, resulting in more porous and less crystalline microstructures. The flow, dimensional change , solubility and film thickness of ERRM comply with ISO standards. [37] ERRM is a biocompatible, antibacterial material with retrograde sealing abilities. [43] The PH value of ERRM was reported to be 12.4; this value is responsible for the antibacterial properties of the material during the curing reaction. ERRM, like BD, forms tag-like structures within the dentinal tubules to create an adhesion with the dentin, creating a micromechanical anchorage. [37] The cement will then be moistened with dentinal fluid and create a mechanical bond with the dentin, inducing a shrinkage limit of the material and ensuring dimensional stability. [33] [44] The marginal adaptation of ERRM depends on the premixed formula of the product, which reduces the air in the mixture, improving the adaptability to the tooth walls. [44] The bioactivity of ERRM is also confirmed. Experimental studies have shown that gingival fibroblasts in contact with ERRM form an overlay similar to the bone matrix. [37] And in vivo studies have shown that ERRM has powerful effects on the differentiation of periodontal ligament and dental pulp stem cells. [27]

4.6.4 GLASS IONOMER CEMENTS

The 1970s and 1980s saw the introduction of polyelectrolytic cements (polycarboxylate and glass ionomer). [45,46] These cements chemically bond to the tooth structure, contain fluoride and quickly became popular mainly because of their ease of mixing, potential to prevent secondary caries and biocompatibility with tooth tissue. [45,46,47] Glass ionomer cements (GIC) were first developed as the product of an acid-base reaction between a basic fluorine-aluminium-silicate glass powder and polycarboxylic acid in the presence of water. [48,49,50] GICs can be supplied as a powder and liquid or as a powder that is mixed with water. In the powder/liquid formula, the powder consists of a sodium aluminium silicate glass of a composition similar to that used in calcium silicate materials. [48] The setting time happens quickly, in 2-6 minutes, once the setting time is complete, several changes take place in the following days or months.

These processes are known as maturation:

- Compressive strength increases asymptotically until it reaches a stable value
- Hardness decreases and the cement becomes more brittle
- Opacity decreases and translucency increases
- The proportion of bound water increases up to a limiting value
- The ionic exchange bond with the tooth surface develops with time

The increase in compressive strength is a desirable factor, as is the improvement in opacity, with a corresponding improvement in aesthetics. Once water bonding has taken place, all unbound water molecules may be lost and the cement begins to take on an unsightly, chalky appearance. To avoid this, it is important to protect the cement by covering it with an appropriate varnish or petroleum jelly. [49,50] GICs are bioactive materials, releasing biologically active ions (fluorine, sodium, phosphate and silicate) into the surrounding aqueous media at levels at which they are biologically useful and under acidic conditions, these ions are released in greater quantities. These ions are crucial in the remineralisation phases of the tooth. Bond strengths are typically higher to enamel than to dentin and develop rapidly, with approximately 80% of the final bond strength achieved within 15 minutes, after which it increases for several days. In the long term, a diffusion process occurs in which ions from the cement and ions from the tooth move into the interfacial zone and create an ion exchange layer, the resulting structure causing the cement and tooth to adhere strongly. (50)

They are versatile materials and are used in dentistry as complete restorative materials, particularly in paediatric dentistry, as sealants and adhesive agents for orthodontic brackets. (46,47,49,50) They are defined as the first choice for atraumatic restorative treatment, in which application they have demonstrated high durability and good clinical results for several years. (49) They can be used effectively as root canal sealants, root exterior filling materials, intra-root barriers, repair of perforations and temporary restorations. (48) It is defined as a substitute for dentine, its ability to bond chemically to the tooth structure provides an excellent marginal seal and its antibacterial activity is demonstrated thanks to release of fluoride. (51) On the contrary, other articles define GICs as materials with poor cavity and wall adaptation; the plasticity and viscosity of GICs prevent condensation and present sensitivity in a humid environment. So susceptibility to hydration, high solubility, low setting speed, low wear resistance, long setting time, difficulty in filling and handling have limited their use in dentistry. (46,51) Chohan H. et al., compare the apical sealing ability in a retrograde filling between conventional GIC, resin-modified glass ionomer (RMGIC), polyacid-modified composite resin and composite resin in 68 incisors. The highest dye penetrations are found with conventional GIC; in descending order we find that composite resin shows the lowest dye loss, followed by RMGIC , polyacid modified composite resin and conventional GIC. (31) Furthermore, for some authors GICs are a poor material in the treatment of root perforations. (41) Many attempts have been made to improve the strength of GICs over the years and so far, few approaches have proved successful. Good results have been obtained with some fibres, in particular hollow glass fibres, and with particular nanoparticles where alteration of the cement has led to significant reductions in porosity. Recent studies show that modification of commercial GICs with bioactive components, such as BAG powders, HAp and bioinert ceramics such as zirconia, help to improve their mechanical properties. Antimicrobial agents such as antiseptics, antibiotics and biomaterials have also been added in an attempt to increase the antibacterial activity of GICs, but the addition of these elements has negatively affected the physical properties of the cement. (46,47) Josna Vinutha Yadiki et al. attempts to improve the antibacterial performance of GIC. This study concludes that the addition of chlorhexidine gluconate to

