

EXTERNAL CERVICAL ROOT RESORPTION: DETERMINANTS & TREATMENT OUTCOMES

by

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Abstract

Objectives: The objectives of this study were to assess if any systemic condition could be a potential predisposing factor for external cervical root resorption (ECRR), and to assess the long-term ECRR treatment outcome and its determinants.

Methods: This study contains data from 76 patients (98 teeth) diagnosed with ECRR at the UBC Graduate Endodontics clinic, from 2008 to 2018. Data regarding the medical and dental history were retrospectively collected from the charts of the ECRR group and an equivalent group of patients without ECRR (control group). Subsequently, the ECRR patients were approached for a follow-up appointment, during which a clinical examination was conducted and intraoral photos were taken. Periapical radiographs, and CBCT if indicated, were taken for the radiographic evaluation. Chi Square test or Fisher's Exact test were used for statistical comparisons at two levels, patient-based and tooth-based level. The Kaplan Meier curves method was used in order to evaluate the overall ECRR survival/failure rates, and how various treatment-related and local predisposing determinants were associated with the ECRR treatment outcome.

Results: Overall, 67 patients were evaluated. The mean follow-up was 3.9 years with the minimum follow-up being one year. The majority of the patients were older than 40 years old (72.4%). The most frequently affected teeth were the maxillary anteriors (31.7%) with the most common diagnosis being Class 2 (38.8%). Half of the cases survived for eight years. Twenty-four teeth failed (i.e. 19 extracted, 5 not functional). The only influencing factor that proved to be statistically significant among the systemic conditions was diabetes, and it was more frequently present in the ECRR group than in the control group. Determinants with statistically significant influence were: the root canal treatment (RCT) and the resorption repair combined with RCT as

local determinants; and the tooth location and the Heithersay classification as treatment-related determinants.

Conclusions: Diabetes may be a potential systemic predisposing factor for ECRR. RCT and the ECRR repair combined with RCT are associated with lower failure rates. Higher failure rates are associated with posterior teeth and higher classes in the Heithersay classification.

Lay summary

External cervical root resorption (ECRR) is a poorly investigated, dynamic process. The key goals of the present study were to assess if any systemic conditions predispose ECRR, and to examine the ECRR treatment outcomes and its determinants.

The study's contribution was to provide a new clinical research approach to this challenging topic. More specifically, there are no previous cohort studies about the association between systemic determinants and ECRR. The present study suggests that diabetes may be a risk factor for ECRR. This indication is of significance because it may have an impact in early diagnosis of ECRR. In addition, cohort studies have not been conducted regarding how various ECRR treatment-related and local determinants may be associated with the treatment outcome. Our findings are of clinical importance because they can provide indications for better treatment planning, and they also highlight the significance of early ECRR diagnosis.

Preface

The present study was designed and completed by the MSc candidate, Eleni Irinakis, under the supervision and guidance of Dr. Markus Haapasalo and Dr. Jolanta Aleksejuniene. The relative contribution of the collaborators in this study was: Dr. Eleni Irinakis 80%, Dr. Jolanta Aleksejuniene 10% and Dr. Markus Haapasalo 10%. The project was approved by the UBC Behavior Research Ethics Board (H17-00885).

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List of Abbreviations

AAE	American Association of Endodontists
CEJ	Cementoenamel junction
CNS	Central nervous system
ECRR	External cervical root resorption
EPT	Electrical pulp test
FeHV-1	Feline herpes virus type 1
GE	Graduate Endodontics
GI	Glass ionomer
MTA	Mineral trioxide aggregate
OPG/RANKL/RANK	Osteoprotegerin/ receptor activator of nuclear factor kappa B ligand/ receptor activator of nuclear factor kappa B
PDL	Periodontal ligament
POE	Portal of entry
PRRS	Pericanalar resorption resistant sheet
RR	Root resorption
SLOB	Same lingual opposite buccal
TCA	Trichloroacetic acid
UBC	University of British Columbia
VRF	Vertical root fracture

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Dedication

This dedication is for my family.

To my mom and dad, for supporting my decisions with all their heart, for teaching me not to give up and for always contributing to my happiness with all their strength. You are the most inspiring role models I could have ever had. To my sister, Vasiliki, for being my best friend since I remember myself and for always standing by me. Your enduring support makes me overcome any obstacles. To my brother, Tasso, for always supporting me and believing in me. Your unwavering support has changed my life. Thank you for everything. To my love, George, for supporting me throughout my education and for being the best company in my life. Without you, this journey would have never been the same. Thank you for making this possible for us.

Chapter 1: Literature review

1.1 Introduction

Root resorption in primary teeth is a physiological process (1). However, in permanent teeth it is a pathological process which may result in loss of dentin, cementum and/or bone and may vary in appearance (2). More specifically, the different types of root resorption which have different clinical and radiographic appearance, and different etiology, are the following: internal inflammatory resorption, external inflammatory resorption, replacement resorption, cervical resorption and transient apical breakdown (2).

The present study is focusing on the external cervical root resorption (ECRR), which is typically located at the cervical area of the root and it is mainly invasive in nature (3). The ECRR starts as a small defect, but it may expand apico-coronally and/or circumferentially around the root canal space (4). As a result, the teeth to maintain their vitality and the patients are often symptom free until the later stages of the resorption process (5).

The exact etiology behind the ECRR is unknown. Two cohort studies have been published presenting ECRR potential local predisposing factors (3,6). However, there is no cohort study examining any systemic conditions as predisposing determinants. In addition, there is only one published study examining the treatment outcome of the ECRR cases (7). This study (7) examines the treatment outcome based only on one local factor (i.e. the Heithersay classification).

The current project will assess if any systemic determinants are associated with an increased prevalence of ECRR. In addition, it will assess if any treatment-related determinants are associated with lower rates of ECRR treatment failure, and if any local determinants are associated with a higher ECRR failure rates.

Understanding the root resorption

1.2 Classification of root resorption

Different attempts to classify root resorption (RR) have been recorded in an effort to organize the different types of RR into distinct categories. An indirect goal of this attempt was to identify the most effective modality of treatment in each category. The following is a brief historical review of different approaches regarding the classification of RR.

Historically, tooth resorption was first mentioned in the 16th century, in a text called “*Artzney Bunchlein*” (8). Since then, multiple different names have been suggested in order to describe external resorptive defects, such as “*spina ventosa*” (9), “*absorption of permanent fangs*” (10,11), “*rarefying periodontitis*” (12), “*idiopathic resorption*” (13), “*spontaneous intermittent resorption*” (14), “*burrowing resorption*” (15).

In 1970, Andreasen (16), approached the topic and classified the RR of injured teeth as follows: internal resorption, which could be inflammatory or replacement, and external resorption, which could be surface, inflammatory or replacement resorption. Two years later, Tronstad (17), classified the inflammatory RR into internal and external, and stated that it can have either transient or progressive character. Furthermore, the cervical and the replacement resorption were added to into his classification in addition to inflammatory. In 1999, Gunraj (18) described the types of RR according to etiologic factors. He stated that surface, inflammatory and replacement resorptions may be present after traumatic incidents and that external RR can be a result of either pulp necrosis and periradicular pathosis, or of pressure in the periodontal ligament (PDL). Internal and cervical resorption were described as well (18). The same year, Ne et al. (19) classified RR according to clinical and histological findings. Internal RR was subdivided into inflammatory and metaplastic (root replacement resorption). External resorption

was classified as surface RR, inflammatory (cervical or apical) RR, ankylosis, replacement RR (separately from ankylosis), and transient apical breakdown. Combined internal and external resorption, as separate individual classification of RR, was also proposed in this paper (19). Fuss et al., in 2003, proposed a classification according to factors that can act as stimuli. Their classification was as follows: pulpal infection RR, periodontal infection RR, orthodontic pressure RR, impacted tooth or tumor pressure RR, ankylotic RR (20). Another classification, which was introduced in 2006 by Lindskog et al. (21), was supported again one year later by Heithersay in a paper about the management of tooth resorption (22). This classification included three main categories: trauma induced, infection induced and hyperplastic resorption. Each category had also subcategories as follows: Trauma induced resorption could be: 1) surface, 2) transient apical internal, 3) pressure, 4) orthodontic, or 5) replacement. Infection induced resorption could be: 1) internal inflammatory, 2) external inflammatory, or 3) communicating internal external. Hyperplastic resorption could be: 1) internal (invasive) replacement or 2) invasive coronal (22).

The most recent classification which will be used throughout this thesis, is the American Association of Endodontists (AAE) classification in 2016 (2). More specifically, the resorption is defined as “*a condition associated with either a physiologic or a pathologic process resulting in a loss of dentin, cementum and/or bone*”. The classification and how each term is defined, are as follows in Figure 1 (2):

American Association of Endodontists - Glossary of Terms

"Internal resorption — An inflammatory process initiated within the pulp space with loss of dentin and possible invasion of the cementum" (a)

"External resorption — Resorption initiated in the periodontium and initially affecting the external surfaces of a tooth; may be further classified as surface, inflammatory or replacement, or by location as cervical, lateral or apical; may or may not invade the dental pulp space"

"Surface resorption — A physiologic process causing small superficial defects in the cementum and underlying dentin that undergo repair by deposition of new cementum"

"Inflammatory resorption — An internal (a) or external (b) pathologic loss of tooth structure and possibly bone, resulting in a defect; occurs as the result of microbial infection; characterized radiographically by radiolucent areas along the root"

"Replacement resorption (ankylosis) — A pathologic loss of cementum, dentin and periodontal ligament with subsequent replacement of such structures by bone, resulting in fusion of bone and tooth" (c)

"Cervical resorption — A type of external resorption that occurs in the coronal third of the root" (d)

"Transient apical breakdown — A response to tooth luxation consisting of radiographic apical bone and root resorption that resolves spontaneously without intervening treatment"

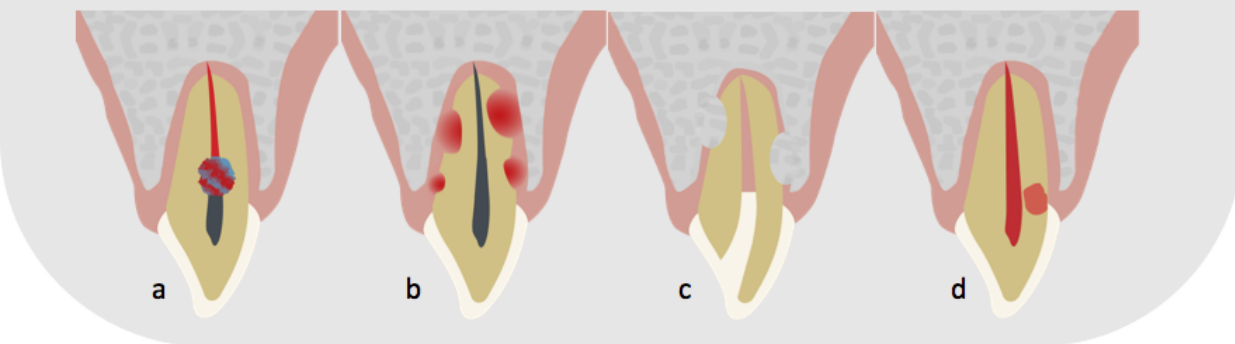


Figure 1. Terminology and classification of root resorption according to the American Association of Endodontists (2). Illustration of different types of root resorption: a) internal inflammatory resorption, b) external inflammatory resorption, c) replacement resorption, d) external cervical resorption.

1.3 Histology of root resorption

Odontoclasts, which are associated with root resorption, exhibit important morphological and functional similarities with osteoclasts (23). These similarities have led some researchers to conclude that odontoclasts and osteoclasts are probably identical. The list of their similarities includes the same contiguous enzymatic function and cytologic characteristics. In addition, they both act on mineralized tissue by causing resorptive defects, known as Howship lacunae (24,25). Furthermore, they are both multinuclear cells, which are the result of mononuclear cell fusion (5,26). Even though mononuclear osteoclasts and odontoclasts have been found in bone and tooth resorptive defects respectively, it is well accepted that as the resorption propagates, multinuclear cells predominate (27,28).

Characteristics that have been suggested as distinguishing factors among these cell types; are the greater size of the cell and its sealing zone and the greater number of nuclei that can be identified in osteoclasts (29). Furseth (30) observed that under an electron microscope, odontoclasts' cytoplasm shows a more vivid staining result than that of its neighbouring cells. This is probably due to the great number of mitochondria, vacuoles and cytoplasmic ribosomes. Their nucleoli are big and symmetrically positioned in the middle of the cell. According to the same researcher, *“where the odontoclast was in contact with the tooth surface, a system of canals extending 2-3 μ m into the cytoplasm was observed, and these canals contained mineral crystals”* (30).

There are different approaches regarding the differentiation of resorptive cells precursors. According to Speziani et al. (31), immature dendritic cells can differentiate their operation into osteoclastic operation and since these cells are present in the pulp tissue, it can be implied that they can also act as odontoclast precursors. According to other researchers, the

OPG/RANKL/RANK transcription factor system has been implied to be responsible for the differentiation of the odontoclasts from their precursors. (32).

It is interesting to examine though, not only the differentiation of resorptive cells which is the molecular starting point for this process, but also the anti-resorption factors. According to Wedenberg et al. (25,33), the expansion of the internal resorption can be prevented by the presence of an odontoblast layer and predentin. Similarly, the expansion of the external resorption can be prevented by the presence of precementum (25,33). In addition, the resorption can only be active when the pulp tissue is vital and at the same time there is a constant bacterial proliferation, probably by partially necrotic pulp tissue (26).

The absence of stimulating factors is critical in order for the resorptive process to cease its progression. The stimulating factors for resorption, can present a concurrent action with the causal factors of the damage on the predentin or precementum of the root. This is a topic that has been examined in the past and it has been shown that there are many different factors (i.e. orthodontic treatment and history of trauma), that can lead to different kinds of resorption (i.e. external or internal) on different areas of the root (cervical, middle or apical third) (20), but it is out of the scope of this thesis to expand further on the topic of causal factors.

1.3.1 Physiological root resorption

Even if the stimulating signals for the physiological root resorption of the deciduous teeth are not well established, it is more likely that this process is a result related to the action of cytokines and transcription factors (1). More specifically, the applied force on the primary teeth by the underlying permanent teeth, is the stimulating factor that activates a sequence of

molecular responses on root and bone tissue, which results in the resorption. However, at the same time, the tooth structure of the permanent adjacent teeth is well protected and instead of being resorbed it develops normally. It is interesting to mention that there is no presence of bacteria during physiological root resorption (26).

1.3.2 Pathological root resorption

Unlike in deciduous teeth, resorption in permanent teeth is a pathologic condition. Permanent teeth cannot undergo physiologic remodeling like bone and regardless the fact that bone resorption may take place around them, they are not usually attacked by clastic cells. However, when this pathological root resorption takes place, the appearance may vary.

Internal root resorption

Throughout the decades, histological studies have been done on extracted teeth diagnosed with internal inflammatory RR, which was initially caused either by natural or experimental forces (34,35). Wedenberg and Zetterqvist (34), in 1987, examined both primary and permanent extracted human teeth and assessed the histologic features of the naturally propagated internal inflammatory RR. According to their findings, the only difference between the two groups of teeth, was that the resorptive defect was propagating faster for the group of primary teeth. Regarding the histological components of the pulp tissue, the researchers found lymphocytes and macrophages to predominate, and some neutrophils to be present. The normal pulp tissue had greater vascularity than the resorptive tissue which was similar to the fibrotic connective tissue of the periodontium. The dentinal walls of resorptive defects were predominated by multinuclear odontoclasts of great size. The adjacent connective tissue was predominated by mononuclear

cells, probably odontoclast precursors. It is interesting to mention that both multinuclear and mononuclear cells, presented tartarate-resistant acid phosphatase (TRAP) activity. It is also fascinating that on the root canal wall of all the examined teeth, mineralized tissue (bone or cementum-like) was present. Furthermore, mineralized tissue islands were present inside the root canal system, which was proposed to be a finding of odontoblast action (34).

External surface root resorption

This type of resorption differs from the others because there is no incessant stimulus. Even though it has been shown that the constant stimulation of the resorbing cells is a requirement for phagocytosis during the resorptive process (36), this kind of resorption is an exception. As a result of the absence of a stimulation force, after a period of a couple of weeks of resorptive action, this phenomenon stops and the area of concern will be repaired by a cementum-like tissue (17) . These resorption defects are present without any PDL inflammation, on normal cementum, and may or may not be identified on a radiograph (37).

External inflammatory root resorption

The histologic appearance of the resorptive defects is bowl-shaped areas, closely related to PDL inflammation. This is probably a result of bacterial antigens from the pulp tissue through tubules. This inflammation results in a growing granulation tissue matrix, which is enclosed in the resorptive defect but at the same time is in contact with the adjacent PDL through the hard tissue loss. This matrix has been shown histologically to consist of plasma cells, lymphocytes and polymorphonuclear leukocytes. The inflammatory reaction can also expand itself into the adjacent capillaries. It is noteworthy that in histologic findings, the odontoclasts are located in the lacunae, in both cementum and dentin, but not in the granulation matrix (37).

Replacement resorption

This type of resorption was named based on the process in which the tooth structure has been replaced in a continuous way by bone. The initial formation of this relationship between bone and tooth structure has not been well described. Yet, on the occasion of a substantiate relationship, the tooth structure either is considered as a “*dead bone transplant*”, so it is replaced, or it is considered as a “*part of the physiological bone remodeling*” (37).

External cervical root resorption

This type of resorption follows the pattern of the other resorptions, with the exception that it is typically located in the cervical area and it is mainly invasive in nature. The location is associated with the level of the junctional epithelium and the probing depths (38). At the beginning of the acute resorptive process, odontoclasts can be found in the lacunae and granulation tissue without inflammatory cells inhabiting the defect (3). However, bacterial proliferation is present at histological images of subsequent stages (4,39). An example of the ECRR histological findings is illustrated in Figure 2.

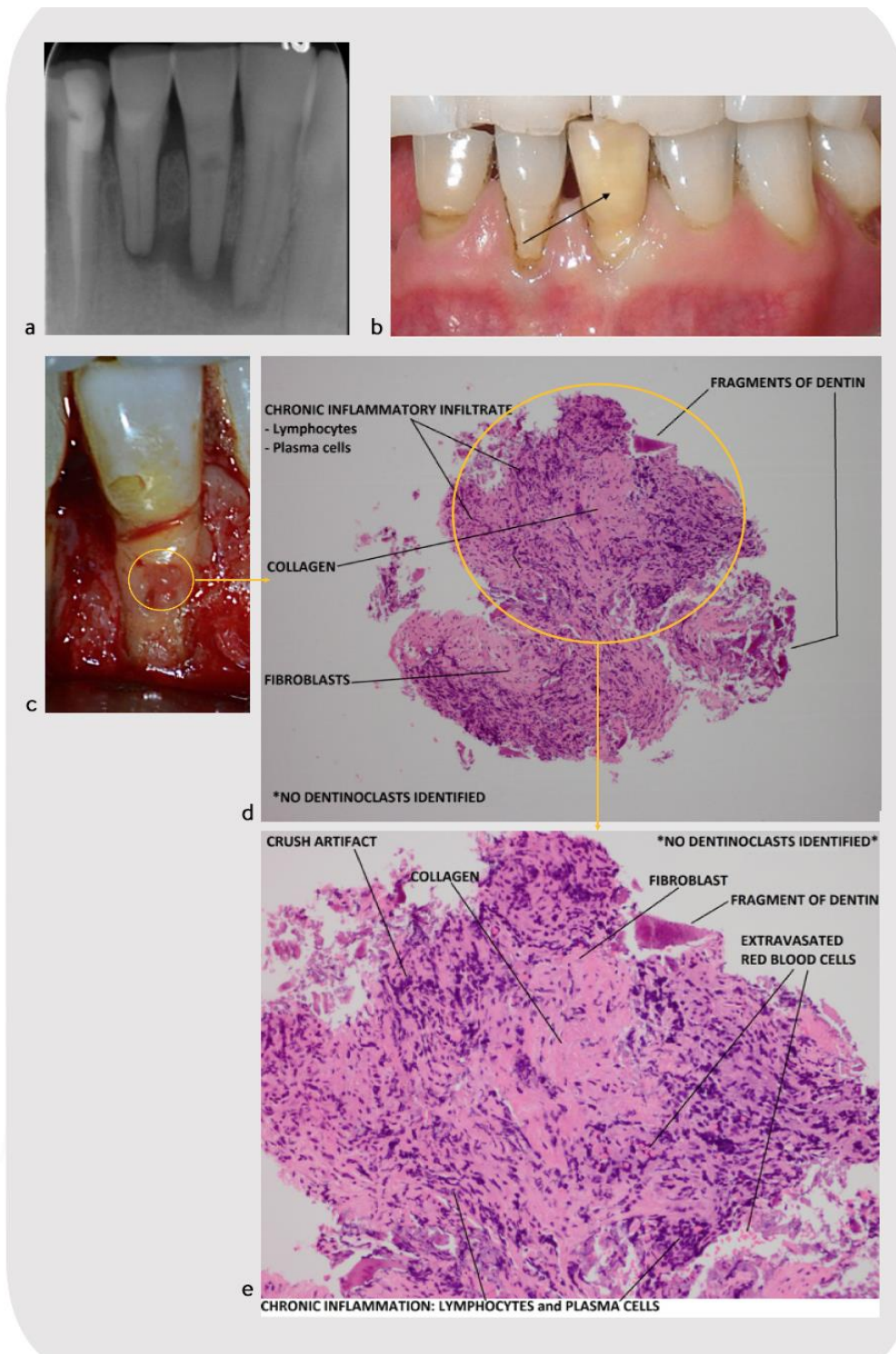


Figure 2. Histological findings. a) periapical radiograph of tooth #31 with external cervical root resorption (ECRR), b) pre-surgical intraoral photo (black arrow shows the tooth with ECRR), c) peri-surgical intraoral photo (yellow circle shows the resorptive defect), d) histological findings, e) magnified area of picture d.