GIC resulted in a restorative material that had increased antimicrobial properties over the conventional GIC alone for S. mutans. [52]

5. DISCUSSION

MTA is considered a material of choice in the endodontics; it is widely present and analysed in today's scientific literature. Therefore, in our study, we took MTA as the standard material for comparison. Comparing the alteration in tooth colour, BD does not cause any difference in colour, making it possible to use it even in aesthetically defined frontal areas. [37] BD maintains colour stability even after 6 months and exhibits minimal discolouration compared to MTA. Almost imperceptible discolouration is observed with BD in the presence of NaOCl and blood. [40]As physical properties, BD exhibits significantly higher hardenss, flexural strength and elastic moduls than ProRoot MTA, MTA Angelus and GCMTA. [33,40] The push-out bond strength, was higher in BD than in Bioaggregate, ProRootMTA and MTA Angelus. [40] Nevertheless of the placement technique used (manual compaction or ultrasonic activation) BD showed higher bond strength values than MTA and MTA+CaCl2. [37,40] This can be explained by the size of the BD particles, which are smaller and more uniform, thus improving interaction with dentin. [37] BD does not vary the push out bond strength in the presence of a contaminated environment unlike MTA and MTA Plus. [38] Even contamination with blood does not alter the marginal adaptation and push out bond strength of BD. [40,41] Metashi Singla et al. make a comparison of the push out bond strength, between GIC, hydroxyapatite, MTA and BD, in 120 extracted teeth.

In a direct comparison between BD and GIC we find that BD has a much higher push out bond strength. In addition, GIC lose adhesion in a contaminated environment and do not show any expansion of the product during the setting time. [41] The compressive strength and surface hardness of BD are superior to other CSCs such as BIOAGGREGATE and MTA. [33] The push-out bond strength and compressive strength of ERRM are comparable to MTA. [33,37] In an experimental apicoectomy model, surface microhardness is evaluated by assessing BD, ERRM and MTA. The results show similar microhardness of BD and ERRM but lower in MTA. [33] In comparison with MTA-Angelus, GCMTA and CEM, BD shows significantly higher compressive strength. [40] The flexural strength and elastic modulus of BD are higher than MTA, and BD is less dense and porous than MTA. [33] BD does not require two steps for its application as in the case of MTA, thanks to fast setting time. [28]

Exposure to different PH (4.4, 5.4, 6.4 and 7.4) for 7 days resulted in BD showing significantly higher compressive strength than White MTA. (40)

When analysing the biocompatibility of each material, BD shows higher biocompatibility than MTA. (30) In this case, the literature is very contradictory and many of the studies analysed show similar biocompatibility among MTA and BD. A study carried out on rat dental pulps revealed odontoblastic differentiation by BD and subsequent formation of a dentinal bridge, similar to MTA, after 14 and 30 days. [(35)] Both BD and MTA can provide a positive environment for the cell by showing both cell proliferation and osteogenic capacity. The cytotoxic effects of BD and MTA on human pulp were tested and declared to be absent for both. Monocyte cell viability improves significantly with time for both MTA and BD, and this would depend on a decrease in cytotoxic substances leached from the materials, thus decreasing the cytotoxic effects on the cells. Both products did not affect the specific function of the target cells and allowed cell viability and proliferation to continue for 72 hours. [(30)] Furthermore, it was mentioned that cells in contact with BD and MTA showed similar cell viability. [(30,40)] In vivo studies have shown that ERRM has potent effects on the differentiation of PDL and dental pulp stem cells in comparison with MTA. [(27)] Cytotoxicity and cytokine expressions are similar between ERRM and MTA. (33) (37) Expression of cytokines like IL-1ß, IL-6, IL-8 and a minimum of TNF-α were found in human osteoblasts in contact with ERRM and MTA. iRoot BP plus was found to be non-toxic to human dental pulp cells, and was able to induce odontoblastic mineralisation and differentiation. [(37)] Only one study contradicts the above, stating that ERRM reduced the viability and alkaline phosphatase activity of human osteoblast-like cells compared to MTA. [(33)] Interleukin (IL)-1α and IL-6 mRNA expression upon contact with BD was similar to MTA-induced expression. [(8,30,40)] In contrast, other studies have developed the idea that BD may be a better biocompatible material than MTA. It was shown that the amount of PDL cells was higher, thus promoting repair and better biocompatibility. The reason for this would be that BD is mainly composed of tri-calcium silicate which would increase the bioactivity on osteoblast and osteoclast-like cells, leading to the release of silicon from the cement. [(30)] When comparing ProRoot MTA and BD, the latter demonstrated significantly better results for survival and proliferation of periodontal ligament cells. [(40)] Compared BD and ERRM promoted increased survival and differentiation of SCAPs and an increase in the odontoblastic marker DSPP.

These two biomaterials can be considered for pulp regenerative and vital therapies. [35,40] Human gingival fibroblasts, mouse fibroblasts, human dermal fibroblasts, PDL fibroblasts and human osteoblasts have been tested in vitro, showing that the biocompatibility of ERRM is similar to that of MTA. [33] Several studies have shown a significantly higher cell viability of BD and MTA, with no significant differences between them, in comparison with GICs, which report a significantly lower cell viability. [37] An increase in Ca2+ release is known to stimulate hard tissue formation. [33] In contact with saline, ERRM creates hydroxyapatite-like precipitates, an alkaline pH comparable to MTA and a calcium release that allows hard tissue deposition. [2,33,43] The post-surgical root healing effect was then compared among MTA and ERRM, both of which were used as root tip filling materials in an animal model. The results reported that ERRM induced better tissue healing than MTA. [40] The improved performance of ERRM probably depends on better tissue mineralisation, inductive/conductive properties thus accelerating cementum-like tissue, PDL-like tissue and bone. [37] Compared to MTA, the use of ERRM has shown similar results, as assessed by micro-CT, and also in histology using an animal model. [27] BD shows a higher release of calcium ions in comparison to Angelus MTA, GCMTA, ProRoot MTA and MTA plus. The higher ion release could be attributed to the presence of pure tricalcium silicate, calcium chloride and higher calcium hydroxide formation. This increased dissolution of calcium ions and in addition silicon ions, makes BD a soluble material, the solubility of BD and ProRootMTA is compared, which proves to be similar up to 10 days of exposure, after 10 days, BD showed a marked increase in its solubility. [40] BD has the ability to release and penetrate a greater amount of Ca2+ than MTA [33,40] and also shows a greater ability to release silicon ions through dentin. This greater release of calcium ions and silicon ions may explain the high push-out bond strength. [41] Several studies have compared the release of calcium ions by BD in comparison with MTA, Endosequence BC sealer, BioAggregate, TCS-Zr and IRM, the results show that BD has a higher release of calcium ions. [37] The biomineralization capacity of BD is also higher than that of MTA. [33,41] Analysing the sealing capacity, we see that BD has a superior sealing ability in comparison to ProRootMTA, RetroMTA, MM-MTA, and ERRM. [38] Other studies confirm that BD has better sealing ability than MTA. [30] By fluid-filtration technique, BD provided a valid and stable apical seal over a period of 12 weeks. [40]