The pattern of expansion for the resorptive defect through the dentin, can be either circumferential around the root canal system or apico-coronal (3). This defect expands itself without invading the root canal system during the first stages, since the presence of predentin acts as an anti-resorption factor as previously mentioned (25,33,40). However, communication between the resorptive defect and the root canal system or the PDL can be noticed at later stages. As a result, the adjacent pulp tissue or the periapical tissue respectively, has normal histologic appearance as long the resorption creates channels only through dentin (3).

The response to the resorptive propagation in some types of cervical resorption and at later stages, is the deposition of bone like tissue in contact with dentin. It was stated that this histologic finding shows an effort of reducing the loss structure (3).

1.4 Classification of external cervical root resorption

Historically, different terminology has been used to describe ECRR, such as “*odontoclastoma*” (41), “*idiopathic external resorption*” (42), “*peripheral cervical resorption*” (43), “*progressive intradental resorption*” (44), “*cervical external resorption*” (45), “*late external resorption*” (46), “*extracanal invasive resorption*” (47), “*supraosseous extracanal invasive resorption*” (48), “*cervical resorption*” (17), or “*peripheral inflammatory root resorption*” (38).

To analyze in depth the phenomenon of ECRR, it is important to understand the different patterns that can be identified in a clinical situation. In 1987, Fank and Bakland classified the “*extracanal invasive resorption*” as intraosseous or supraosseous, based on the possible location of the POE (48). A year later, Frank and Torabinejad further categorized the “*extracanal invasive*

rerorption”, again based on the location of the POE, but this time they suggested 3 classes, i.e. intraosseous, crestal and supraosseous (49).

In 1999, Heithersay published a clinical classification of ECRR, which became the gold standard in the following years. This classification was based on the extension and the pattern of the resorptive defect, as grouped in Figure 3 (3):

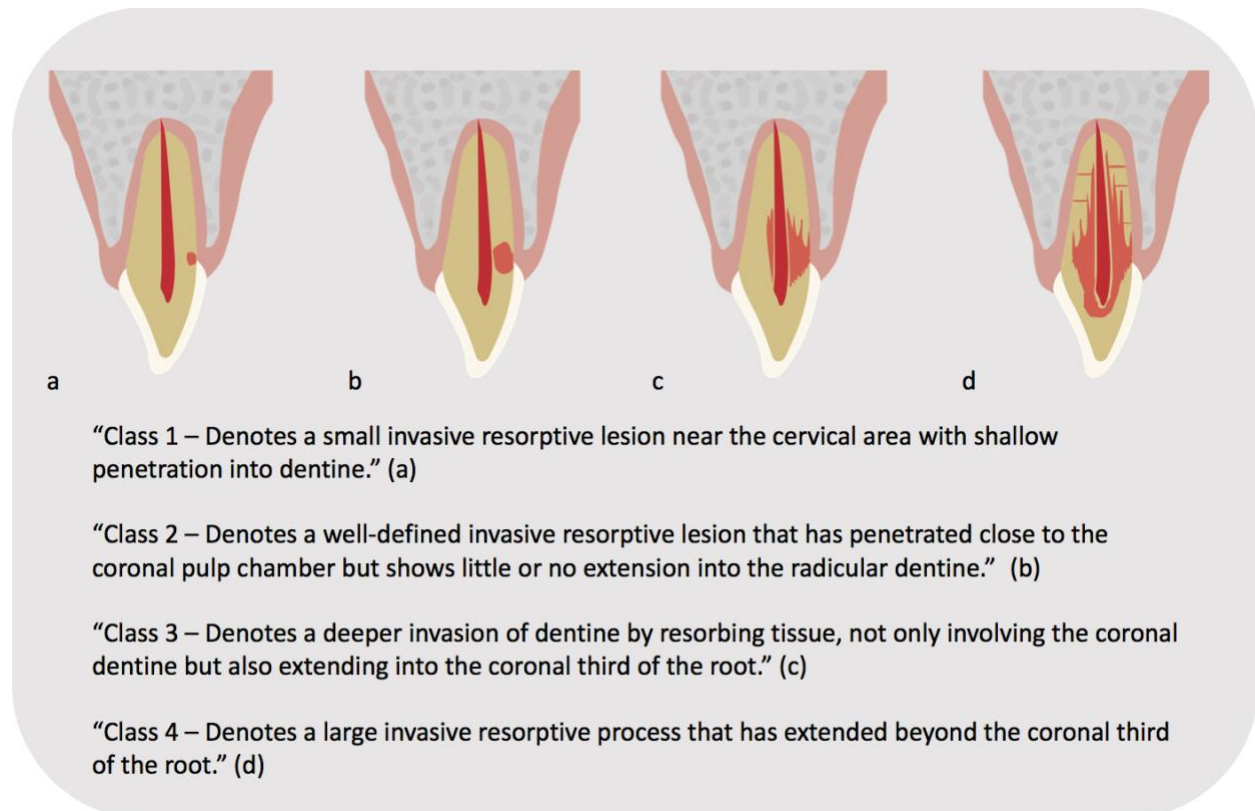


Figure 3. Illustration of the Heithersay classification of external cervical root resorption (3).

In 2018, after the recommended use of CBCT as a means to determine prognosis and treatment plan in root resorption cases (50), two different “three dimensional” classifications have been proposed (51,52). The first one (51) recommended a descriptive classification based on the combination of three measurements on the CBCT image: the height of the lesion , the

circumferential spread and the proximity to the root canal. More specifically, the authors proposed the use of a number from 1 to 4 in order to describe the height of the lesion (i.e. 1: at CEJ or supracrestally, 2: extension into coronal third and subcrestally, 3: extension into middle third, 4: extension into apical third of the root). In addition to that, they proposed the use of a capital letter from A to D in order to describe the circumferential spread (i.e. A: $\leq 90^\circ$, B: $> 90^\circ$ to $\leq 180^\circ$, C: $> 180^\circ$ to $\leq 270^\circ$, D: $> 270^\circ$), and finally a lower-case letter was used to describe the proximity to the root canal (i.e. d: lesion restricted to dentine, p: possible pulpal involvement) (Fig. 4). According to the authors, the combination of the number, the capital and the lower-case letter will provide an effective way of sharing information between colleagues accurately. It seems to be a precise, albeit complicated way of classification, and it requires that a CBCT of good quality is available. The second paper (52) proposed the Rohde Classification System, which is based on the findings of the axial slides of the CBCT images. More specifically, this classification is focused on the amount of dentin loss in the cervical third and the external surface of the tooth. The proposed three classes are based on the circumferential extent of the resorptive defect:

class 1: in less than 1/3 of the tooth,

class 2: in less than 1/3 of the tooth with a perforation defect $\geq 2.5\text{mm}$ in any dimension,

class 3: in more than 1/3 of the tooth.

According to the authors, this classification system may be useful for treatment planning.



Height	At the CEJ or <u>supracrestal</u>	1
Circumferential spread	$\leq 90^\circ$	A
Proximity to the root canal	Lesion confined to dentine	d
Classification		1Ad

Figure 4. Illustration of a novel 3D classification (51). The yellow arrows point the external cervical root resorption.
a) periapical radiograph, b) sagittal CBCT view, c) axial CBCT view of a Class 1Ad case.

Throughout this thesis, the Heithersay classification will be followed.

Understanding the external cervical root resorption

1.5 Mechanism of action of external cervical root resorption

Two recently published studies provide information regarding the mechanism of action of ECRR in vital (53) and previously endodontically treated teeth (54). In both cases, the ECRR is progressing in three main sequential phases. The first phase is named the “*resorption initiation*”, the second the “*resorption progression*”, and the last one the “*repair*” phase. It seems that resorption and repair can take place simultaneously on a root, but at different areas of it. Even if the phases are common in both vital and previously treated teeth, considerable differences between them exist.

1.5.1 External cervical root resorption in vital teeth

Initially, localized PDL breakdown takes place (38) leading to inflammation limited to that area. Activated macrophages travel to the breakdown area and assist in the formation of granulation tissue (55). A potential uncovered dentin area at the level of the cemento-enamel junction (CEJ) could be vulnerable if it comes into contact with the granulation tissue (56). If indeed the dentin is exposed at the level of the CEJ, then this area is a potential portal of entry (POE) for cervical resorption. There are three possible scenarios that can take place, based on the type of tissue adjacent to the POE (57). The first scenario takes place when the injured area is reconstructed by bone cells, which results in replacement resorption (55). In the second scenario, the area is reconstructed by PDL cells that results in the regeneration of the periodontium (55). The last scenario, in which there is no repair, takes place when gingival connective tissue comes into contact with the exposed dentin (55). According to Mavridou et al. (53), PDL is usually not

present at the POE of ECRR, but the area is predominated by fusion and augmentation of the alveolar bone into the resorptive lacunae. However, a stimulus, such as infection or mechanical force, is required in order for the ECRR to propagate (38). It has been hypothesized, that hypoxia at the resorptive microenvironment possibly plays a significant role at this first stage of ECRR (53).

During the second phase, the resorption spreads towards the pulp, by tearing down cementum, dentin and enamel; without invading the pulp space per se, due to a resistant layer. It then creates resorptive channels in all three dimensions and expands with a more circumferential spread. By using micro-CT, the mean thickness of the residual circumpulpal/pericanalar dentin has been found to be 210 μm , and the contrast of this area has been shown to differ from the rest of the dentin; which could be interpreted as an area with a distinctive mineral substance (58). According to Mavridou et al. (53), the pulp plays a role during the resorptive process by propagating calcification of the extracellular matrix, especially at the areas close to the active sites of ECRR. The authors named the residual circumpulpal layer as pericanalar resorption resistant sheet (PRRS). They advocated that the occurrence of the PRRS of this high impedance is due to two main reasons. Either due to vitality of the pulp, which provides normoxia in the PRRS, versus hypoxia in the resorptive areas, or due to the way the mineralization of this layer is distributed, being more mineralized at the external surface and gradually less mineralized in the internal surface (53).

During the third stage, bone like tissue travels through the POE and grows into the resorptive lacunae towards the pulp, a process that has been interpreted as healing (14,53,59). Also, in areas where the PDL is disintegrated, a localized fusion between the neighboring alveolar bone and the newly formed bone like tissue takes place. It has been noticed that osteoid tissue apposition and remodeling processes can coexist (53).

1.5.2 External cervical root resorption in endodontically treated teeth

During the initiation stage of ECRR in endodontically treated teeth, all the steps described for the vital teeth take place. The main difference is that in previously treated teeth, there is no bone tissue coming through the POE into the resorptive lacunae, and as such there is no fusion between the root and the adjacent alveolar bone (54). An explanation supported by the authors, is that due to lack of vitality these teeth are also lacking the balanced action of normoxia; and as a result hypoxia predominates (54). It has also been suggested that under hypoxia, angiogenesis is high which potentially leads to a successive growth of a highly vascularized granulation tissue in the area (60).

During the second stage, a similar pattern of ECRR has been noticed in both vital and previously treated teeth. The main difference is that the resorption proceeds in a more expansive way for the endodontically treated teeth. Two potential explanations have been given, the absence of a PRRS (53,54) and the different chemical composition of root dentin after its exposure to irrigants during the RCT (54,61).

During the third stage, remodelling still takes place, similarly to the vital teeth, but it is less extensive (54).

1.6 Etiology and predisposing factors

The precise etiology of ECRR remains a mystery that has not been solved. However, it is generally recognized that a deficiency or damage on the cementum layer at the cervical area of the root, bellow the epithelial attachment, could be described as a requirement for a resorption to initiate (38). This has been confirmed by animal studies (55). This deficiency on cementum layer can be either a result of developmental insufficiency that allows a POE at the CEJ level (62), or a result of chemical or mechanical breakdown (54,56).

In an effort to identify the predisposing factors of ECRR, several studies have been conducted. However, due to the complex character of the topic, the vast majority of these studies were case reports and case series. Hitherto, only two cohort studies have been carried out (3,6). In this section all these studies will be analyzed in a comprehensive way, with an emphasis on the cohort ones.

To the best of our knowledge, there are no published cohort studies examining systemic determinants as potential predisposing factors for ECRR. However, in this section case reports suggesting an association between systemic conditions and ECRR will be presented. Two systemic conditions (i.e. the use of bisphosphonates and viral infections) were examined as predisposing factors for ECRR in a recent cohort study (6). However, this study included these factors based on existing literature and more specifically based on published case reports. That emphasizes the lack of cohort studies examining which systemic conditions could potentially be predisposing factors for ECRR.

1.6.1 Predisposing factors based on cohort studies

Heithersay published a retrospective study in 1999 (3), where 257 teeth diagnosed with ECRR in 222 patients were analyzed for the presence of possible predisposing factors to ECRR. More specifically, information regarding trauma, intracoronal bleaching, surgery in the area, orthodontic treatment, periodontal root scaling or planing, bruxism, delayed eruption, developmental defects, other treatments or incidents, and intracoronal restorations was collected. Also age, gender, medical and dental history were recorded as well. According to the results of this study, orthodontic treatment was the most common predisposing factor (24.1% of the teeth). Trauma and intracoronal restoration were the next on the list (15.1% and 14.4% of the teeth,

respectively). Surgical procedures at the level of the CEJ and intracoronal bleaching were other two factors that have been associated with the occurrence of ECRR (5.4% and 3.9% of the teeth, respectively). All the other factors that were analyzed in this study were present with low frequency and were the following: bruxism (2.4% of the teeth), eruption disorders (1.6% of the teeth), developmental disorders i.e. grooves or invaginations (0.8% of the teeth), and interproximal stripping (0.6% of the teeth). However, another important finding of this study is that in 16.4% of the teeth with ECRR there was no correlation with any predisposing factor. The author commented that those teeth “*may have had undetectable developmental defects of cementum*”, and therefore categorized the ECRR as idiopathic. In 28.9% of the cases more than one predisposing factor was present, a finding that suggests a multifactorial character of the ECRR (3).

Mavridou et al. (6), collected data from 337 teeth diagnosed with ECRR, in 284 patients. Overall, the evidence was tested on the following potential predisposing factors: cracks, poor oral health, developmental disorders, malocclusion, frenulum tension at cervical gingiva, eruption disorders, extraction of adjacent tooth, nonvital bleaching, orthodontic therapy, orthognathic surgery, parafunctional habits, periodontal surgery, previous traumatic injury, restorative and endodontic procedures, systemic diseases, medication, viral infections and playing of wind instruments. The authors included items to the list based on the existing literature. Orthodontic therapy was the most common factor (45.7% of the teeth). Trauma, parafunctional habits and poor oral health were frequent factors as well (28.5%, 23.2% and 22.9% of the teeth, respectively). Less frequent factors were malocclusion (17.5% of the teeth) and extraction of an adjacent tooth (14.0% of the teeth). Other factors with a low rate of frequency but still noteworthy were the following: eruption disorders (2.7% of the teeth), cracks

(2.1% of the teeth), developmental disorders (1.5% of the teeth), intracoronal restorations (1.2% of the teeth) and frenulum tension at the cervical area (0.6% of the teeth). An interesting observation was also that 59.0% of the cases had more than one predisposing factor, potentially indicating a multifactorial nature for ECRR. Gender appeared to play no role as a predisposing factor for ECRR, while the tooth site seemed to have an impact, with maxillary central incisors being the most frequent diagnosed teeth. Age showed to have a different distribution for each potential predisposing factor. For instance, when orthodontics was the examined determinant, the majority of the patients were found in the age group of 15-19 years, whereas when the determinant was poor oral health, the majority of the patients were found in the age group of above 65 years (6).

1.6.2 Predisposing factors based on case and case series reports

Orthodontic treatment

In 1984, a study on 87 post-orthodontic patients, concluded that ECRR is not a frequent complication since only one patient presented with it (63). This is in agreement with a more recent 8-year orthodontic follow-up study, where only one out of 108 patients was diagnosed with ECRR (64).

Two other studies (65,66) followed an experimental model (67) and applied a variation of forces for different time intervals on teeth that would be later extracted based on the orthodontic treatment plan. There was a control group and all extracted teeth eventually underwent volumetric analysis (65,66). The first study (65) was published in 2006, and assessed the physical properties of root cementum. This study shed light on the frequency of ECRR occurrence, based on the different surfaces of the root in association with different types of force

applied (i.e. compression, tension). The heavy-force group (225g of buccal tipping orthodontic forces) was found to have eight times the amount of resorption at the buccal cervical area, than the light-force group (25g). When the middle and apical surfaces of the root were examined for different force levels, there was no significant difference for the occurred RR (65). The second study in 2017 (66), showed that the extent of ECRR was related to the extent of the tooth movement. Significant ECRR was noted when, for a period of two months, a force of 2 N was applied. Moreover, the mandibular teeth showed more resorption than the maxillary ones (66).

A case series in 2013 examined the influence of failed orthodontic treatment on impacted canines (68). The sample consisted of 14 patients that were referred by other orthodontists after the failure to move impacted canines. The number of teeth examined was 15 since one patient had two canines with ECRR, bilaterally (68). The presence of more than one tooth with ECRR in orthodontic patients has been reported more recently as well (69). It is noteworthy that the ECRR on the impacted canines presented regardless the severity of tooth displacement, and was already class 3 or 4 when patients were referred for a second opinion (68). It is interesting to mention that most of the teeth underwent an open surgical approach during the orthodontic treatment, which means that either mechanical forces or orthophosphoric acid leakage could have potentially initiated a cementum breakdown at the CEJ area. All teeth in this study had to be extracted and the authors made a clear point by concluding that early diagnosis of ECRR is critical (68).

Trauma

ECRR is a frequent unfortunate result of traumatic injuries on teeth (3,6,70). Cvek (46) has described it as “*late*” external resorption because it can be identified during a clinical examination years after the traumatic event took place. It was suggested that patients with a history of dental trauma should continue to be followed up radiographically (70), even when they do not have clinical signs or symptoms. Patients with history of intrusion and avulsion have a higher likelihood of presenting root resorption (not specifically ECRR) after a traumatic incident (71,72), and the need of strict follow-up is higher. The multidisciplinary approach seems to be a requirement for a good treatment outcome in more complicated trauma cases (73).

Bleaching

An unfortunate aftermath of RCT is sometimes the crown discoloration (74), and a common solution offered to this problem is bleaching. However, bleaching may have another unwanted consequence, which is the occurrence of ECRR. One of the first and well described predisposing factors for ECRR is bleaching of pulpless teeth (75). Harrington and Natkin (75) in 1979, presented a case series study where patients had a history of trauma and the RCT was done at a young age. These patients underwent bleaching with a caustic agent and heat source 6 to 15 years (with one exception of 6 months) after trauma. Incident of a second trauma was excluded based on the dental history. The fact that both mesial and distal cervical areas were affected in most of these cases and the timewise close proximity of ECRR to the bleaching procedure supported the hypothesis of predisposition. Two factors may have been involved: first, Superoxol may have diffused through patent dentinal tubules to reach the cervical PDL. Secondly, in 10.0% of the teeth the dentin is exposed to PDL tissue because the enamel and cementum do not meet

(76). These two factors were discussed in “*Inflammatory resorptive response in the cervical area appears a reasonable hypothesis*” by the authors, in addition to the possibility that heat at the cervical area can also be a causative factor for ECRR (75). Four years later, another research team supported this hypothesis (77). The main two differences between the two studies is firstly that this case series included teeth that underwent RCT while the patients were adults, and secondly the absence of history of trauma in the patients’ dental history (77). Similar cases of ECRR after bleaching have been reported (4,78–83). Superoxol is “*a 35% hydrogen peroxide formula to bleach non-vital teeth that can be mixed with sodium perborate for the walking bleach method*” (84), as stated in the manufacturer’s web page. It is not presently known what the role of sodium perborate could be in the initiation of the resorptive process. In 1998, an *in vitro* study suggested an answer to this question by assessing the adherence index of sodium perborate on rat inflammatory macrophages. Due to its inhibitory action on macrophage adhesion, sodium perborate may be involved in the process of ECRR (85). A recent case report in 2017, presented a patient diagnosed with multiple ECRR on mandibular and maxillary incisors, after using a home bleaching kit with 22.0% carbamide peroxide-based gel for 4 nights consecutively (86).