Yanti Johari et al. in vitro study evaluated the sealing ability by comparing injectable dental composite, BD and MTA, in 68 extracted teeth. BD, shows a similar composition to MTA but with better chemical-physical characteristics and a faster setting time, MTA and BD show more Gap than injectable dental composite, but when analysing the sealing ability of both, MTA shows more Gap than BD. (53) Using dye penetration technique, it was reported that BD exhibits less significant microleakage, compared to MTA, but significantly higher than Pro Root MTA, MM-MTA, GIC and ERRM. (40) ERRM on the other hand, through in vitro studies, shows marginal adaptation, as retrograde material, comparable to MTA. (33) In contrast, however, Anish Kumar Lagisetti at. All. compare ERRM, GIC (ZIRCONOMER) and MTA, in the treatment of root perforations, through an in vitro study, where 48 maxillary first teeth were selected. The results show that the least amount of dye loss is present with ERRM, followed by MTA and finally zircomer.(44) BD demonstrated a lower sealing capacity than MTA when inserted as an apical plug. Comparison, other studies claim that BD has a superior sealing capacity and marginal adaptation with a 4 mm thick apical plug. (38) The sealing ability of BD at the cement-dentin interface in a sandwich technique restoration (in vitro) is comparable to the sealing ability of RMGIC. (33) BD showed very good sealing ability as retrograde filling materials in comparison to GIC, which showed a significantly weaker sealing ability. In addition, BD showed less porosity and better cement-dentin adhesion than GI. (38) Only one in vitro study contrasts the ability of BD with GIC. Furthermore Acid-etched BD demonstrated structural and chemical changes. Both acid-etched and non-etched BD demonstrated statistically significant losses at the cement-dentin interface compared to acid-etched GIC and non-etched, under resin composite. (33) BD is defined as a preferred material for root end filling over MTA and GIC and compared to GIC, has less microleakage. Comparing MTA Angelus, BD, MTA Plus and GIC, MTA Angelus shows less microfiltration and a higher sealing capacity, followed by BD and MTA Plus, while GIC shows a much lower sealing capacity. (38) Bolbolian M. et al. using a sample of 15 teeth, compares the marginal adaptation of BD, ProRoot MTA and Retro MTA in retrograde fillings. Longitudinally, BD shows fewer gaps than ProRootMTA and Retro MTA, but transversely it shows more gaps than ProRootMTA and Retro MTA. (.32) Evaluating the marginal adaptation by comparing MTA, BD and GIC, 30 premolars are used, the results show that the smallest gaps are obtained with the marginal fit made by BD, followed by MTA and GIC presenting the worst results. (51) The antibacterial ability of BD compared to MTA is stronger against S. sanguinis strains.

Weaker, or almost null, was seen against S. mutans. In comparison with Angelus MTA and ProRoot MTA, BD showed significantly less antibacterial activity against S. salivarius. Furthermore, the antibacterial activity of BD was like MTA Angelus but significantly higher than ProRoot MTA and MTA Plus. Against E. faecalis and E. coli BD showed similar results compared to MTA Angelus but significantly superior compared to ProRoot MTA. The antifungal activity of BD against C. albicans was similar to MTA Angelus and MTA Plus but significantly superior to ProRoot MTA. (40) Another study attempts to compare the antimicrobial activity of MTA, GIC and BD. The results show that BD has high antimicrobial activity compared to MTA and the antimicrobial activity of MTA and BD was significantly higher than GIC. The results suggest that BD possesses higher antibacterial and antifungal potential than MTA. (39) The antimicrobial activities and PH values of iRoot BP plus compared to MTA are evaluated. IRoot BP Plus shows a better antibacterial activity against E. Faecalis. E. Faecum. S. Aureus. S. Mutans and P. anaerobius, it shows no effect on P. gingivalis. MTA, on the other hand, shows greater antibacterial activity against C.Albicans. Finally, the particularly high PH value of IRoot BP Plus translated into a greater alkaline effect is highlighted after 5 and 60 minutes. (34) Whereas the antibacterial activity of ERRM against E. faecalis was like MTA. The antibacterial effects between MTA and ERRM were similar on planktonic E. and Faecalis cells. Finally, other recent studies report that ERRM and MTA show the same antifungal activity. One study compared PH changes in simulated root resorption defects filled with MTA and ERRM, and it was concluded that intracanal placement of MTA reported a higher PH level than ERRM. (33,37) Analysing the induction capacity in the change of PH, Stephen W. Hansen et al. did a comparison between ERRM and Pro Root MTA, in a sample of 24 extracted teeth. After 24 hours, the diffusion of ions by both products was stable, but afterwards ERRM saw a significant drop compared to MTA, so it is hypothesised that this difference depends on the initial and final setting time of the two products. MTA demonstrated a continuous diffusion of ions over the next 4 weeks, thus maintaining a higher and longer lasting pH. (42) The antibacterial effects of GIC are analysed in comparison with MTA and BD, where, however, GIC show poor results; there is a significant difference in antibacterial activity between BD and GIC against E.Faecalis, E.Colli, S. Mutans and Candida Albicans. (39)

6 CONCLUSIONS

According to the studies in the literature, BD and ERRM, exhibit better properties than GIC, in the resolution of ERR. Especially BD, exhibited the best performance, we can therefore identify it as a worthy substitute for MTA and above all a suitable and more effective material for solving ERRS.

ERRM, compared to BD is a lesser cited material in the literature, but from the sources found, showed high-level physicochemical properties, although in all the studies analysed it never exceeded the performance of BD, it equalled its properties.

ERRM was also found to be superior to MTA in certain mechanical properties without the disadvantages of MTA such as malleability and setting time.

Both CSCs showed very good sealing properties, very good antimicrobial properties, very good malleability and a fast-setting time, which appeared to be lacking in MTA.

Finally, when analysing GICs, since the required performance was poor and attempted improvements have not yet led to concrete results, nowadays they are not identified as a suitable material in ERR management.

7. BIBLIOGRAPHY

1. Sikri VK. Root Resorption - an Enigma. Indian Journal of Comprehensive Dental Care (IJCDC) 2011 Jul [cited 2021 Sep 2];1(1):15–8.
2. Vivekananda Pai A, Khosla M. Root resection under the surgical field employed for extraction of impacted tooth and management of external resorption. J Conserv Dent. 2012;15(3):298.
3. Kheirieh S, Fazlyab M, Torabzadeh H, Eghbal MJ. Extraoral Retrograde Root Canal Filling of an Orthodontic-induced External Root Resorption Using CEM Cement. *Iran Endod J*. 2014;9(2):149-152.
4. Bartok RI, Văideanu T, Dimitriu B, Vârlan CM, Suciu I, Podoleanu D. External radicular resorption: selected cases and review of the literature. *J Med Life*. 2012;5(2):145-148.
5. Mohammadi Z, C Cehreli Z, Shalavi S, Giardino L, Palazzi F, Asgary S. Management of Root Resorption Using Chemical Agents: A Review. Iran Endod J. 2016 Winter;11(1):1-7.
6. Darcey J, Qualtrough A. Root Resorption: Simplifying Diagnosis and Improving Outcomes. *Prim Dent J*. 2016;5(2):36-45.
7. Popescu SM, MercuŢ V, Scrieciu M, et al. Radiological and optical coherence tomography aspects in external root resorption. *Rom J Morphol Embryol*. 2017;58(1):131-137.
8. Ahangari Z, Nasser M, Mahdian M, Fedorowicz Z, Marchesan MA. Interventions for the management of external root resorption. *Cochrane Database Syst Rev*. 2015;2015(11):CD008003. Published 2015 Nov 24.
9. Sengar E, Mulay S, Kulloli A, Ligade S. Management of internal and external resorption with open apex. J Interdiscip Dent. 2019;9(2):83.
10. Al Khatib Z, Besner E. Dental traumatic injuries. In: Jain P, curatore. Current Therapy in Endodontics [Internet]. Hoboken, New Jersey: John Wiley & Sons, Inc.; 2016 [cited 12 May 2021]. pag. 153–91.

11. Yi J, Sun Y, Li Y, Li C, Li X, Zhao Z. Cone-beam computed tomography versus periapical radiograph for diagnosing external root resorption: A systematic review and meta-analysis. Angle Orthod. 1 march 2017;87(2):328–37.

12. Mona M, Abbasi Z, Kobeissy F, Chahbandar A, Pileggi R. A Bioinformatics Systems Biology Analysis of the Current Oral Proteomic Biomarkers and Implications for Diagnosis and Treatment of External Root Resorption. Int J Mol Sci. 20 march 2021;22(6):3181.