In 1988, Friedman et al. (79) found that occurrence of ECRR after bleaching, and without history of trauma in 6.9% of cases (4 out of 58 patients). They drew the attention to the appropriate bleaching case selection and most importantly to the significance of preventive measures and follow-up (79). As a response to the need for prevention, different approaches have been proposed for intracoronal bleaching, in order to avoid ECRR (77,82).

Traumatic occlusion

In a case report of ECRR on tooth #21, a patient presented with traumatic occlusion on that tooth. Tooth #21 was labially displaced and had occlusal interference throughout protrusive movements and fremitus on centric occlusion. However, this specific case also presented with poor oral hygiene and a pyogenic granuloma in the area of the ECRR. (87). Occlusal trauma with the presence of periodontal findings (i.e. localized gingival overgrowth) had been reported previously as well (88). Malocclusion has frequently (17.5%) been found to be a predisposing factor for ECRR (6).

Periodontal findings

Poor oral hygiene or the presence of plaque is a factor often mentioned in cases of ECRR (87–91) and is well described as a significant possible predisposing factor (22.9%) for ECRR (6). Periodontal therapy (i.e. deep scaling including the area of the CEJ) has been seldom mentioned as a predisposing factor (3). Surgical periodontal therapy, on the other hand, has been found to be present as a predisposing factor from 1.8% of the teeth (6) to 5.4% of the teeth (3). Other periodontal findings, such as pyogenic granulomas (87), peripheral giant cell granulomas (recurrent or not) (38,92), localized gingival overgrowth (88) and gingival inflammation with crestal bone resorption (93) have also been associated with ECRR.

Extraction of a neighboring tooth

Extraction of a neighboring tooth has been described as a predisposing factor, since mechanical trauma to the remaining teeth can be caused during such procedure. A case report was published where a tooth adjacent to an extracted mandibular molar developed ECRR (94). However, in this particular case, orthodontic movement and a final tilted position of the tooth

(i.e. increased possibility of occlusal trauma), were reported after the extraction of the adjacent tooth. In a prospective cohort study, extraction of a neighboring tooth was found to have 14.0% frequency among the predisposing factors (6).

Playing wind instruments

A case series study hypothesized that pressure forces applied on the cervical area of the root by a wind instrument could trigger the initiation of ECRR (95). This hypothesis was supported by a cohort study which found 9 out of 337 teeth (2.7%) were diagnosed with ECRR in patients who play wind instruments (6). Another case of a clarinet player having ECRR on a lateral incisor was also published in 1992 (38).

Orofacial cleft

A retrospective cohort study shed light on the prevalence of ECRR in orofacial cleft patients. Out of 558 patients examined, 14 were diagnosed with ECRR (2.4%), six with unilateral and eight with bilateral cleft lip and palate. All 17 teeth affected were maxillary anterior teeth. All patients had undergone orthodontic treatment, and a significant number of them presented with dental history of periodontal surgery (n=12) or osteotomy (n=7) (96).

Bisphosphonates

In an effort to identify etiologic factors, Patel and Saberi (97) examined the effect of specific systemic medications. As they stated in their case series paper, bisphosphonates were related with “*an acute phase response and the release of proinflammatory cytokines*”, which could be identified as a possible causal factor for ECRR.

Viral infections

There are three different types of viral infections that have been related to ECRR, the Varicella zoster virus, the Feline herpes virus type 1 (FeHV-1) and the Hepatitis B virus infection.

The varicella zoster virus was first associated with internal root resorption in 1986 (98), and then later in 2007 (99) and 2015 (100). It was only in 2016, that the varicella zoster virus was associated with an ECRR case (101). In this case report (101), a patient was hospitalized due to a severe trigeminal (right V3 branch) herpes zoster episode 19 years prior, and a mild anesthesia in the right lower area of patient's face was reported. The day that the patient was examined (19 years after the hospitalization), all teeth from the central incisor (#41) to the second molar (#47) located on the forth quadrant (right side of dentition of lower jaw) did not respond to vitality tests (both EPT and cold test). With one exception of a previously treated tooth, all other teeth were found to be without any clinical indication of necrosis, such as deep caries. As a consequence of the zoster virus, multiple periapical radiolucencies presented in the affected area, along with a ECRR in the mandibular canine of the affected side. It is noteworthy that the existence of varicella zoster virus in the RC system, with the absence of bacteria, was confirmed by molecular and culture tests. Other predisposing factors, such as history of trauma or orthodontic treatment were excluded according to the patient's dental history (101). Based on a review paper (102), there are no other reported cases of varicella zoster virus detected in patients with any kind of root resorption.

The second type of viral infections related to ECRR is the Feline herpes virus type 1 (FeHV-1). An interesting observation is that feline (domestic, captive and wild ones) odontoclastic resorptive lesions in the cervical area of teeth is a frequent clinical finding for

veterinary dentists (103,104). In a case series report (105), four patients were diagnosed with multiple ECRR and no predisposing factor was found on their dental or medical history. The authors having the background knowledge of feline odontoclastic resorptive lesions and in an effort to identify the etiology of ECRR, asked their patients whether they had been an encounter with cats. They received a positive response from all the patients, and blood samples were collected for neutralization testing of FeHV-1, which verified the transmission. This report highlights the possibility of transmission of FeHV-1 to humans (105).

The third and most recently published type of viral infections related to ECRR is the Hepatitis B virus. This case reported on a patient where a multiple idiopathic ECRR affected 20 teeth. No other predisposing factors, except the viral infection, were found in the medical or dental history of the patient (106).

Systemic sclerosis

A case report of a patient with multiple ECRR lesions identified a potential correlation of ECRR with systemic sclerosis, after other possible predisposing factors were excluded based on the patient's dental history (107). Systemic sclerosis is an autoimmune disease, characterized by microvascular breakdown and generalized fibrosis. The authors described a potential correlation between the high osteoclastogenesis (108,109) of the mandible and the distal phalanges of fingers (a result of the systemic sclerosis), with the mechanism of action of ECRR (107).

Familial pattern

The effect of genetic predisposition has been discussed in a case where a father and his son and daughter, two out of his six children, were all diagnosed with multiple idiopathic ECRR (110). In the study of Gold and Hasselgren (38) published in 1992, the authors made a comment

about a potential link between idiopathic ECRR and genetic factors. According to the authors, idiopathic cases of ECRR have been diagnosed in family members.

Diet

According to a case report, a patient developed ECRR lesions after having an acid enriched diet for two years (94). The patient also presented inflammation of the gingiva and resorption of the crestal bone. The authors proceeded with periodontal treatment and recommended alterations to the patient's diet. At the one year follow-up examination, repair of the resorptive defects with bone-like tissue was noticed (93).

1.6.3 Idiopathic external cervical root resorption

When none of the known predisposing factors can be identified through the patients' dental or medical history or by a thorough clinical examination, ECRR is diagnosed as idiopathic (13,111,112). It is notable that when Heithersay (3) investigated ECRR potential predisposing factors, 16.4% of the teeth (15.3% of the patients) examined were not related to any of the investigated factors. Case reports of idiopathic ECRR (113) have been previously published. However, a recent cohort study (6) which examined a wide range of predisposing factors as they were indicated by the literature, concluded that known predisposing factors were not identified in only 1.0% of the cases.

Multiple idiopathic external cervical root resorption

Multiple idiopathic resorption is an extended version of ECRR. It was, initially reported in 1930 (114). It can affect from 3 (115) or more teeth per patient (106,115,116), to all of patient's teeth in extreme cases, including even impacted third molars (117). No etiological

factors have been identified through these patients' medical and dental histories. However, a potential link to the feline virus (105) and the Hepatitis B virus (106) has been suggested as a potential factor. A hereditary link was also proposed (110). Multiple idiopathic ECRR is a rare condition, and only 25 case reports or case series reports, including 34 patients, have been published between 1930 to 2018 (93,106,118–120). Multiple idiopathic ECRR has been more frequently diagnosed in female patients (121). Multiple idiopathic root resorptions at the middle and apical third of the root have been reported as well (122,123).

1.6.4 Multifactorial etiology

The process of understanding the etiology of ECRR is fascinating not only because of the mystery behind it, but also due to the common coexistence of more than one etiologic factor simultaneously. As mentioned earlier, it has been found that the multifactorial character of ECRR is a frequent finding (28.9% of the patients (3) and 59.0% of the cases (6)). Patients presenting with two etiologic factors (38.0% of the cases) are nearly as common as those presenting with one factor (40.0%). Three factors were present in 17.0% of the cases and more than 3 factors were found in 4.0% of the cases (6).

1.7 Diagnosis

The clinical and radiographic findings of ECRR can present a substantial variation regarding the dimensions and the location of resorptive defect, which depends on the class/ stage of ECRR (5).

1.7.1 Clinical findings

Patients diagnosed with ECRR are often symptom free, i.e. ECRR is frequently only an incidental radiographic finding (5,38,47–49,90,124–129). This is supported by a cohort study that found the majority of patients with ECRR, diagnosed when the resorptive defect was already at class 3 (3). A vital pulp is a frequent finding in ECRR cases too (17,38,47–49,53,89,90,94,95,124,126,127,130–138) and a pink spot on a crown (Fig. 5) can be present (5,94,95,124,126,129,130,134,135) as well.

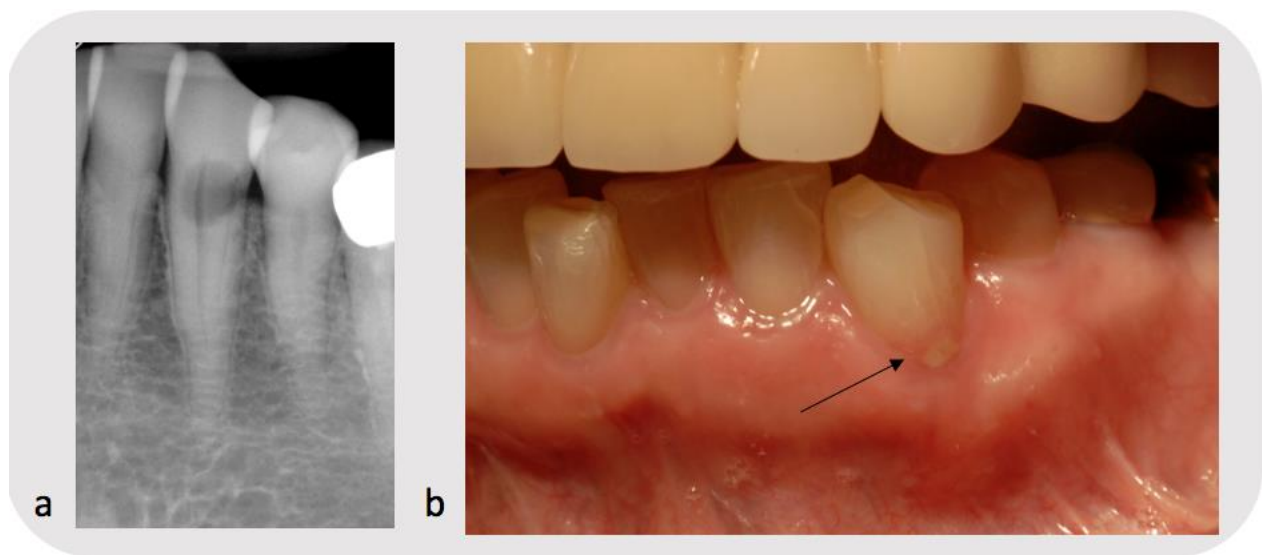


Figure 5. Periapical radiograph and clinical photo of tooth with pink spot at the cervical area.

a) Periapical radiograph b) Intraoral picture. Black arrow shows a pink spot on the cervical area of tooth #33.

However, a clinician should not rush to diagnose ECRR based on a pink spot on the crown and the positive response to vitality tests, because that can also be a clinical finding of an internal inflammatory root resorption (48,139). The presence of discoloration of a crown can be related to the location of the resorptive defect (49). When the defect is located interproximally it is more difficult to identify it. The POE of the resorptive defect can be associated with the presence of

granulation tissue, and therefore localized bleeding on probing frequently occurs in ECRR cases (38,49). However, the POE is not always easy to locate, even after elevating a surgical flap, because it is often very small (even $< 1 \text{ mm}^2$), and because it is not necessarily associated with periodontal bone breakdown and apical migration (49).

Clinically, it is important for a clinician to be able to diagnostically differentiate ECRR from root caries. The first sign, according to Singla (137), is the presence of bleeding on probing in ECRR cases due to the granulation tissue related to the area. The second clinical sign during probing, is that the bottom of the “concavity” is hard in ECRR and soft in caries, when examined with a sharp dental explorer. In addition, in cases of root caries the root surface often shows yellow discoloration around the area. The third clinical sign is that ECRR defects are rarely exposed clinically, while root caries is usually accompanied with recession of the gingival tissue (137).

1.7.2 Radiographic findings and tools

Periapical radiographs are crucial for the ECRR localization, diagnosis and differential diagnosis, albeit these provide only a two dimensional view. In order to overcome this limitation, a clinician can take a combination of two periapical radiographs, one straight and one with a horizontal angulation, and combine the findings from these two views. The multiple angulation periapical radiographs can be used to differentiate internal RR from ECRR, by following the continuation of the root canal, which is intact in the ECRR cases while it is expanded in internal RR cases (38,137). In ECRR, the outline of the root canal remains uninterrupted even if it is superimposed by the defect (48,49). The horizontal parallax radiographic technique, following the SLOB rule, can be used to check if the resorptive defect remained centered on the root canal

space on multiple (more than one) radiographs taken with different angulation, which indicates internal root resorption (26,137,140). In contrast, in ECRR, when different radiographs are taken with a more mesial or distal angulation, the defect will move accordingly and will be projected on the external surface of the root (49,137). Another radiographic finding in ECRR of endodontically treated teeth, is that the root filling material follows the normal shape of the root canal, without expanding into the resorptive defect (49). Also, ECRR defects tend to be asymmetrical, while the internal RR defects are more often symmetrical (137).

ECRR can be present as a mottled area on the radiograph due to depositing of osteoid tissue (15). ECRR can also look like a caries-like lesion in a radiograph(43), which is why differential diagnosis is critical. In addition to multiple radiographs with different angulation of one tooth, a full mouth radiographic examination has been suggested as a diagnostic tool in cases of multiple idiopathic resorption (5). Another advantage of taking periapical radiographs with more than one angulations is the ability to rule out the presence of cervical resorption or cervical burnout, and avoid possible overtreatment (75,141).

According to Andreasen et al. (142) *in vitro* study, periapical radiographs are reliable for the diagnosis of an external root resorption only when the size of the defect is bigger than 1.2 to 1.8 mm in diameter and 0.6 to 0.9 mm in depth. None of the “small” artificial cavities, with dimensions 0.6 mm x 0.3 mm, were detectable on the periapical radiographs. This study also proved that high contrast and multiple horizontal angulations provide a diagnostically superior result; when compared to lower contrast and single angulation radiographs. Another conclusion of this study was that resorptive defects located proximally (mesio-distal plane) were easier to detect than those on the bucco-lingual plane when periapical radiographs are used (142). More recent *in vivo* (140) and *ex vivo* studies (143–145) have demonstrated that periapical radiographs

are not always good enough in detecting and providing adequate information about natural or artificial external resorption cavities because of geometric distortions and two dimensional views.

Despite the fact that periapical radiographs provide an acceptable level of accuracy regarding the diagnosis of resorptive defects, CBCT is more trustworthy for an accurate and early diagnosis which can lead to better treatment planning and more predictable clinical results (50,146). A detailed dynamic view that provides information about the geometrical associations in all three dimensions simultaneously, allows a more thorough evaluation (147) of the defect. By “reading” carefully a CBCT scan, a clinician can gain information about the size of the ECRR, its circumferential spread and location, how close it is to the root canal system, and if the ECRR can be approached from outside or inside the tooth. By having this information, a clinician has all the necessary tools for optimal treatment planning. A clinical study which included 115 patients diagnosed with ECRR and compared the clinical value of their periapical radiographs and CBCT scans, concluded that a CBCT provides information for better treatment planning in ECRR cases (148). In addition, a CBCT scan visualizes, in a three-dimensional way, the resorptive channelling formation and the potential communication with the PDL. The channels can contain granulation tissue, resorptive cells, bone-like tissue and vasculature (148,149). In this context, it becomes clear how important it is for the clinician to be able to visualize in advance the extent of the resorptive defect, in order to prevent any active resorptive remnants hidden by the newly formed bone-like tissue in the main lesion and the tiny channels, which could lead to treatment failure (150). The diagnostic superiority of CBCT over periapical radiographs in ECRR cases has been documented by multiple clinical studies (51,148), and in some of them the treatment plan was changed after a CBCT was taken (52), or the likelihood of

correct treatment planning increased (23). Furthermore, in another clinical study, periapical lesions related to ECRR cases were identified only after the CBCT was taken (150). In agreement, *ex vivo* studies have shown that CBCT scans were more likely to localize (143) and correctly identify the type (classification) of ECRR defects (145), regardless of the tooth and dimensions of the defect (144). Multiple case reports and case series publications have used the CBCT as a means for better treatment planning (91,94,95,125,126,131,132,151–153).

1.8 Treatment management

The management of ECRR is fascinating and can be challenging as well, if one considers that each ECRR case is unique regarding significant factors such as the location, the accessibility, the extension of the resorptive defect, or the potential symptoms and the chief complaint of the patient. In 1987, Frank and Bakland (48) described in detail the suggested treatment in cases of supraosseous ECRR, where the POE is detected within the periodontium. Specifically, it was recommended that after confirming the diagnosis of ECRR as described at the diagnosis section earlier, to surgically expose the resorptive defect area and curette the resorptive granulation tissue by using slow-speed burs until only sound dentin is left on the defect's walls. The use of spoon excavators was recommended in order to avoid any accidental disturbance of the root canal continuity with the bur. After that, the use of hard-setting calcium hydroxide paste and silver amalgam was recommended as a means of restoration. Reposition of the flap, education of the patient how to avoid plaque formation, and finally follow-up appointments were suggested (48). Even if RCT was not strongly recommended during those steps, one year later, Frank and Torabinejad (49) made the comment that simultaneous RCT may be beneficial since it may be required later. This latter article also provided a well-organized

review of treatment options, beyond the supraosseous ECRR cases. Specifically, for the crestal ECRR cases where the POE is detected at the crestal level, a surgical approach after the RCT is recommended, because the internal approach may result in probing defects. For the intraosseous cases, where the POE is detected within the crestal bone and there is no contact with the oral cavity, the authors provide two options depending on the accessibility: an intracanal approach through the access cavity or intentional replantation. The intracanal approach, as described, has as its main goal to access the POE from the pulp chamber and/or coronal root canal, then completely clean the resorption area by chemomechanical curettage, and hermetically seal the POE. It is important not to gauge overzealously the root with the long shank round bur, in order to minimize damage to periodontal tissues and any structural weakening of the root. After all these steps have been followed, the resorptive defect can be filled with GI, super-EBA or MTA. The authors made the comment that unsuccessfully cases treated intraorally, end up in failure due to bacterial contamination. In ECRR cases when none of the previously described treatment methods is attainable and when the resorptive defect is not extensive making the extraction in one piece feasible, intentional replantation can be offered as a treatment option and can be discussed thoroughly with the patient (49). An updated paper published by Frank (154) in 1995 is in agreement with all the above steps.

Since 1999, when Heithersay (3) introduced the ECRR classification system, most treatment recommendations are based on the class of each ECRR case. In general, as it was recommended by Haapasalo et al. (155), the main objectives for an effective treatment are: “ i) *remove the resorptive tissue, ii) prevent the return of the resorption; and iii) maintain or regain a strong tooth structure*”.

1.8.1 External cervical root resorption defects Class 1 and 2

An external approach is widely recommended for these categories of ECRR cases. One way to proceed, is after raising a full thickness flap and removing the resorptive tissue by using a curette or a bur, to restore the defect with a material of choice and reposition the flap. In this way, the blood supply to the resorptive cells is eliminated (71). Another way to proceed, is to apply a protective stroma of glycerol on the surrounding soft tissue, and then apply 90.0% aqueous solution of TCA on small cotton pellet for 1-2 minutes with mild pressure. This stops bleeding and results in coagulation necrosis of the resorptive tissue, which can then be easily removed. After adjusting the margins of the resorptive defect, it is filled e.g. with GI and then a layer of light-activated bonded resin and composite filling (5).