13. Pruthi P, Dharmani U, Roongta R, Talwar S. Management of external perforating root resorption by intentional replantation followed by Biodentine restoration. Dent Res J. 2015;12(5):488.

14. Rangwala A. Clinical Management of Severe External Root Resorption and Immature Open Apex with MTA and Calcium Hydroxide. Clinical Dentistry (0974-3979) [Internet]. 2014 Jan [cited 2021 Sep 2];8(1):27–31.

15. Galler KM, Grätz E-M, Widbiller M, Buchalla W, Knüttel H. Pathophysiological mechanisms of root resorption after dental trauma: a systematic scoping review. BMC Oral Health. December 2021;21(1):163.

16. Abbott P. Prevention and management of external inflammatory resorption following trauma to teeth. Aust Dent J. march 2016; 61:82–94.

17. Lu J, Liu H, Lu Z, Kahler B, Lin LM. Regenerative Endodontic Procedures for Traumatized Immature Permanent Teeth with Severe External Root Resorption and Root Perforation. J Endod. november 2020;46(11):1610–5.

18. Bellini-Pereira SA, Almeida J, Aliaga-Del Castillo A, dos Santos CCO, Henriques JFC, Janson G. Evaluation of root resorption following orthodontic intrusion: a systematic review and meta-analysis. Eur J Orthod. 3 august 2021;43(4):432–41.

19. Samandara A, Papageorgiou SN, Ioannidou-Marathiotou I, Kavvadia-Tsatala S, Papadopoulos MA. Evaluation of orthodontically induced external root resorption following orthodontic treatment using cone beam computed tomography (CBCT): a systematic review and meta-analysis. Eur J Orthod. 23 january 2019;41(1):67–79.

20. Iglesias-Linares A, Hartsfield JK. Cellular and Molecular Pathways Leading to External Root Resorption. J Dent Res. february 2017;96(2):145–52.

21. Udagawa N, Koide M, Nakamura M, Nakamichi Y, Yamashita T, Uehara S, et al. Osteoclast differentiation by RANKL and OPG signaling pathways. J Bone Miner Metab. january 2021;39(1):19–26.

22. Nakano Y, Yamaguchi M, Fujita S, Asano M, Saito K, Kasai K. Expressions of RANKL/RANK and M-CSF/c-fms in root resorption lacunae in rat molar by heavy orthodontic force. Eur J Orthod. 1 august 2011;33(4):335–43.

23. Wang Z, McCauley L. Osteoclasts and odontoclasts: signaling pathways to development and disease: Osteoclasts and odontoclasts. Oral Dis. march 2011;17(2):129–42.

24. Ximenes, Gabriela Wagner; SILVA, Alessandra Dutra da and Borba, Paulo Oliva de. Immunopathological response in external dental resorption. *Stomatos* [online]. 2015, vol.21, n.41, pp. 29-34.

25. Fernandes M, de Ataide I. Nonsurgical management of a large periapical lesion associated with an immature tooth displaying external inflammatory resorption. J Conserv Dent. 2015;18(4):349.

26. Shah P, Arora A, Kapoor S. Accessory branch of canalis sinuosus mimicking external root resorption: A diagnostic dilemma. J Conserv Dent. 2017;20(6):479.

27. Bahabri R. Combined Surgical and Endodontic Therapy to Repair the External Root Resorption Defect Using a Condensable Bioceramic Material. A Case Report. International Journal of Medical Dentistry [Internet]. 2020 Oct [cited 2021 Sep 2];24(4):547–51.

28. Sayyad Soufdoost R, Jamali Ghomi A, Labbaf H. Endodontic management of a tooth with apical overfilling and perforating external root resorption: A case report. Clin Case Rep. December 2020;8(12):3278–83.

29. Kim S-Y, Yang S-E. Surgical repair of external inflammatory root resorption with resin-modified glass ionomer cement. Oral Surg Oral Med Oral Pathol Oral Radiol Endodontology. april 2011;111(4):e33–6.

30. Solanki NP, Venkappa KK, Shah NC. Biocompatibility and sealing ability of mineral trioxide aggregate and biodentine as root-end filling material: A systematic review. J Conserv Dent. 2018 Jan-Feb;21(1):10-15.