1.8.2 External cervical root resorption defects Class 3 and 4

Class 3 and 4 ECRR lesions are larger and more spread than types 1 and 2. They also have narrow, vertical channels extending towards the crown and the root. The size and shape of class 3 and 4 lesions makes them clinically challenging to treat. The following treatment options should be considered: no treatment (follow up with annual checks), internal approach and external surgical approach. In cases where the internal approach is chosen, the clinician should try to reach the POE, induce coagulation necrosis by applying TCA, and fill the defect with an appropriate material e.g. GI or MTA (5). In cases where there is a large POE and destruction of adjacent bone, an external approach should be considered either as the sole treatment or together with RCT and an internal approach. In the external approach, a full mucoperiosteal flap is raised and the granulation and osteoid tissues are cleaned out through an access point at the most apical part of the defect, in order to preserve some cementum and increase the chances of PDL re-

attachment to the root. One of the main difficulties in type 4 ECRR treatments, is loss of tooth substance and the difficulty to detect where osteoid tissue ends and healthy dentin starts. After removing the resorptive soft tissue and the hard bone-like osteoid tissue from the defect, it can be filled with the material of choice (71) or can remain unfilled (156). The root surface is covered with bone grafting material and after the area is covered with a Goretex membrane, the flap is re-attached (71). In this way, Rankow introduced the advantages of guided tissue regeneration to ECRR cases that require endodontic surgery (156). Another option, as mentioned earlier, is the combination of external and internal approach, with elective RCT (5,71). A two-step external/internal approach has been described, where during the first step the resorptive tissue is removed only from the bony defect and a barrier membrane is placed before the flap is repositioned. At a later time, the resorptive defect is removed from the root resorptive defect through an internal access restored with MTA, but without raising a flap. It has been advocated that this should be the technique of choice in order to preserve the periodontal attachment (71).

Complementary options can be forced eruption (orthodontic extrusion), in cases with long roots (5,20,71), or forced eruption combined with re-intrusion, when the crown-root ratio is not adequate (71), or even intentional replantation in cases with low risk for root fracture during extraction (71).

In summary, as recommended by Haapasalo et al. (155) in the most recent paper providing treatment guidance, for the class 1 and 2 ECRR cases the external (surgical) approach is the treatment of choice. In these cases, resin composite or GI can be used to fill the resorptive defect. However, when the portal of entry is small and in proximity to the pulp space, the internal approach (through the root canal) is recommended, in combination with either bioceramic cement, GI or composite. For class 3 and 4 cases, which have guarded or poor prognosis, RCT

and an internal approach for the resorptive defect is recommended together with use of bioceramic cements.

1.8.3 Treatment considerations and prognosis

The American Association of Endodontists, in the Position of Statement regarding the “*Treatment options for the compromised tooth: a decision guide*”, have included a table which summarizes all the significant points a clinician should consider before providing any treatment option to their patient diagnosed with external resorption. For instance, in cases of minor missing tooth structure and with straight access to the supraosseous lesion, the prognosis is favorable. On the other hand, when the majority of the root structure is resorbed, not accessible surgically and associated with periodontal problems, the prognosis is unfavorable (157).

Even though many different approaches have been described regarding the management of ECRR cases, there is no specific gold standard, which a clinician can follow. A review conducted by the Cochrane Collaboration group regarding the management of external root resorption of all types, emphasized the lack of credible evidence. Consequently, it was suggested that dentists should use their clinical experience, based on patients’ needs and considering each case individually (158).

1.9 Treatment outcome

To the best of our knowledge, there is only one published study that examined the treatment outcome of ECRR cases. This study was done in 1999 by Heithersay (159), and analyzed the clinical results of 94 patients, with 101 affected teeth, that have been treated non surgically. The first step was the protection of the surrounding soft tissue by application of glycerol, then a topical application of 90.0% aqueous TCA and the subsequent removal of the resorptive tissue. Following that, the defect was filled with GI. RCT was provided only when it was required. In this study, the patients had to have attended a follow-up of 3 years or more in order to be included. An exception was made for the cases that failed in less than 3 years, which were also included. The cases were divided in four groups, according to the Heithersay classification (3). Overall, 4 teeth (4 patients) were allocated in Class 1, 18 teeth (16 patients) in Class 2, 63 teeth (61 patients) in Class 3, and 16 teeth (13 patients) were allocated in Class 4. The success was defined as an “*absence of resorption or signs of periapical or periodontal pathosis*”. Based on the results, Class 1 and Class 2 cases showed 100.0% success, Class 3 showed 77.8%, while Class 4 showed 12.5% success. The author emphasized the importance of an early diagnosis (159).

Other than the aforementioned cohort study (159), there is a plethora of case and case series reports (38,47,49,73,83,88–91,124–126,128–135,150–153,156,160–171) that provide information collected during the follow-up appointments, albeit this information is of low level of evidence; due to the type of these studies (172).

Chapter 2: Hypotheses and objectives

Three study hypotheses were postulated.

Study hypothesis 1: systemic determinants such as medication, systemic diseases, and allergies are associated with an increased prevalence of external cervical root resorptions (ECRR).

Study hypothesis 2: treatment-related determinants such as presence and type of external repair of ECRR, root canal treatment, resorption repair combined with root canal treatment are associated with lower rates of failure of teeth with ECRR.

Study hypothesis 3: local determinants such as location of tooth, location of portal of entry, Heithersay classification, trauma, orthodontic treatment, extraction of adjacent tooth, irregular forces and presence of restoration are associated with higher failure rates of teeth with ECRR.

In order to test the aforementioned hypotheses, the study objectives were as follows:

Objective 1: to identify all patients who were diagnosed with ECRR at the Graduate Endodontics clinic of UBC, during a 10-year period of time (2008-2018).

Objective 2: to retrospectively review the medical charts of the ECRR patients, all information provided regarding their medical and dental history. Then, to analyze this information at a tooth and a patient level, and assess if it is associated with the presence of ECRR.

Objective 3: to follow-up all patients in the ECRR group and assess the long term treatment outcome and its potential determinants.

Chapter 3: Materials and methods

The current study included all patients who were referred to the UBC Graduate Endodontics (GE) clinic and who were diagnosed with ECRR, during the time period of 2008-2018. The inclusion criteria were: having a minimum of two periapical radiographs showing the defect, even taken at different times, or one periapical radiograph and one CBCT scan from the area of interest. The data were collected in two separate stages of the study. The first stage was a retrospective approach (retrospective chart review), where information was collected from the charts of patients with and without resorption. The group of patients without resorptions was the control group. The second stage was a prospective approach and included a follow-up of patients with ECRR. Inclusion criteria for the second stage was a follow-up interval not less than 1 year. The project was approved by the UBC Behavior Research Ethics Board (H17-00885).

3.1 Sample selection

Romexis software (Planmeca, Helsinki, Finland) was used to search for and identify patients with ECRR from the general pool of patients of the GE clinic. Romexis is the software suite used in the UBC faculty of dentistry, where all radiographs and other patient information, such as medical and dental history, are saved by chronological order in a patient's digital chart.

The first step in sample selection, was to use nine terms as key search terms that potentially can have been used in patients' digital charts. The following key terms were used: 1) resorp, 2) resorb, 3) resorption, 4) cervical resorption, 5) root resorption, 6) internal resorption, 7) internal root resorption, 8) external resorption, and 9) external root resorption. The objective of this step was to collect all patient charts that were including those key terms. Internal and cervical resorption can in some cases be difficult to differentiate from each other. Therefore, by

including both internal and external resorption key terms, the possibility of not identifying an ECRR case because of previous misinterpretation of the resorption type was minimized. After searching these nine terms in all GE patient charts (Fig. 6), two groups of information were collected. The first group of data showed the chart numbers of the cases where any of these key terms was used in the “Condition notes” section. That means that Graduate Endodontics residents used one or more of the terms while documenting their cases in the prelisted options in Romexis. The second group of data was showing if any of these key terms was used in “Free text notes”, which means that residents used the key terms when adding comments in the free text notes area. Overall, 398 chart numbers were collected in the “Condition notes” group and a total of 308 in the “Free text notes” group. These chart numbers were combined and the duplicates excluded. This resulted in a total of 398 charts being collected from the first step of the sample selection. For the majority of these charts, the context in which that the key word was used was included and shown in the results, presented in an excel sheet (Fig. 7).

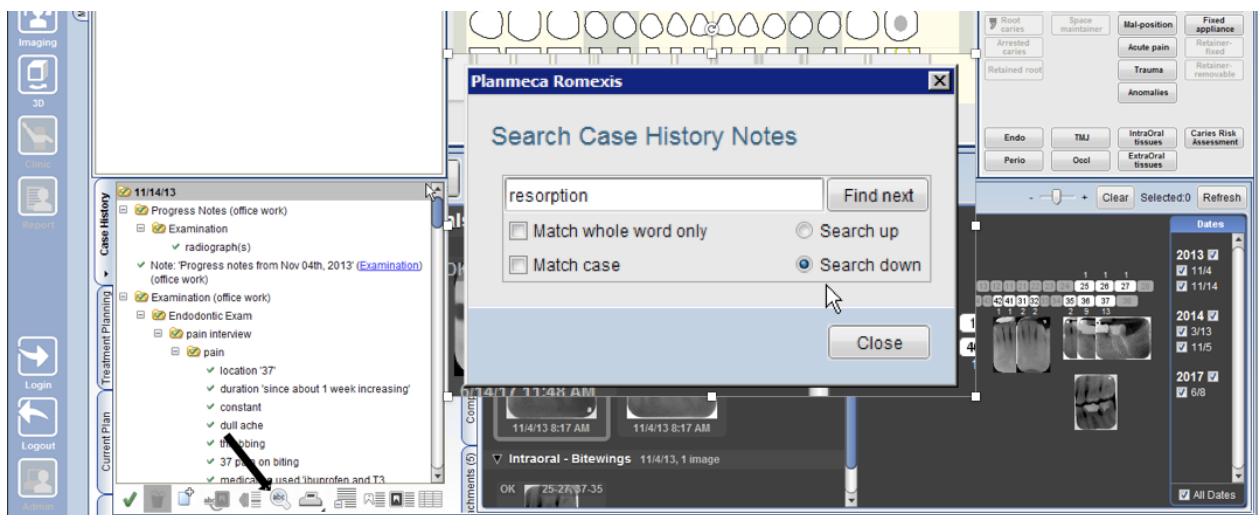


Figure 6. A print screen of a patient’s chart in Romexis. The black arrow shows where one should “click” for the “search case history notes” option, which is a “search machine” for the key terms.

During the second step, 131 charts were excluded as irrelevant to the current research. For instance, charts in which the term ‘resorption’ was used in a different context such as: bone resorption, sutures resorption or resorbable membrane were excluded (Fig.7). At the end of the second step of the sample selection, 267 charts with cases of RR or cases with unknown context of the key word were collected.

	A	B	C	D
610	33312	2E+07	100740000	external cervical resorption - class 3
611		2E+07	160746062	
612		2E+07	160759906	
613	33431	2E+07	223357250	root resorption
614	33463	2E+07	170258057	external root resorption
615	33481	2E+07	92626671	bone resorption
				internal root resorption
616	33562	2E+07	100726890	
617	33731	2E+07	180803754	tooth has a resorbed endodontically tx root
618		2E+07	104756288	apical resorption,
619	33788	2E+07	161747700	inflammatory root resorption
620	33862	2E+07	84834681	resorption of apical bone
621	33977	2E+07	111451306	internal and external resorption
622	34112	2E+07	130834290	resorption
				either root resorption or iatrogenic damage during surgical extraction of 17 (more consistent with trauma/iatrogenic trauma
623	34167	2E+07	121152540	during extraction of molar)
624		2E+07	121152650	

Figure 7. Excel sheet illustrates the organization of the information given about the key terms found in Romexis “Free text notes”. Note that in some cases the context and/or the tooth number is provided.

During the third step of the sample selection, the 267 charts were thoroughly examined. Each patient was given a code number in order to be identifiable only by the research team. At this stage, 98 charts were excluded as irrelevant to the current project. Then the RR group was divided into two subcategories, 1) resorption at the cervical and/or middle root third (Fig. 8a) and 2) resorption at the apical third (Fig. 8b). Seventy-eight cases with an apical resorption were excluded as irrelevant to ECRR. At the end of the third step of selection, the remaining sample was 91 patients with radiolucency at the cervical or middle third of a root of at least one tooth.

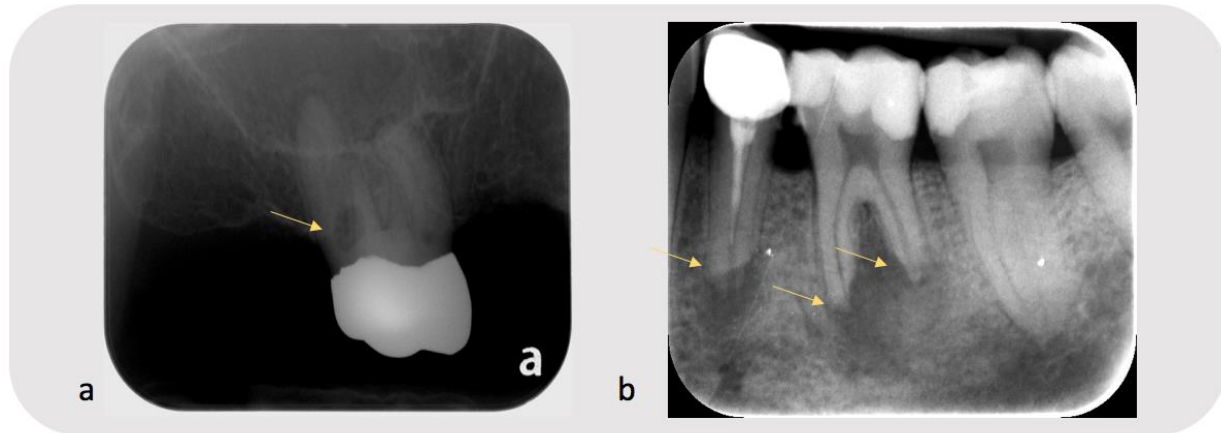


Figure 8. Examples of different locations of root resorption (pointed by a yellow arrow): a) cervical root third b) apical root third.

During the fourth step, radiographs of 91 patients were exported from the Romexis digital patients' charts, and organized per patient and per date taken. Multiple periapical radiographs of each patient, and panoramic or CBCT scans, if available, were imported into a Power Point presentation (Microsoft® PowerPoint). A black background was used for the slides. Every time a new case was to be presented, the first slide was a total black slide with only a patient's code number, making the transition clear. In the second slide of each patient, periapical radiographs were added with information of the year these radiographs were taken. If panoramic radiographs or CBCT scans were available, they were presented on the following slides. This PowerPoint-based information was assessed twice, six months apart. The first time it was presented on a 13-inch MacBook Air with a screen resolution of 2560 by 1600 pixels. The second time, six months later, the radiographs in the PowerPoint presentation were viewed on a 40-inch Samsung monitor. Two examiners (one supervisor and the MSc candidate) assessed all cases. In the assessment a decision was made on the following parameters: location of the RR (internal/external) and the Heithersay classification. In cases where there were doubts or

disagreement, the whole CBCT scan, and not only a print screen, was examined. If a CBCT was not available, the clinical description provided in a patient's chart was used. Due to the limitation of Heithersay classification, which is based on a two dimensional scale, the examiners came to an agreement on how to classify a specific type of lesion. More specifically, the cases that were “*well-defined*” (part of the definition of Class 2) and at the same time “*extending at least at the coronal third of the root*” (part of the definition of Class 3). The examiners concluded that all cases that had well-defined borders, without the typical channeling of Classes 3 and 4 around the root canal, should be defined as Class 2 (Fig. 9).

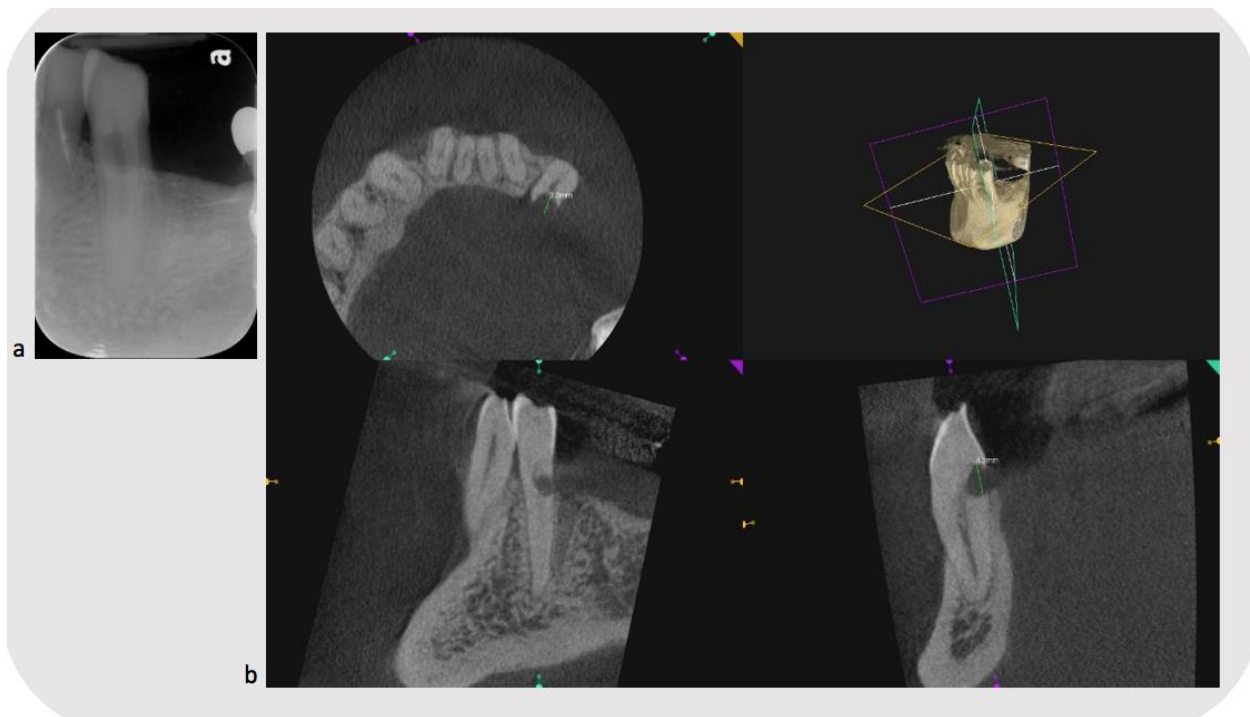


Figure 9. Example of Class 2 cases with well-defined borders and without a channeling spread:

a) periapical radiograph and b) CBCT axial, coronal, and sagittal views of the same Class 2 case.

At this stage, 16 cases were excluded as internal inflammatory RR cases. Another four cases with radiolucent defects on the cervical or middle third of the root were also excluded. One

case was excluded because there was only one periapical radiograph in a patient's chart, and the second one because the resorptive defect was present only in one of the periapical radiographs (Fig. 10a), leading to a possible false positive diagnosis of ECRR (Fig. 10b). The third and the fourth cases were excluded because they were obvious incorrect diagnoses, not ECRR, in contrast to the clinical notes. Finally, by the end of the summer of 2017 when all data were collected, the group of patients diagnosed with ECRR at the UBC GE clinic consisted of 71 patients and 92 teeth.

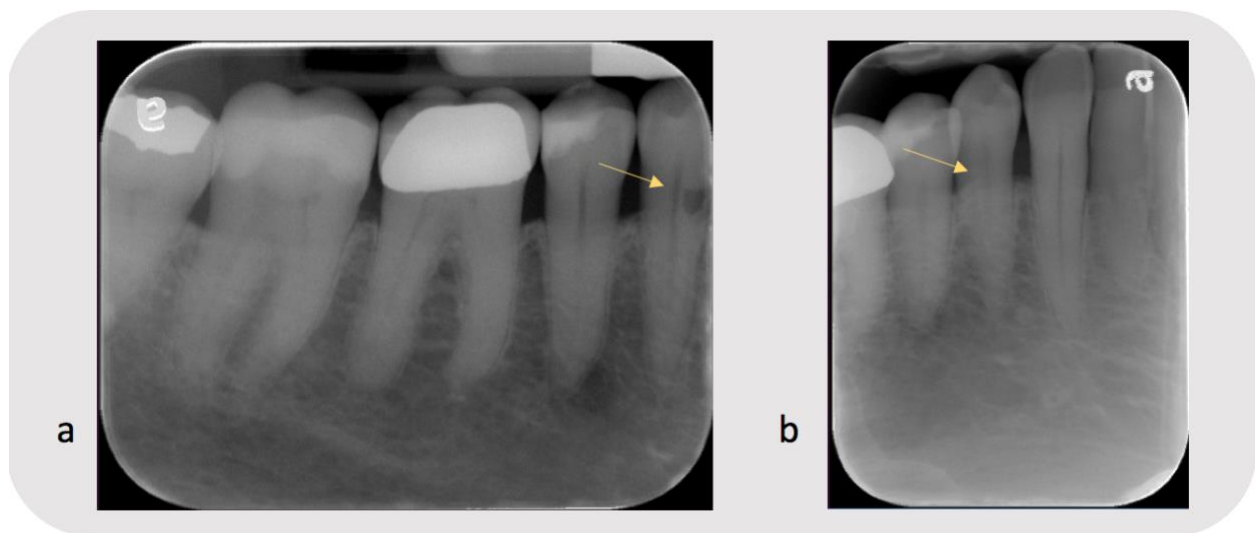


Figure 10. An excluded case, showing an example of false positive diagnosis of external cervical root resorption (yellow arrows point the tooth of interest): a and b periapical radiographs were taken the same day.

The fifth step was to keep the sample updated while this project was still ongoing. For that reason, five recently referred patients, from September 2017 till May 2018, to the UBC GE clinic and newly diagnosed with ECRR, were also included in the sample.

After these five steps were followed (Fig. 11), a total of 76 patients and 98 teeth diagnosed with ECRR were included in the sample.

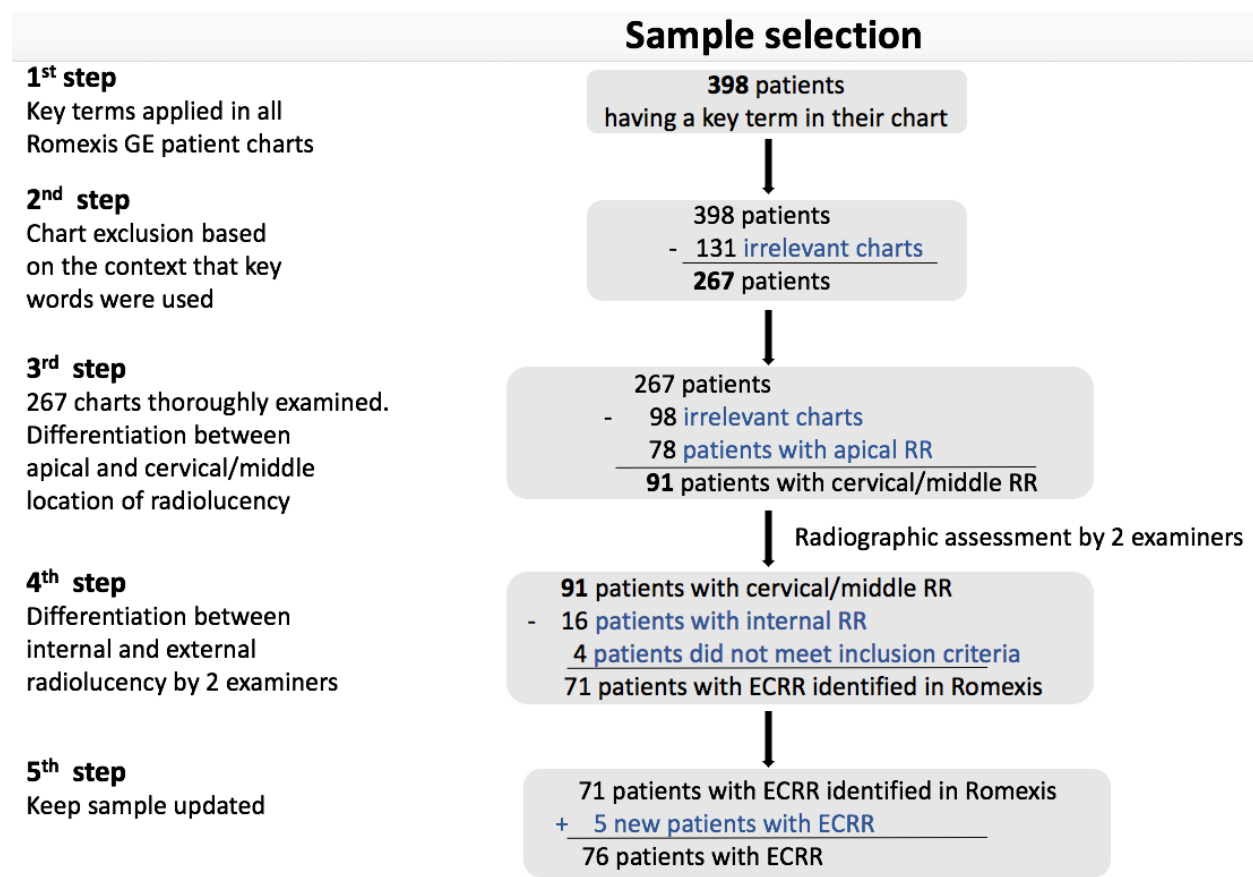


Figure 11. Chart illustrates the 5 steps followed for the sample selection of the external cervical root resorption group (ECRR).

Finally, after the ECRR group was identified, another group of patients (control group), with an equal number of participants, was created. The inclusion criteria for this group were exactly the same as for the study group: first a participant had to be chosen from the pool of patients of GE clinic and secondly the patient had to have two radiographs from the area of concern. However, none of the patients included in the control group had ECRR. During this selection process, a total of 76 patients without ECRR, each with two periapical radiographs were included in the control group.

3.2 Data collection

Data were collected at two different stages of the study for two different purposes. In the first stage, the MSc candidate retrospectively collected information from the patients' charts when they were first diagnosed with ECRR. The second stage of data collection (prospective review) included information of the most recent follow-up appointment, which had to be at least one year after the initial diagnosis.

After the group of patients with ECRR was identified, data from their charts were collected and recorded on an Excel sheet (Microsoft® Excel). The following retrospective data was collected:

1. year of birth
2. gender
3. detailed information regarding their medical history (list of 21 medical conditions)
4. medication use
5. allergies
6. number of a tooth diagnosed with ECRR
7. year of diagnosis of ECRR
8. potential predisposing factors: trauma, orthodontics, extraction of adjacent tooth restoration (direct, indirect, post) and irregular forces (bruxism, eruption disorders)
9. patient's chief complaint
10. if two periapical radiographs were available
11. if CBCT scan of the area of interest was available
12. radiographic findings indicating where the resorption was located (mesial, distal, palatal/lingual, buccal)
13. class of ECRR based on the Heithersay classification

14. pulpal diagnosis
15. periapical diagnosis
16. initial ECRR repair/treatment: no treatment, internal approach, external approach, extraction, root amputation
17. the material(s) used for the resorption repair

The same information, except for the items 6, 7, 12, 13, 16 and 17, were retrospectively collected for the control group.

After all information was collected, patients identified with ECRR were contacted, in order to arrange a follow-up appointment. The MSc candidate tried to contact all patients who were diagnosed with ECRR at least one year earlier. Patients who were recently diagnosed with ECRR and did not meet the criterion of a minimum one-year follow-up, were not contacted. However, these patients remained in the patients' list for future follow-up. In addition, if a recent follow-up had taken place during the last year (173,174), these patients were not contacted, but the ECRR related information was retrieved from their Romexis digital charts. The MSc candidate tried to contact all eligible participants via phone, initial contact letter and an initial contact email in order to arrange a follow-up appointment. For the patients that were willing to participate but were living in remote areas, thus not able to visit the UBC clinic, a different solution was found. Initially, a verbal permission was acquired from these patients, followed by their dentist's contact information. The next step was to contact their dentists and ask them to provide chart information and copies of radiographs of the area of interest. In cases where dentists did not have radiographs of a tooth with ECRR or if patients did not have a dentist or they were unwilling to provide their contact information, a quick interview over the phone took place. During this

interview, the patients or their dentists (without periapical radiographs but with clinical charts), were asked to answer the following questions: 1. Is a tooth (with ECRR) still in place? 2. If extracted, when and why did that happen? 3. If a tooth is still present, does a patient have any symptoms or clinical findings? 4. Could you describe the chief complaint?

Compensation was offered to all patients for the lost working hours and travel expenses. To partially compensate participants, each of them received a 10 CAD Save on Foods groceries gift card. The follow-up appointments were free of charge, based on the protocol of the UBC GE clinic.

Follow-up appointment and collection of data was not conducted for the control group, because the assessment of endodontic treatment outcome was out of the scope of the present study. During the follow-up appointments, the protocol of the UBC GE clinic was followed. First, all participants signed an informed consent before the examination took place. During the clinical examination of the tooth of interest and its adjacent teeth; chief complaint, probing, palpation test, percussion test, bite test, vitality test were conducted and intraoral photos were taken by using a digital camera and the dental operating microscope. During the radiographic examination, periapical radiographs were taken, and if needed for treatment purposes, a CBCT scan was taken as well.

After several efforts were made to contact all patients for a recent follow-up, the following data was collected:

1. year of the last follow-up
2. if there was no follow-up, why
3. clinical findings /chief complaint
4. radiolucency in bone, related to ECRR
5. presence of RCT at the final follow-up

6. year of extraction
7. reason for the extraction
8. change of size of the ECRR
9. failed or functional tooth.

For optimal evaluation of the change in size of the ECRR, different CBCT scans should ideally be used. The digital subtraction radiography technique has been used, in a case report, in order to compare the size of the ECRR radiolucency in the initial and the final CBCT slices (131). As mentioned earlier, CBCT is better suited for the evaluation of the size of ECRR lesions than conventional 2D radiographs. However, not all of the patients in our sample had a CBCT scan. Due to this limitation, the initial and the latest periapical radiographs of each case were used. The radiographs were presented on a Power Point presentation after all the follow-up appointments were completed. For each case, a single slide with black background was used to present the initial and the latest periapical radiographs. The comparisons were made by the MSc candidate and the supervisor. There was 100% agreement between the two examiners. If the size of ECRR defect changed during the follow-up period in untreated cases, or a new radiolucency was detected around the ECRR restoration in treated cases, this information was recorded. No other comment on the extension of the ECRR was made, because it was not possible to make quantitative measurements of the changes (Fig. 12).

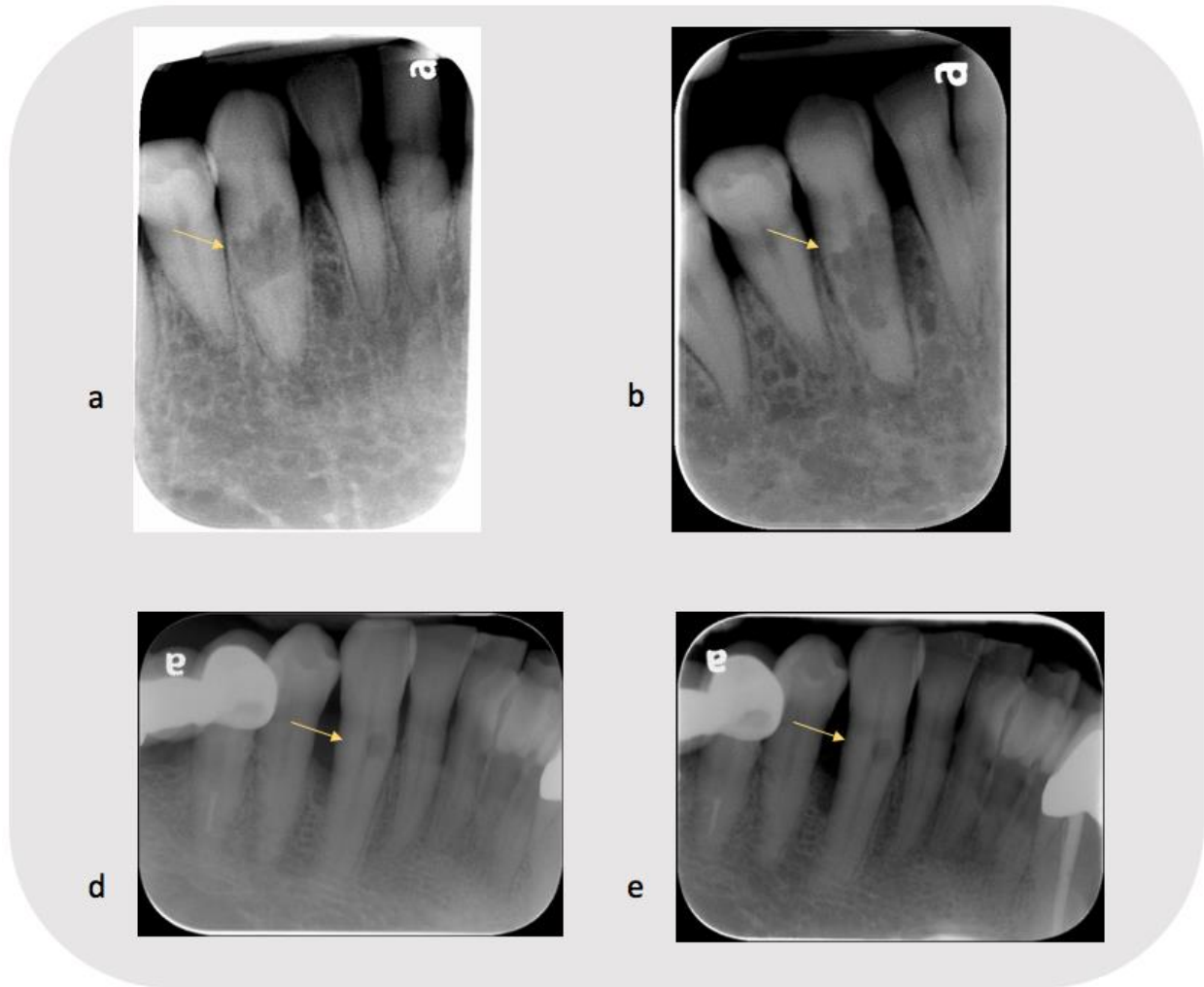


Figure 12. Examples of two untreated cases with external cervical root resorption (ECRR), and the changes noted in size over the years (yellow arrows point the tooth with ECRR).

Case 1: a) initial periapical radiograph taken in 2013 and b) latest periapical radiograph taken in 2018. Note the increase in the ECRR size.

Case 2: c) initial periapical radiograph taken in 2016, and d) latest periapical radiograph taken in 2018. The ECRR lesion seems unchanged in the 2D radiographs.

For the outcome assessment, it was critical to define the difference between a functional and a failed tooth. For that reason, Friedman's classification for treatment outcome was used, and a functional tooth was defined when “ *the clinical presentation was normal, while radiolucency might be absent or present – newly emerged or persisting*” (175–177). Accordingly, as failed was defined a tooth when it was extracted or it was a non-functional (tooth without normal clinical presentation).

3.3 Data analyses

The data was analyzed with the SPSS version 25.0 software (IBM, New York, United States) and the level for statistical significance was set at $p < 0.05$. Data were analyzed at two levels: patient as a unit of analysis and tooth as a unit of analysis. The analysis of patient level data used comparisons between the patients with external cervical root resorption (study group) and the patients without external cervical root resorption (control group). For both type of statistical comparisons (patient- or tooth-based data) Chi Square test or Fisher's Exact test were used to compare proportions. To get insight into time-related failure rates, survival analyses employing Kaplan Meier curves method was used, where different local treatment-related and predisposing risk factors (determinants) were considered.

Chapter 4: Results

4.1 Patient level of analysis

In this section, the collected data and the analysis regarding all the patients diagnosed with ECRR, irrespective of the existence of follow-up information, is reported. The results on a patient level will be presented in three different approaches:

- 1) presentation of retrospectively collected information from patients' charts, related to their medical and dental history. The results are visually illustrated in Figure 13.
- 2) comparison between the retrospectively collected findings of ECRR and the control groups. The results are visually illustrated in Figures 14 and 15, and Table 1.
- 3) presentation of the time intervals and the number of patients who were followed-up. The results are visually illustrated in Figures 16 and 17.

Univariate descriptive analyses: Patient level of analysis, Retrospective approach

This first approach analyzed the data at a patient level; based on the list of retrospectively collected information presented previously. Regarding the prevalence of ECRR, 2.3% of all patients at GE clinic were diagnosed with at least one tooth with ECRR. The sample age-related distribution (age of patient when initially diagnosed with ECRR) was as follows: 12-39 years (n=12, 15.3%), 40-59 years (n=28, 36.7%) and 60-89 years (n=27, 35.7%) (Fig. 13). Of the 76 patients, 31 were women and 45 were men. Fifteen patients were diagnosed with more than one tooth with ECRR (ten patients with two teeth, four patients with three teeth and one patient with five teeth with ECRR). Twenty-four patients had a non-contributory medical history (no systemic condition), while 52 patients had at least one systemic disease, which will be discussed in further detail. Nineteen patients had a complex medication regimen, while 57 took either no

medications or light medications such as vitamins or painkillers only when needed. Fifty-one patients did not report any allergies, while 16 patients had allergies. Regarding the initial patient's chief complaint, 48 patients had none, 24 expressed some pain or sensitivity, while four patients were concerned about the aesthetics of a tooth due to a pink discoloration. All patients finally included in the study had at least two periapical radiographs of the tooth of interest, and 46 patients also had a CBCT scan from the area of concern.

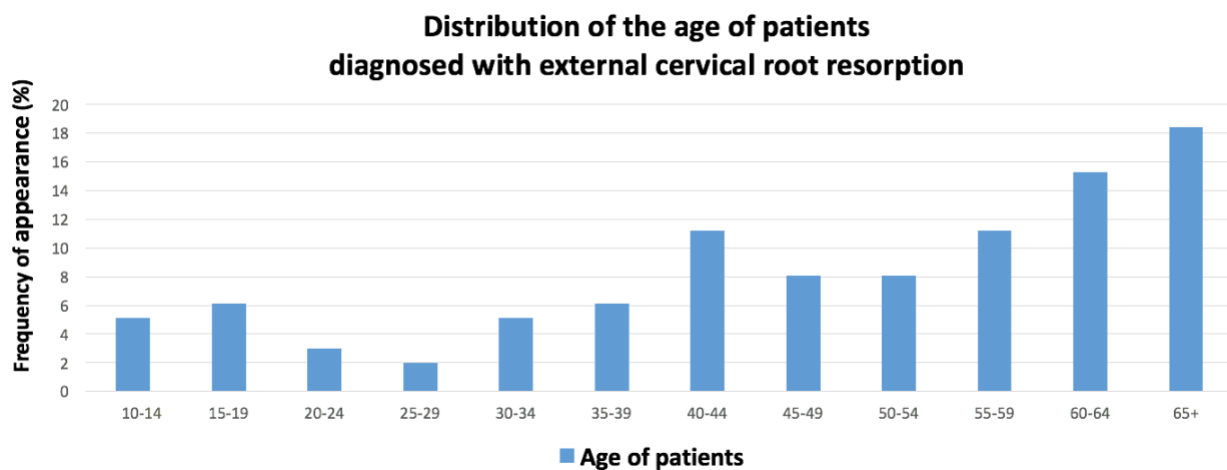


Figure 13. Distribution of the age of patients at the time of external cervical root resorption (ECRR) diagnosis.

Bivariate analyses: Patient level of analysis, Case-control study approach

The second approach provides information regarding the medical and dental history of the ECRR group and of the control group. Chi square test was conducted to compare proportions. The results of the systemic determinants are presented in Table 1.

Overall, the patients in the control group had more systemic conditions than the patients in the ECRR group (Table 1). More specifically, a higher number of patients in the control group, compared to the patients of the ECRR group, presented with a medical history related to

musculoskeletal disorder, high blood pressure, orofacial pain, gastrointestinal disorder, heart vascular disease, thyroid disorder, CNS disorder, hemorrhagic disease, dermatological problems, chemotherapy, eating disorders, presence of allergies and need for medication. However, the differences regarding the presence of the aforementioned conditions among the two groups were not statistically significant. In addition, for some medical conditions, the number of patients presenting them were identical between the two groups. More specifically, the disorders with equal proportions between the groups were: kidney disease, liver disease, mental health problem, sleep disorder, rheumatoid disorder, organ transplantation and dry mouth. There were four systemic conditions which presented the opposite trend and were observed more frequently in the ECRR group than in the control group. Three of them, respiratory disease, head/neck radiotherapy and implants (not dental) did not present significant differences between the control and ECRR group. The presence of diabetes was the only statistically significant difference between the two groups (study and control group).

In summary, there was a tendency for more systemic health conditions in the control group, but no significant differences between the two groups were detected except for diabetes. The number of diabetics in the ECRR group was three times higher when compared to the control group.