31. Chohan H, Dewan H, Annapoorna B, Manjunath M. Comparative evaluation of sealing ability of glass ionomer-resin continuum as root-end filling materials: An in vitro study. J Int Soc Prev Community Dent. 2015;5(6):488.

32. Bolbolian M, Mostafaei F, Faegh S. Evaluation of the Marginal Adaptation of ProRoot MTA, Biodentine, and RetroMTA as Root-end Filling Materials. Dent Hypotheses. 2020;11(4):97.

33. Dawood AE, Parashos P, Wong RHK, Reynolds EC, Manton DJ. Calcium silicate-based cements: composition, properties, and clinical applications. J Investig Clin Dent. may 2017;8(2):e12195.

34. ElReash AA, Hamama H, Eldars W, Lingwei G, Zaen El-Din AM, Xiaoli X. Antimicrobial activity and pH measurement of calcium silicate cements versus new bioactive resin composite restorative material. BMC Oral Health. december 2019;19(1):235.

35. Estrela C, Decurcio D de A, Rossi-Fedele G, Silva JA, Guedes OA, Borges ÁH. Root perforations: a review of diagnosis, prognosis and materials. Braz Oral Res [Internet]. 18 october 2018 [citato 16 May 2021];32(suppl 1).

36. Donnermeyer D, Bürklein S, Dammaschke T, Schäfer E. Endodontic sealers based on calcium silicates: a systematic review. Odontology. October 2019;107(4):421–36.

37. Wang Z. Bioceramic materials in endodontics. Endod Top. 2015;32(1):3–30.

38. BAHABRI R, KRSOUM M. Biodentine: Perforation, Retrograde Filling, and Vital Pulp Therapy. A Review. International Journal of Medical Dentistry [Internet]. 2020 Jul [cited 2021 Sep 2];24(3):394–7

39. Bhavana V, Chaitanya K, Dola B, Gandi P, Patil J, Reddy R. Evaluation of antibacterial and antifungal activity of new calcium-based cement (Biodentine) compared to MTA and glass ionomer cement. J Conserv Dent. 2015;18(1):44.

40. Rajasekharan S, Martens LC, Cauwels RGEC, Anthonappa RP. Biodentine™ material characteristics and clinical applications: a 3-year literature review and update. Eur Arch Paediatr Dent. February 2018;19(1):1–22.

41. Singla M, Verma KG, Goyal V, Jusuja P, Kakkar A, Ahuja L. Comparison of Push-Out Bond Strength of Furcation Perforation Repair Materials - Glass Ionomer Cement Type II, Hydroxyapatite, Mineral Trioxide Aggregate, and Biodentine: An *in vitro* Study. Contemp Clin Dent. 2018 Jul-Sep;9(3):410-414.

42. Hansen SW, Marshall JG, Sedgley CM. Comparison of Intracanal EndoSequence Root Repair Material and ProRoot MTA to Induce pH Changes in Simulated Root Resorption Defects over 4 Weeks in Matched Pairs of Human Teeth. J Endod. april 2011;37(4):502–6.

43. Shokouhinejad N, Nekoofar MH, Ashoftehyazdi K, Zahraee S, Khoshkhounejad M. Marginal adaptation of new bioceramic materials and mineral trioxide aggregate: a scanning electron microscopy study. *Iran Endod J*. 2014;9(2):144-148.

44. Lagisetti AK, Hegde P, Hegde MN. Evaluation of bioceramics and zirconia-reinforced glass ionomer cement in repair of furcation perforations: An *in vitro* study. *J Conserv Dent*. 2018;21(2):184-189.

45. Sulaiman TA, Abdulmajeed AA, Altitinchi A, Ahmed SN, Donovan TE. Physical Properties, Film Thickness, and Bond Strengths of Resin-Modified Glass Ionomer Cements According to Their Delivery Method: Cement Properties with Different Delivery Methods. J Prosthodont. gennaio 2019;28(1):85–90.

46. Ching HS, Luddin N, Kannan TP, Ab Rahman I, Abdul Ghani NRN. Modification of glass ionomer cements on their physical-mechanical and antimicrobial properties. J Esthet Restor Dent. novembre 2018;30(6):557–71.

47. Nicholson JW, Sidhu SK, Czarnecka B. Enhancing the Mechanical Properties of Glass-Ionomer Dental Cements: A Review. Materials (Basel, Switzerland) [Internet]. 2020 May 31 [cited 2021 Sep 2];13(11)

48. Mohammadi Z, Shalavi S. Clinical applications of glass ionomers in endodontics: a review. *Int Dent J*. 2012;62(5):244-250.

49. Nicholson JW. Maturation processes in glass-ionomer dental cements. Acta Biomater Odontol Scand. 1 January 2018;4(1):63–71.

50. Sidhu S, Nicholson J. A Review of Glass-Ionomer Cements for Clinical Dentistry. J Funct Biomater. 28 giugno 2016;7(3):16

51. P V R, Vemisetty H, K D, et al. Comparative Evaluation of Marginal Adaptation of Biodentine(TM) and Other Commonly Used Root End Filling Materials-An Invitro Study. *J Clin Diagn Res*. 2014;8(3):243-245

52. Chimata VK, Yadiki JV, Jampanapalli SR, Konda S, Inguva HC. Comparative Evaluation of the Antimicrobial Properties of Glass Ionomer Cements with and without Chlorhexidine Gluconate. Int J Clin Pediatr Dent. june 2016;9(2):99–103.

53. Johari Y, Pungut NA, Wong Xiu Yin V, Khamis MF, Yusoff MNM. Sealing Ability of Injectable Dental Composites, Biodentine and MTA in Repairing Furcal Perforation of Permanent Molar Teeth. Journal of International Dental & Medical Research [Internet]. 2020 Oct [cited 2021 Sep 2];13(4):1428–34

Preflight Results

Document Information

Title: untitled
Author: Rui Emanuel Barbosa de Sousa
Creator: Microsoft® Word per Microsoft 365
Producer: Microsoft® Word per Microsoft 365

Preflight Information

Profile: Convert to PDF/A-2b
Version: Qoppa jPDFPreflight v2021R1.00
Date: Sep 21, 2021 9:51:14 AM

Legend: (X) - Can NOT be fixed by PDF/A-2b conversion.
(!X) - Could be fixed by PDF/A-2b conversion. User chose to be warned in PDF/A settings.

Page 6 Results

(X) Font TimesNewRomanPSMT is not embedded. Could not find matching font to embedFont TimesNewRomanPSMT can not be embedded because: Could not find matching font to embed

Page 12 Results

(X) Font TimesNewRomanPSMT is not embedded. Could not find matching font to embedFont TimesNewRomanPSMT can not be embedded because: Could not find matching font to embed

Page 13 Results

(X) Font TimesNewRomanPS-BoldMT is not embedded. Could not find matching font to embedFont TimesNewRomanPS-BoldMT can not be embedded because: Could not find matching font to embed

Page 17 Results

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed

Page 18 Results

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed

Page 18 Results (contd.)

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed

Page 20 Results

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed

Page 21 Results

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed

Page 23 Results

(X) Font TimesNewRomanPSMT is not embedded. Could not find matching font to embedFont TimesNewRomanPSMT can not be embedded because: Could not find matching font to embed
(X) Font TimesNewRomanPSMT is not embedded. Could not find matching font to embedFont TimesNewRomanPSMT can not be embedded because: Could not find matching font to embed
(X) Font TimesNewRomanPSMT is not embedded. Could not find matching font to embedFont TimesNewRomanPSMT can not be embedded because: Could not find matching font to embed

Page 24 Results

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed

Page 26 Results

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed

Page 27 Results

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed

Page 27 Results (contd.)

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed

Page 35 Results

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed

Page 36 Results

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed

Page 37 Results

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed

Page 37 Results (contd.)

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed

Page 38 Results

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed

Page 39 Results

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed

Page 44 Results

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed

Page 52 Results

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed

Page 53 Results

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed

Page 54 Results

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed

Page 54 Results (contd.)

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed

Page 55 Results

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed

Page 56 Results

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed

Page 57 Results

(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed
(X) Font ArialMT is not embedded. Could not find matching font to embedFont ArialMT can not be embedded because: Could not find matching font to embed