Table 1. Potential determinants: presence of systemic conditions

Systemic condition	Control group n (%)	ECRR group n (%)	Significance # (p-value)
Medical condition (any)	58 (76.3)	52 (68.4)	0.276
Musculoskeletal	26 (34)	16 (21.1)	0.070
High blood pressure	23 (30.3)	21 (27.6)	0.721
Respiratory disease	6 (7.9)	9 (11.8)	0.415
Kidney disease	4 (5.3)	4 (5.3)	1.000
Liver disease	3 (3.9)	3 (3.9)	1.000
Mental health	12 (15.8)	12 (15.8)	1.000
Orofacial pain	4 (5.3)	3 (3.9)	0.699
Gastrointestinal	16 (21.1)	8 (10.5)	0.075
Sleep disorder	12 (15.8)	12 (15.8)	1.000
Heart vascular disease	16 (21.1)	15 (19.7)	0.840
Thyroid	12 (15.8)	10 (13.2)	0.645
Central nervous system	7 (9.2)	5 (6.6)	0.547
Hemorrhagic disease	4 (5.3)	3 (3.9)	0.699
Diabetes	4 (5.3)	12 (15.8)	0.034
Dermatology	13 (17.1)	11 (14.5)	0.656
Rheumatoid disorder	4 (5.3)	4 (5.3)	1.000

Chemotherapy	4 (5.3)	1 (1.3)	0.172
Head/neck radiotherapy	0 (0.0)	3 (3.9)	0.080
Organ transplantation	1 (1.3)	1 (1.3)	1.000
Dry mouth	10 (13.2)	10 (13.2)	1.000
Implants (non-dental)	4 (5.3)	5 (6.6)	0.731
Eating disorders	4 (5.3)	3 (3.9)	0.699
Allergies	28 (36.8)	25 (32.9)	0.610
Medication	26 (34.2)	19 (25.0)	0.214

#Chi-Square Test

Comparison of local risk factors revealed that the ECRR group presented more patients with a history of trauma and less patients with any kind of restoration, when compared to the control group. Other local determinants presented similar numbers for both groups (Fig. 14).

Number of patients with potential local predisposing factors

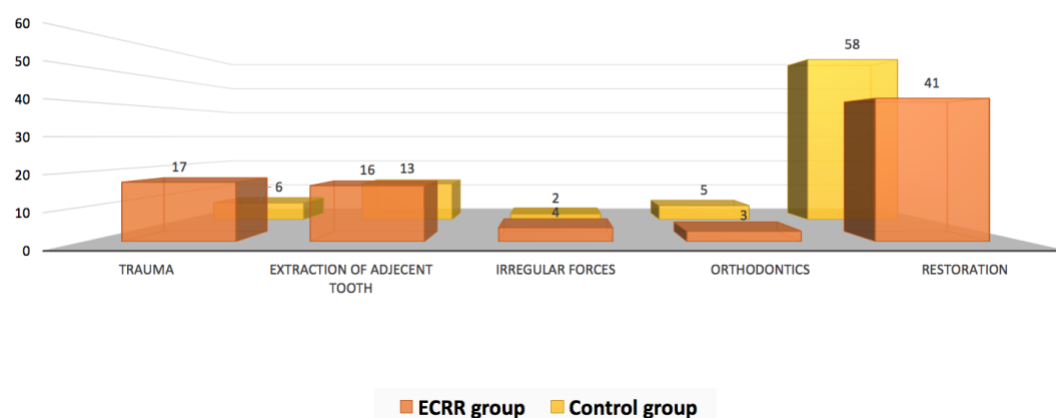


Figure 14. Bar chart illustrates the number of patients presenting different potential local predisposing factors in the control and the external cervical root resorption (ECRR) groups.

A single local factor rather than several factors was more frequently present, 48.0% in the ECRR and 67.0% in the control group (Fig. 15). Also, both groups had comparable proportions for the presence of two local factors, with 29.0% for the ECRR group and 24.0% for the control group. The ECRR group had a few cases with 3 or 4 local determinants (1.0%) (Fig. 15).

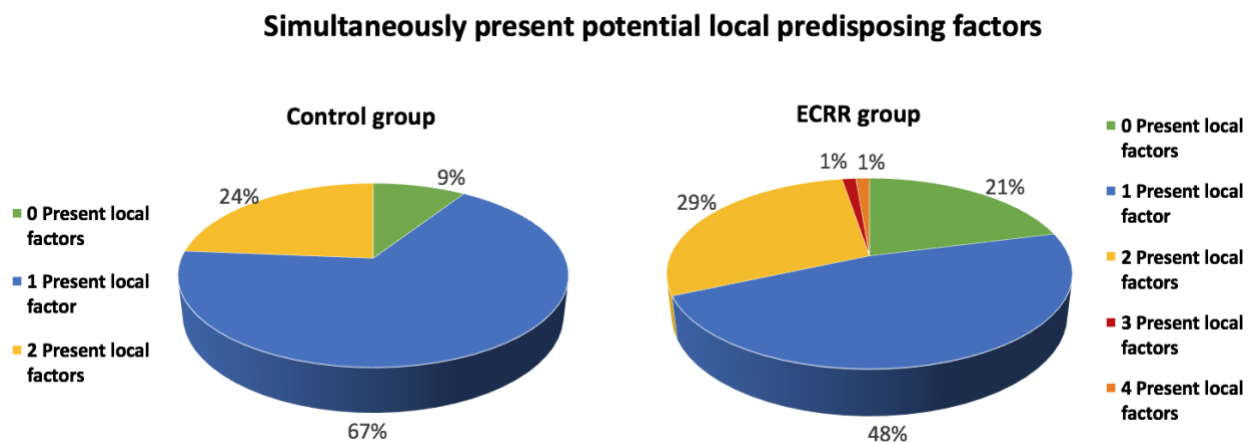


Figure 15. Pie charts illustrate the frequency of simultaneous presence of different potential local predisposing factors in the control and external cervical root resorption (ECRR) groups.

Univariate descriptive analyses: Patient level of analysis, Prospective approach – Follow-up

The third approach to analysis provides information regarding the number of patients who were examined at one or more follow-up appointments. The mean follow-up time was 3.9 years (SD=3.1 years, minimum 6 months and maximum 10 years). Out of the 76 patients with ECRR, 20 patients were not recently followed-up, because five were newly diagnosed, 14 had relocated and could not be contacted or did not respond, and one was deceased. Overall, 73.7% of the patients with ECRR were recently followed-up. Out of the 56 recent follow-up appointments, 23 took place at the UBC faculty of dentistry, 8 were conducted by other dentists who provided radiographic and clinical information, and 8 were interviewed by phone. From the

overall group, 17 patients had their teeth extracted. The extraction was confirmed either by information provided in the patients' chart (n=15 patients) or during the phone interview (n=2 patients). Two patients with more than one teeth with ECRR had one of them extracted (Fig. 16).

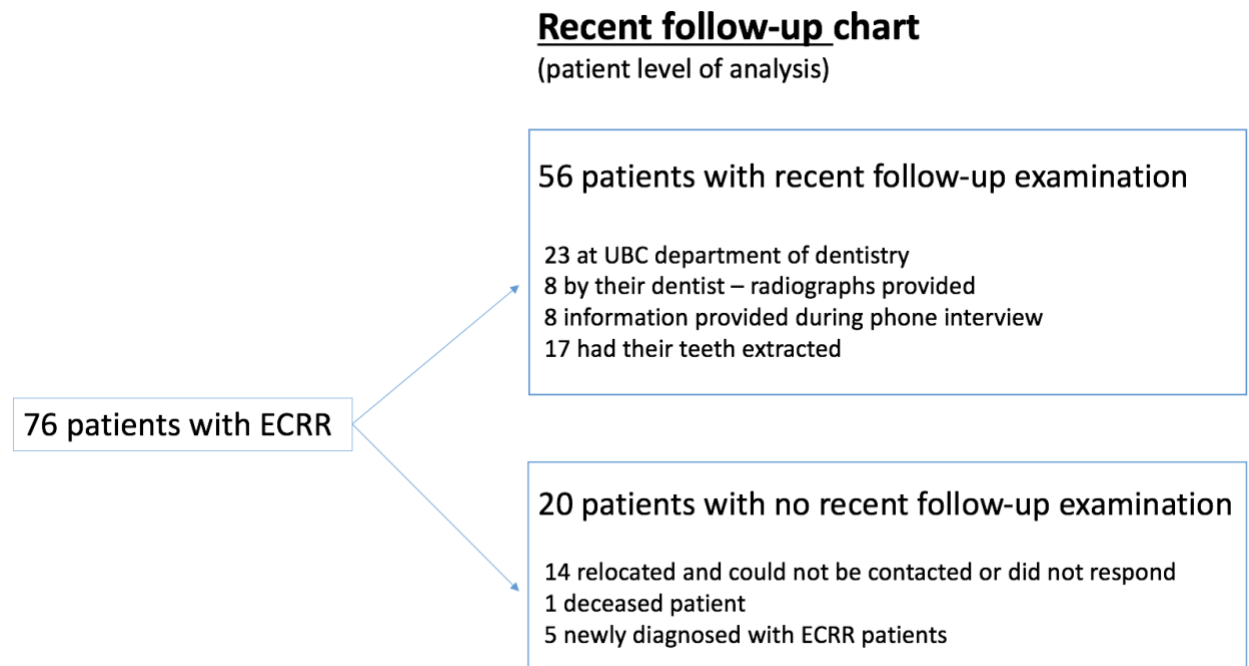


Figure 16. Chart illustrating the number of patients who were or were not recently examined at a follow-up appointment.

Eleven out of the 20 patients that we were unable to follow-up within the last year, had a follow-up information provided in their charts. This information was used as their last follow-up. This way, the overall follow-up information was available for 67 patients (88.2% follow-up rate). From the nine patients that were never re-examined in a follow-up appointment, five were newly diagnosed with ECRR, three had relocated and therefore could not be contacted and one was terminally ill at the time of the original ECRR diagnosis (Fig. 17).

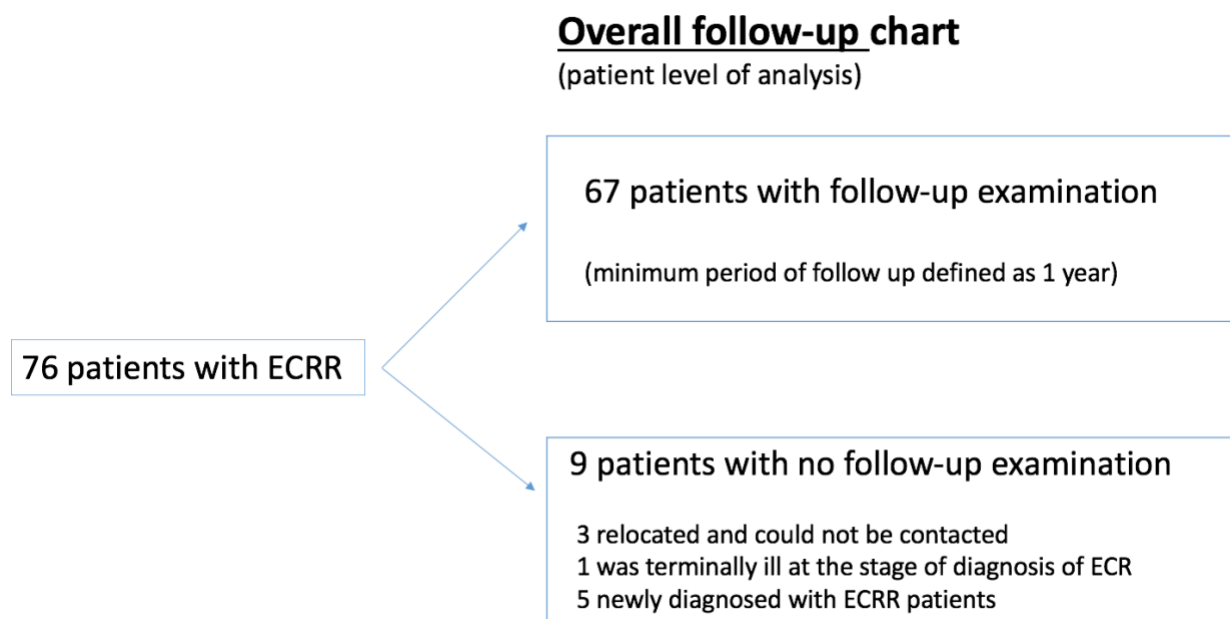


Figure 17. Chart illustrating the number of patients who were or were not examined at a follow-up appointment.

4.2 Tooth level of analysis

In this section, the unit of analysis was the tooth. In these analyses, control group patients were not included. The results on the tooth level will be presented in four different approaches:

- 1) presentation of the retrospectively collected data of all teeth diagnosed with ECRR. The results are visually illustrated in Figures 18 – 21.
- 2) presentation of findings collected at the follow up appointments (prospective approach).
- 3) presentation of the survival rates of teeth having at least a one-year follow-up, based on different local determinants. The results are interpreted in Tables 2 and 3. Bivariate analysis was used to present this information.
- 4) presentation of the survival rates of teeth having at least a one-year follow-up, based on different local determinants. The visual analysis of failure rates is illustrated in Figures 23 – 30. Hazard ratio curves were used to present this information.

For the last two approaches, the survival rates of teeth from different ECRR subgroups (regarding the presence of local determinants) were compared to each other.

Univariate descriptive analyses: Tooth level of analysis, Retrospective approach

Fifty-six of the 98 teeth with ECRR were anterior teeth (31 maxillary and 25 mandibular), and 42 were posterior teeth (20 maxillary and 22 mandibular). The distribution of the teeth is presented in Figure 18.

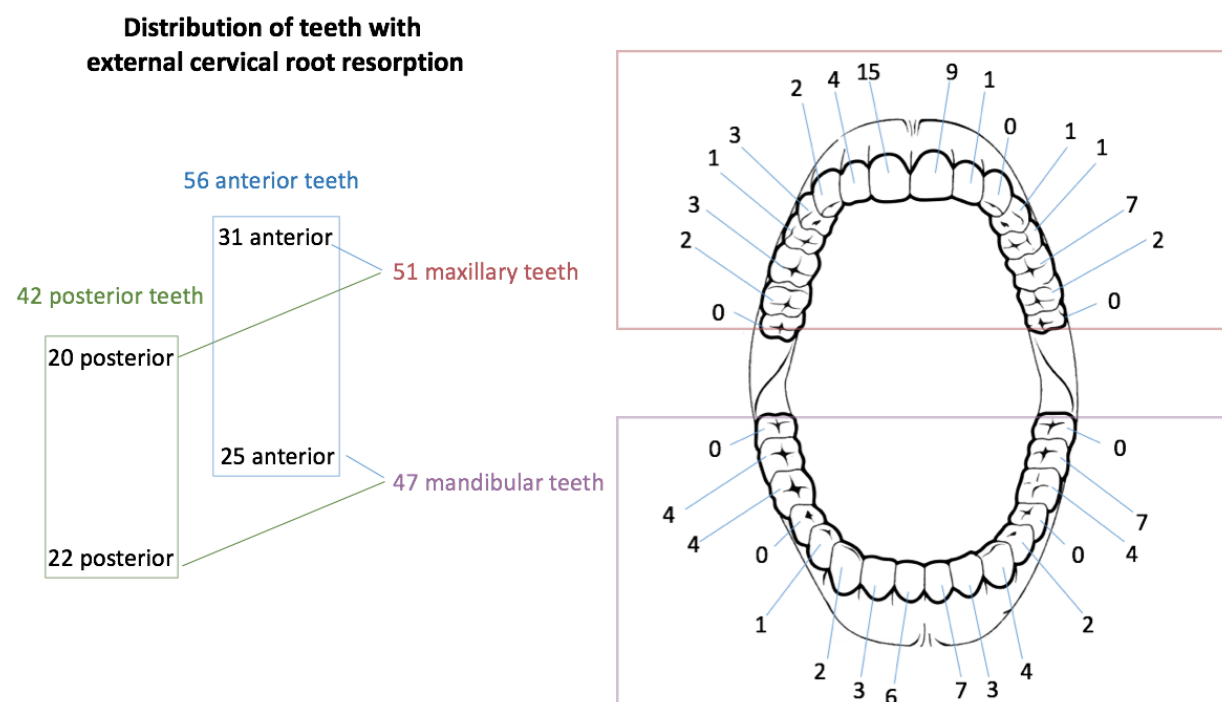


Figure 18. Distribution of teeth with external cervical root resorption.

There was an almost equal distribution among teeth with “normal pulp” (n=29 teeth, 29.5%), “pulp necrosis” (n=33 teeth, 33.7%) and “root filled teeth” (n=28 teeth, 28.6%). The diagnosis of “irreversible pulpitis” (symptomatic or asymptomatic) was less frequent (n=7 teeth, 7.1%), and the least frequent diagnosis was the “previously initiated RCT” (n=1 tooth, 1.1%).

The majority of the teeth, 68 out of 98 teeth (69.4%), were symptom free at the time of the diagnosis. The “normal apical tissues” was the most predominant finding (n=48 teeth, 49.0%); followed by an “asymptomatic apical periodontitis” (n=20 teeth, 20.4%). Slightly less frequent than the asymptomatic assigned finding, was the “symptomatic apical periodontitis” (n=16 teeth, 16.3%), and even less common was the “chronic apical abscess” (n=11 teeth, 11.2%) finding. The presence of “acute apical abscess”, presented an opposite trend from the predominant asymptomatic conditions (n=3 teeth, 3.1%).

The POE was located on the buccal surface of the tooth in 25 cases (25.5%), on the palatal or lingual surface in 23 cases (23.5%), on the mesial side in 26 cases (26.5%) and on the distal side on 21 cases (21.4%). In 3 cases (3.1%) the location of the POE was not identifiable because the extend of the resorptive channels was 360°, circumferentially around the root canal space. In 5 cases (5.1%) the resorptive defect covered 3 surfaces of the root and in 16 cases (16.3%) covered 2 surfaces. Seventy-four cases (75.5%), the majority of the resorptive defects, had a single surface presentation. When the location of the POE was not identifiable, the center of the resorptive defect was noted instead (Fig. 19).

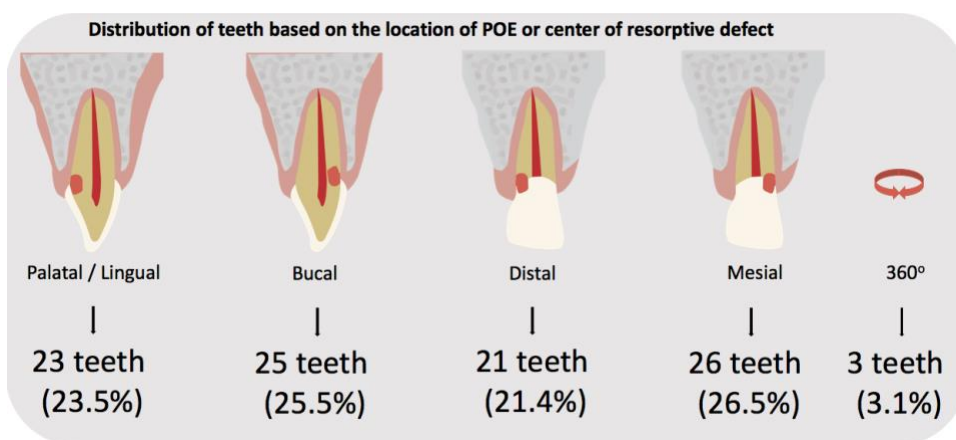


Figure 19. Distribution of teeth based on the location of the portal of entry (POE) or, when it is not visible, the center of the resorptive defect.

The frequencies of the different Heithersay ECRR classes 1, 2, 3 and 4 were 12.2% (n=12 teeth), 38.8% (n=38 teeth), 23.5% (n=23 teeth) and 25.5% (n=25 teeth) respectively (Fig. 20).

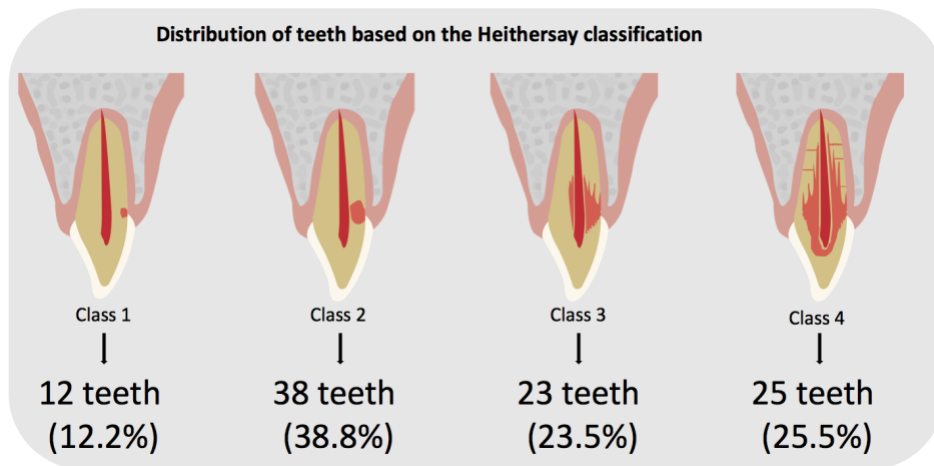


Figure 20. Distribution of teeth based on the Heithersay classification.

The sample was divided almost equally in numbers of teeth that received no resorption repair (49.0%) and teeth that received some kind of resorption treatment (51.0%). More specifically, 24 teeth (24.5%) received internal repair and in 17 teeth (17.3%) the resorptive process was accessed from outside (external approach, directly from external root surface). Six teeth with ECRR (6.1%) were extracted, and in three multi-rooted teeth (3.1%) amputation of one root was performed. For the internally repaired teeth, the following materials were used: MTA in 17 teeth (70.1%), resin composite in three teeth (13.4%), Biodentine in two teeth (8.3%), GI in one tooth (4.1%), and unknown material in one tooth (4.1%). For the externally repaired ECRR defects, resin composite was used in ten teeth (59.0%), Geristore in four teeth (23.6%), and MTA (5.8%), GI (5.8%) and amalgam (5.8%) on one tooth each. Overall, MTA was the most frequently used material for the internal repair and resin composite for the external repair (Fig. 21).

Initial ECRR treatment management

(tooth level of analysis)

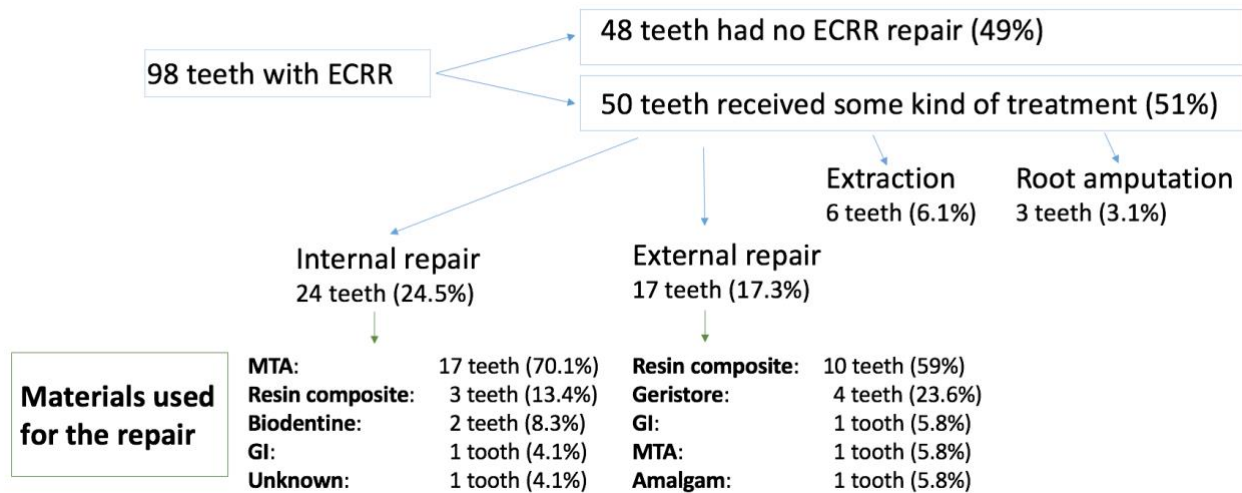


Figure 21. Chart illustrating the number of teeth which did or not receive initial treatment of the external cervical root resorption (ECRR). The materials used for the internal and the external repair and their frequencies are also pictured.

Univariate analyses: Tooth level analysis, Prospective approach

Survival rates were calculated for all teeth with at least one-year follow-up (n=89 teeth). Thirteen teeth developed new or increased periodontal radiolucency, five of them were related to the ECRR area and eight to periapical area. Five teeth presented with increased ECRR size, based on the radiographic findings, all of them without ECRR repair or RCT. Overall, 24 teeth were categorized as failed, and 19 of them were already extracted at the time of the follow-up procedure. The remaining five teeth were categorized as not functional based on the follow-up findings, even if they were still present in the oral cavity. Out of the 19 extracted already teeth, four were extracted due to periodontal reasons, eight because they were not restorable, and seven due to a poor prognosis. Out of the five still present but failed teeth, two failed due to periodontal

problems (Fig. 22), two because they cracked, and one due to vertical root fracture which was not related to the resorption side. All above categorizations, for instance the three etiological factors for extraction (i.e. periodontal problems, restorability and poor prognosis), are organized based on the clinical notes or phone interview findings.



Figure 22. Clinical pictures of a tooth (pointed by a black arrow) failed due to a periodontal problem.

a) intraoral picture of tooth #43 taken during the follow-up. b, c and d) intraoral pictures taken three months later than picture a. Pictures b and c show the periodontal inflammation and d) shows the tooth before the completion of the extraction. Note the extend of external cervical root resorption, and the root canal space in the center of the resorptive defect (yellow arrow). For the radiographic interpretation of the case, see Figure 12 a and b.

Bivariate analyses: Tooth level analysis, Failure rates regarding different local determinants

Two treatment related local factors showed statistically significant differences regarding the ECRR failure rates. The first factor was the RCT, and it showed that root canal treated teeth had a lower risk of failure than the teeth without such treatment. The second factor was the ECRR repair, whether combined or not with RCT. The comparison showed that teeth with ECRR repair and RCT had lower failure rates than teeth with ECRR repair but no RCT. Overall, the presence of ECRR repair and whether internal or external approach was used, showed no statistically significant difference in the ECRR failure rates (Table 2).

Table 2. Treatment related determinants in association with failure rates (tooth level analysis)

Treatment related determinants	Failure rates n (%)	Significance # (p-value)
Repair of External Root resorption		
Internal	3 (13.6)	0.372
External	4 (25.0)	
Root canal treatment		
Yes	9 (17.3)	0.007
No	15 (44.1)	
Resorption repair & Root canal treatment		
Yes	6 (15.0)	0.013
No	18 (39.1)	
Initial root resorption repair		
Yes	11 (23.4)	0.307
No	13 (33.3)	

Chi Square test

The “location of the portal of entry”, “history of trauma”, “orthodontic treatment”, “extraction of the adjacent tooth” and the “presence of restoration” were local determinants without statistically significant difference in the ECRR failure rates. The factor “irregular forces” was statistically significantly related to the failure rates ($p=0.032$). However, the 75% of teeth with irregular forces that failed, represents only three teeth. Because of the small number of teeth, this finding cannot be considered as truly significant.

Two local determinants, tooth location and Heithersay class, showed statistically significant differences regarding the ECRR failure rates: posterior teeth with ECRR had higher failure rates compared to anterior teeth, and the higher the Heithersay class, the higher the risk of failure (Table 3).

Table 3. Local determinants in association with failure rates (tooth level analysis)

Local determinants	Failure rates n (%)	Significance # (p-value)
Location (tooth)		
Anterior	8 (16.7)	0.009
Posterior	16 (42.1)	
Location (portal of entry)		
Buccal	7 (31.8)	0.802
Distal	4 (21.1)	
Palatal/lingual	4 (21.1)	
Mesial	8 (34.8)	
360	1 (33.3)	

Classification		
Class 1	0 (0.0)	0.020
Class 2	6 (18.2)	
Class 3	7 (33.3)	
Class 4	11 (47.8)	
Trauma		
Yes	4 (16.7)	0.148
No	20 (32.3)	
Orthodontic treatment		
Yes	1 (20.0)	0.685
No	23 (28.4)	
Extraction of adjacent tooth		
Yes	5 (33.3)	0.606
No	19 (26.8)	
Restoration		
Yes	12 (26.1)	0.526
No	12 (32.4)	
Irregular forces		
Yes	3 (75.0)	0.032
No	21 (25.6)	

Chi Square test

Visual analyses of failure rates: Tooth level analysis, hazard ratio curves

The cumulative hazard, meaning the cumulative probability of failure in different follow-up years, is demonstrated in a subsequent series of graphs. Within the first year there was a 12.0% probability of failure (Fig. 23). Corresponding failure probabilities were for the 2nd, 3rd, 4th and 5th years were 14.0%, 16.0%, 23.0% and 26.0% accordingly. At the 6th year a substantial increase in failure rates was observed, when half of the cases showed an increased probability of failure at 8 years, which could otherwise be interpreted that half of the cases survived 8 years. The highest 80.0% cumulative failure rate was at the 10th follow-up year (Fig. 23).

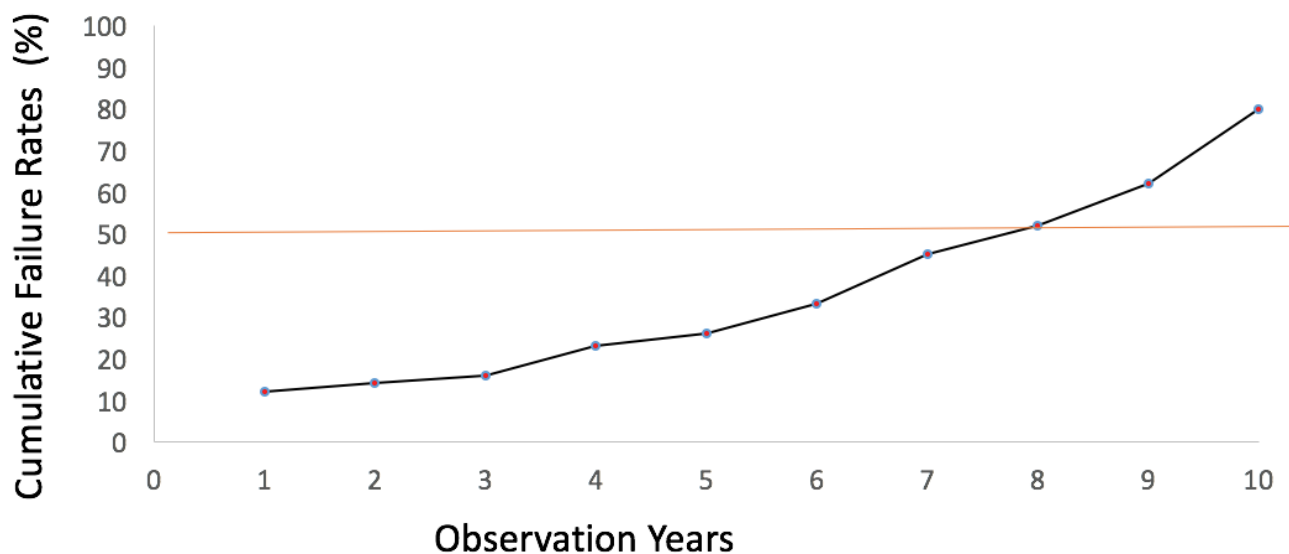


Figure 23. Treatment outcome and probability during a failure of a 10-year follow-up period.

Risk probability (cumulative hazard) illustrated in Figure 24 compares cases with no ECRR repair to the cases with some ECRR treatment (internal or external approach, root amputation or immediate recommended extraction). The probability of risk was relatively similar for both groups throughout the first 7 years. For the last 2 years, the probability of failure was high in both treatment groups (Fig. 24).

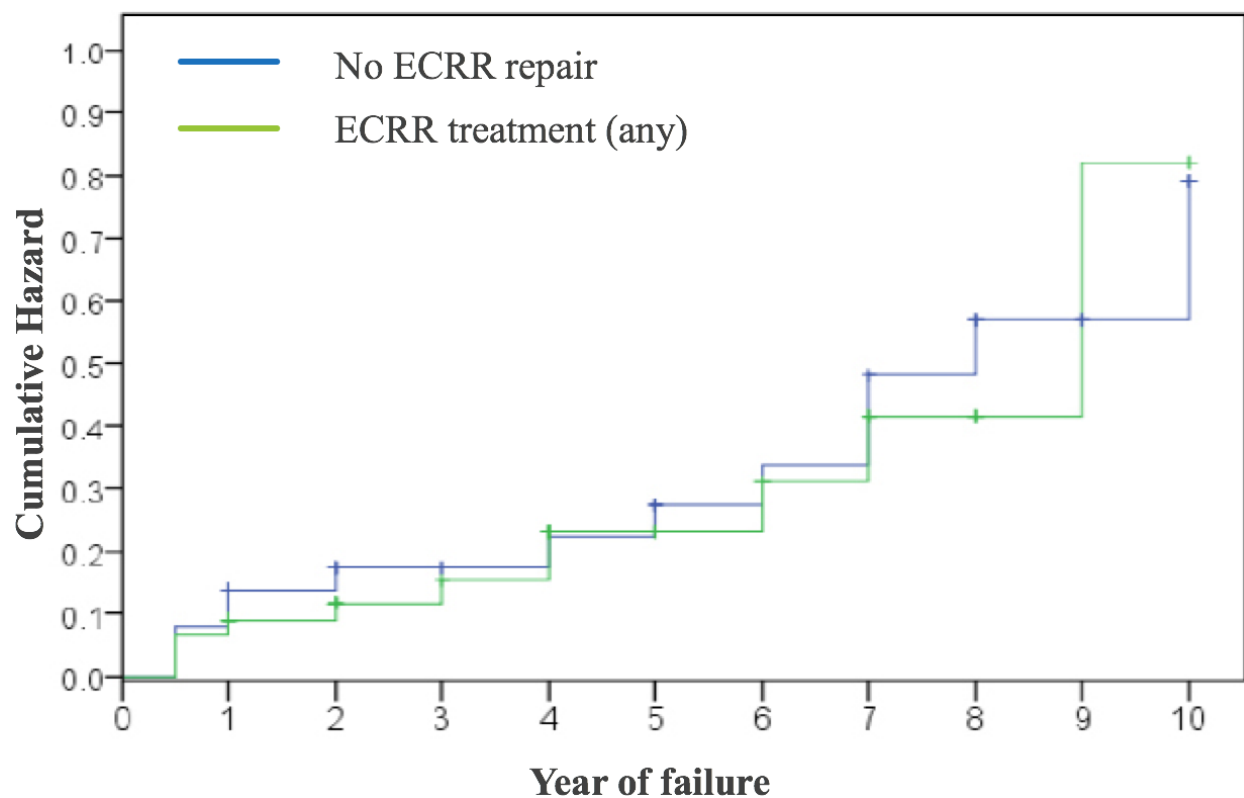


Figure 24. Treatment outcome. Determinant: external cervical root resorption (ECRR) repair.

The failure rates were compared between the teeth which were restored either via internal or external access (Fig. 25). For the first four years there were no obvious differences between the two groups of repair. However, after the 7th year the external repair group showed an increased risk of failure. The internal repair did not show any increased risk after the first four years.

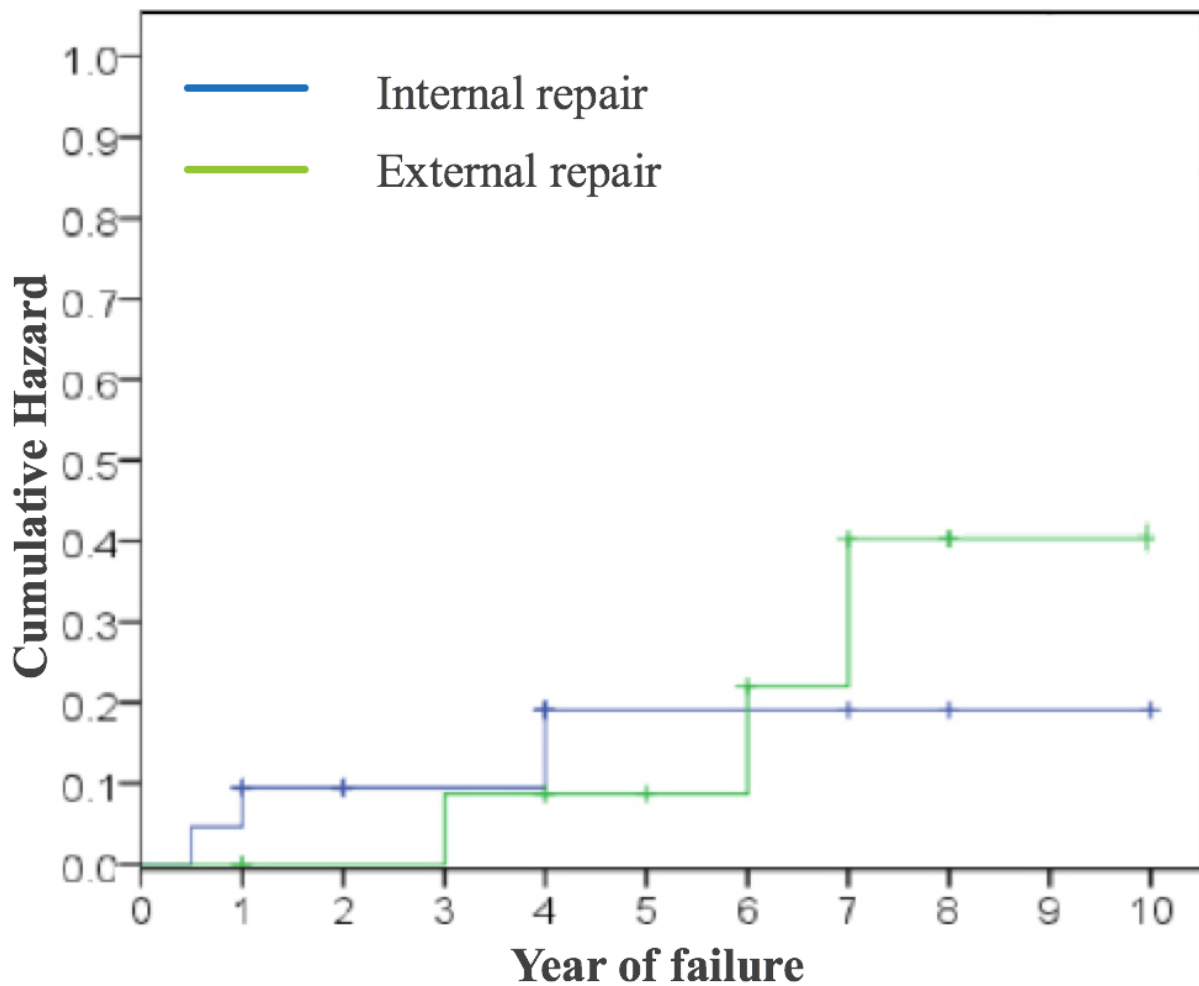


Figure 25. Treatment outcome. Determinant: Type of repair of external cervical root resorption repair.

When risk rates were compared between different locations (Fig. 26), the anterior teeth showed lower probability of failure than the posterior teeth. More specifically, the probability of failure was below 30.0% for the anterior teeth up to the 8th to 10th years of follow-up, which was similar to failure rates of posterior teeth at the 4th and 5th year of follow-ups. For the posterior teeth, the probability of failure was around 90.0% at the 7th to 10th year of follow-ups.

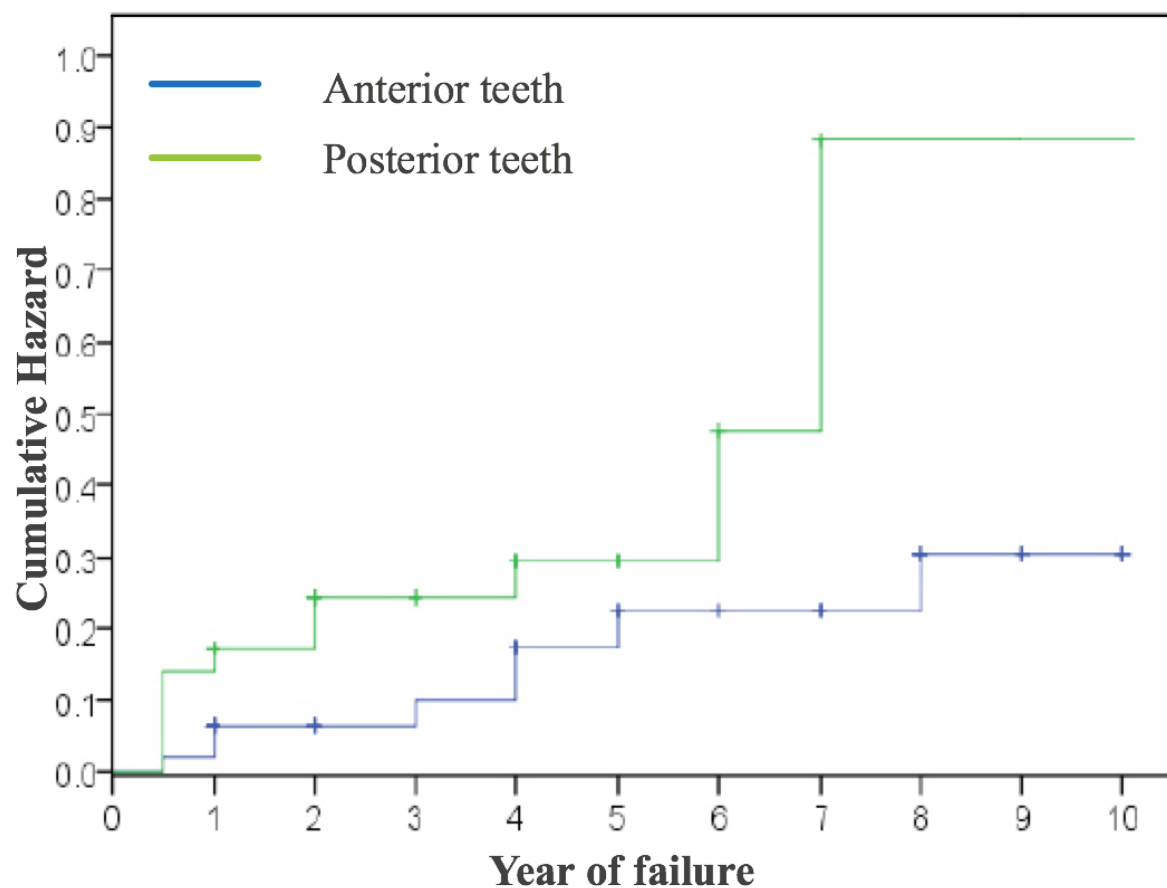


Figure 26. Treatment outcome. Determinant: Location of the tooth, anterior or posterior.

The treatment outcomes were also evaluated based on tooth vitality (Fig. 27) by comparing risk rates between teeth that received and those that did not receive root canal treatment (RCT). Overall, the probability of failure was higher for the teeth without RCT, e.g. at the 2nd year of follow-up the probability of failure was 35.0% for the teeth without RCT, while it was 5.0% for the teeth with RCT. The risk of failure was 70.0% for the teeth without RCT and 40.0% with RCT at the 8th year of follow-up.

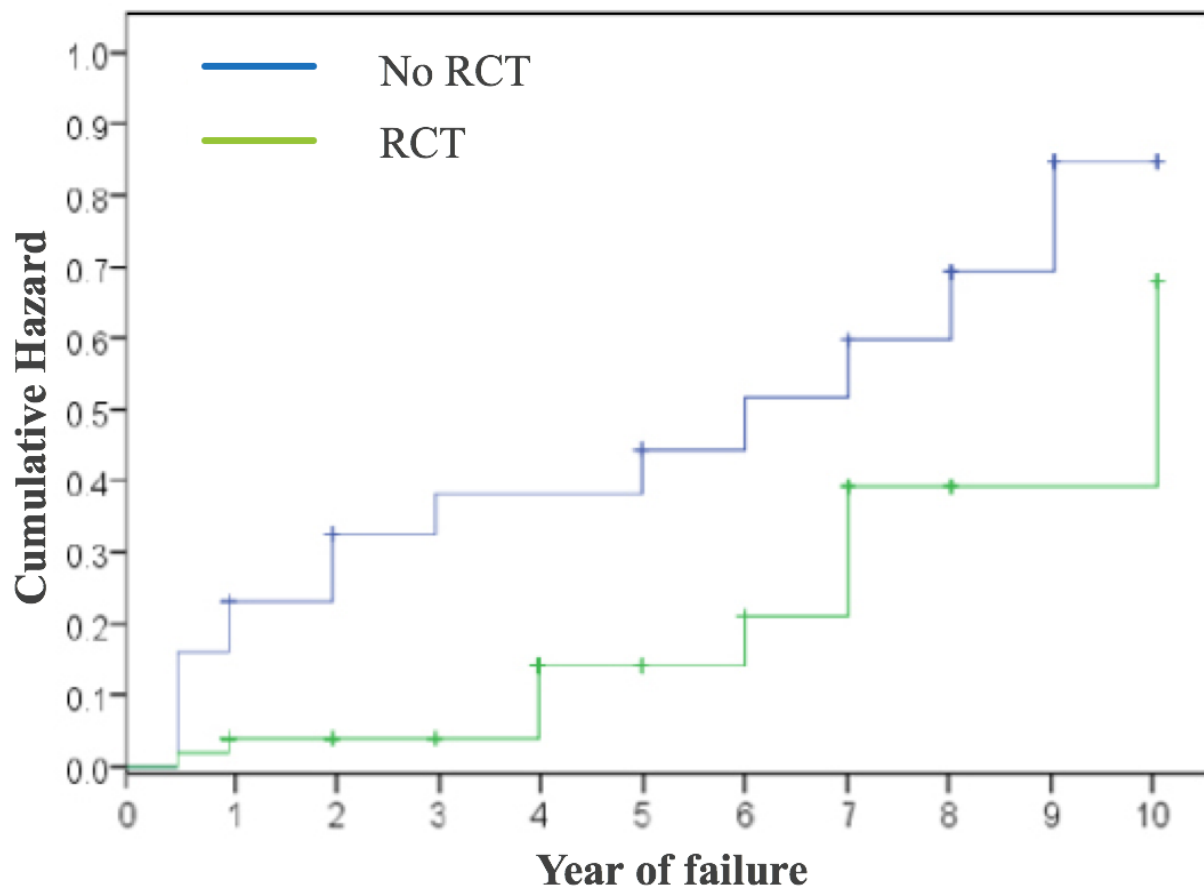


Figure 27. Treatment outcome. Determinant: Root canal treatment (RCT).

The probability of failure was also examined based on resorption repair with or without RCT (Fig. 28). Overall, the teeth without RCT but with repaired ECRR showed a substantially higher probability of failure, i.e. the risk of failure at the 5th year was 35.0% vs. 15.0%, while for the 8th year it is 65.0% and 35.0% respectively, for the teeth without RCT teeth and for the teeth with RCT (Fig. 28).

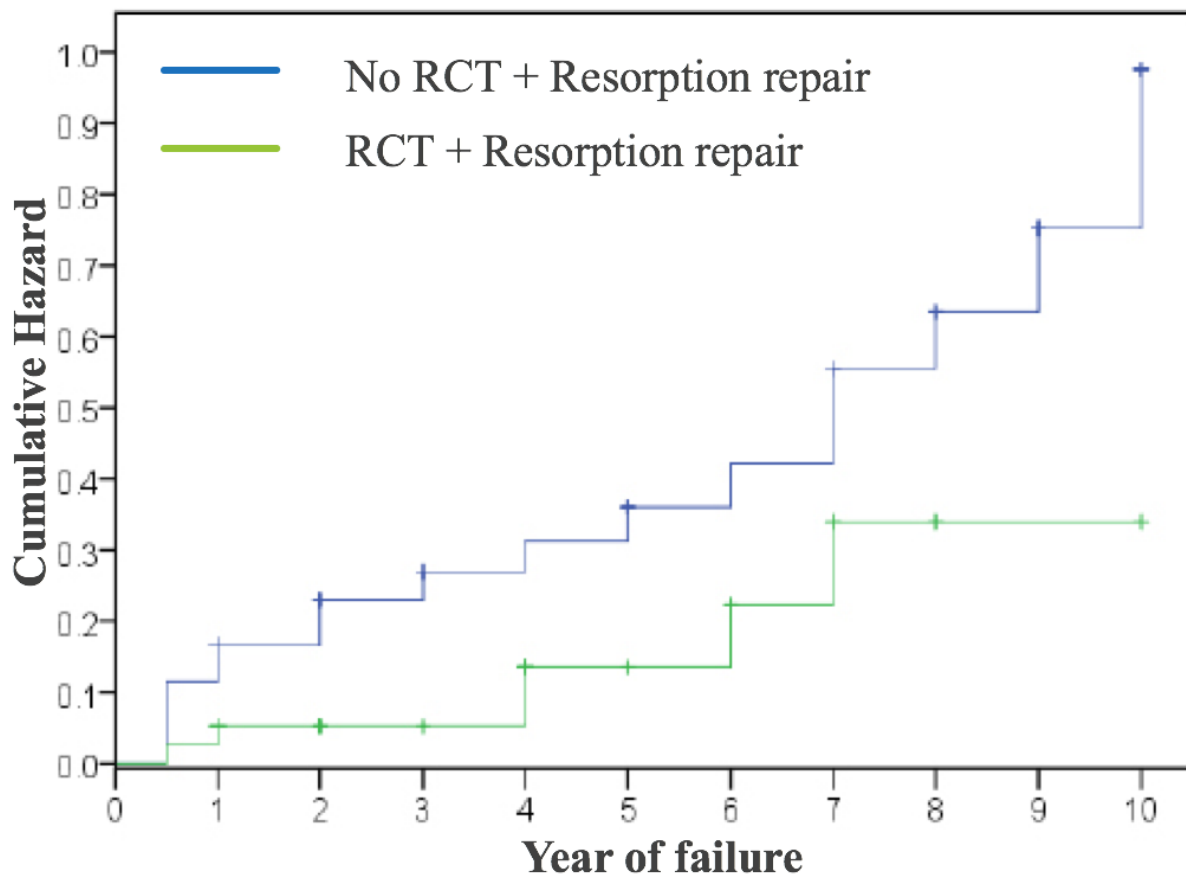


Figure 28. Treatment outcome. Determinant: External cervical root resorption repair combined with or without root canal treatment (RCT).

The failure rates were also assessed based on the location of the portal of entry (POE) or, if it was not visible, the center of the resorptive lesion as well as the number of tooth surface affected (Fig. 29). When the resorption spread was circumferential (360° around the root canal system), the risk of failure was substantial and reached 70.0% at the 1st year. At the end of the follow-up period, the risk of failure was higher when the POE was located on an interproximal surface compared to the location at the buccal and palatal/lingual surface.

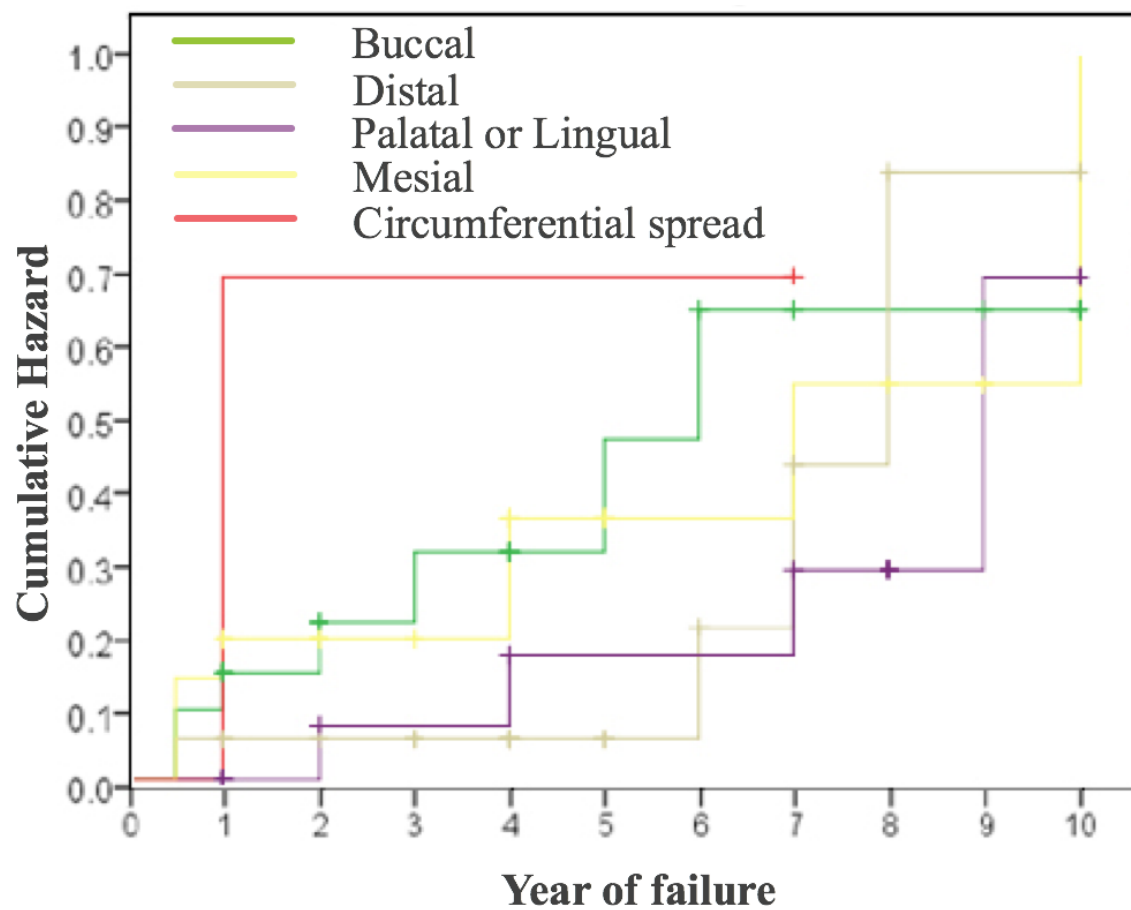


Figure 29. Treatment outcome. Determinant: Number of surface affected, location of portal of entry (POE), or if not visible, center of resorptive defect.

The failure rates in teeth with a different Heithersay ECRR class were compared (Fig. 30). Class 4 teeth showed the highest risk of failure, starting with 25.0% the 1st year, and reaching the 100.0% the 5th year. Class 1 showed 0.0% risk of failure throughout the whole 10year follow-up period. At the 5th year, class 3 teeth showed a 5.0% risk of failure in comparison to 20.0% for class 2. After the 7th year the risk pattern changed. At the 10th year, class 3 teeth had 70.0% and class 2 had 40.0% failure rates (Fig. 30).

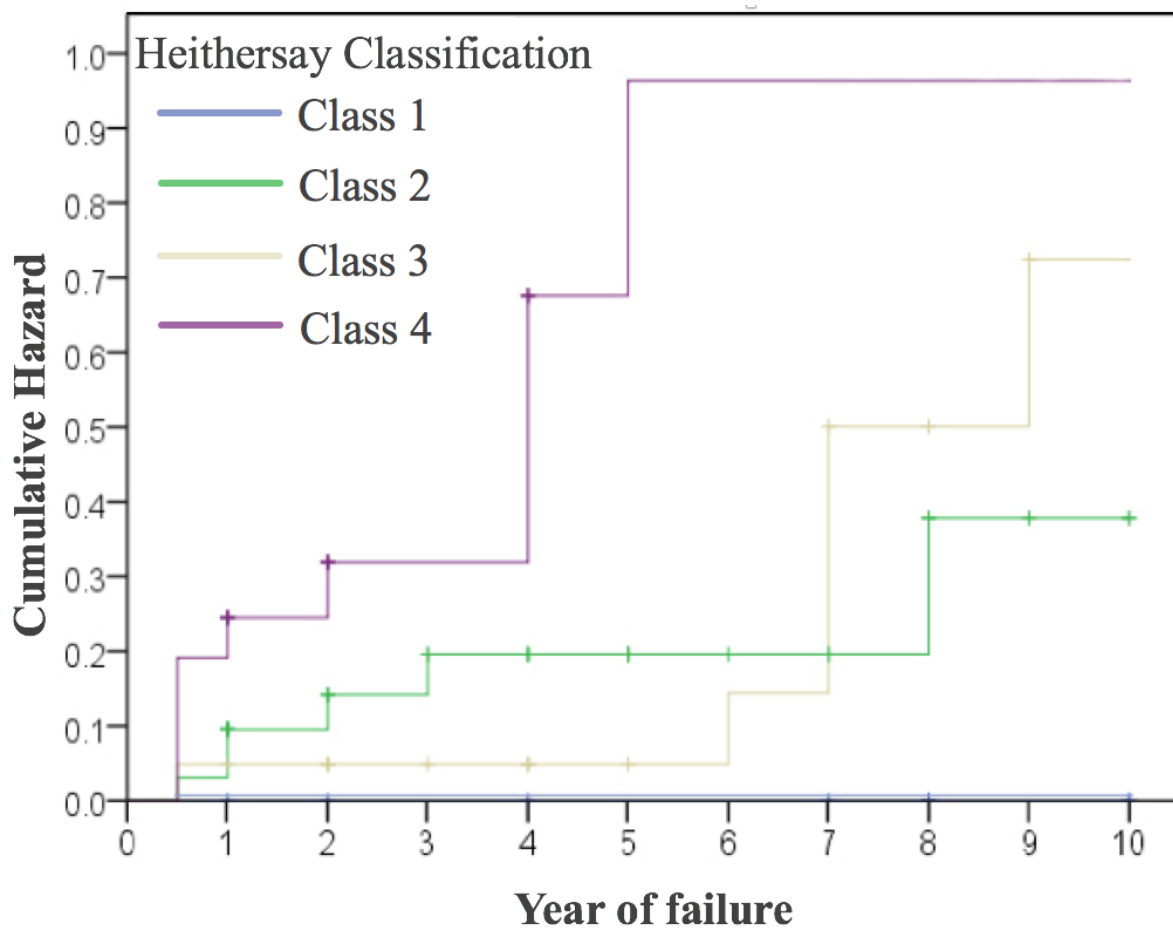


Figure 30. Treatment outcome. Determinant: Heithersay classification.

Chapter 5: Discussion

5.1 Discussion

First study hypothesis

The first study hypothesis was that systemic determinants are associated with higher rates of presence of external cervical root resorptions. To the best of our knowledge, this hypothesis has not been examined in previous studies. Systemic factors included presence of allergies, use of medication and 21 different medical conditions were assessed with a case-control study approach. Although the control group patients were unhealthier overall, there were no statistically significant differences between the study group (external cervical root resorption) and the control group (no external root resorption), except for one systemic condition. Diabetes was statistically significantly more frequent in the ECRR patients than in the control group. This finding indicates that diabetes may be a risk factor for ECRR, which partially supports the first study hypothesis. A potential link between ECRR and diabetes, could be hypoxia as oxidative stress and inflammation seem to be related to hypoxic cellular microenvironment in diabetic patients (178). In other studies, hypoxia has been proposed to predominate during the first steps of ECRR (53,54).

There are no previous studies assessing the systemic determinants of ECRR, however, there are two cohort studies regarding the potential local predisposing factors related to ECRR (3,6). In these two studies and the current study, the gender distribution was similar with the percentage of women diagnosed with ECRR being 40.8% (present study), 48.0% (6) and 51.3% (3). However, there was a difference in the age distribution at the time of the diagnosis of ECRR. In our study, the majority of cases was almost equally distributed in two age groups: 40-59 years

(n=28, 36.7%) and 60-89 years (n=27, 35.7%), whereas in the study of Mavridou et al. (6) the majority of the patients were between 15 and 54 years, and in Hethersay's study between 20 and 50 years (3). The age of patients in our study sample was higher at the time of the diagnosis of the ECRR than in the other two cohort studies. This age difference could be due to the relatively small number of patients in our sample (76 patients), in comparison to the other two studies, which had 284 (6) and 222 patients (3). All three studies showed that the maxillary central incisors were the most commonly affected teeth. The prevalence of ECRR in our study was 2.3%, which was calculated as the percentage that was diagnosed with ECRR from all patients in the graduate endodontic program during the last 10 years. In Heithersay's study (3), the ECRR prevalence was 0.02%, and it was calculated as the percentage of people living in Adelaide (Australia) in 1999 (1.2 million people) that were diagnosed with ECRR. The difference in the prevalence could be explained by that fact that Heithersay (3) used a significantly larger population (Adelaide population) than in our study for the calculations.

Second study hypothesis

The second hypothesis of the present study was that treatment-related determinants are associated with lower rates of failure. Based on the results of the present study, no statistically significant difference between the internal and the external repair of the ECRR was found. Two statistically significant differences regarding the ECRR treatment outcome were identified: "ECRR repair combined with or without RCT", and "RCT present vs. absent". Time interval for the presence of the RCT is the latest appointment recorded in a patient's chart, not the initial diagnosis. The two statistically significant findings were the following: first, teeth with ECRR repair combined with RCT, and second, root canal treated teeth regardless of the presence of

ECRR repair, showed lower failure rates. These two factors had Kaplan Meier hazard curves with similar patterns. When the determinant was “ECRR repair or not”, there was no statistically significant difference between the “ECRR repair” and the “no repair group”. This is a finding of great clinical interest as the result indicates that the “no treatment” potentially could be a valid treatment option for some ECRR cases. However, it should be mentioned that in our sample, the five teeth presenting with increased size of ECRR, were all untreated cases. Overall, the second hypothesis was partially accepted, since some ECRR treatment-related factors, but not all, were associated with lower failure rates. To the best of our knowledge, there are no published studies which have examined the relationship of ECRR treatment-related factors and treatment outcome.

Third study hypothesis

The third hypothesis was that local determinants are associated with higher failure rates. No statistically significant differences in ECRR treatment outcome were found when the determinants were evaluated: “location of portal of entry or center of resorptive defect”, “trauma”, “orthodontic treatment”, “extraction of adjacent tooth” and “restoration”. When the “irregular forces” was examined as a determinant, it was statistically significantly associated with the treatment outcome (75.0% failure rate). However, one must pay attention on how this information is interpreted. This high percentage of failures (75.0%) represents three failed cases out of total four cases with “irregular forces”. Due to the small sample size of the present study, potential misleading outcomes should be assessed in depth before confirming this as valid evidence. A statistically significant difference regarding the treatment outcome was found when the determinant “tooth location” was evaluated. More specifically, the failure rate was significantly higher for the posterior teeth than the anterior teeth. The difference in failures

increased substantially after the 6th year. This could potentially be related to the higher frequency of cracks on posterior teeth (179). To the best of our knowledge, there are no previously published studies which have examined the aforementioned local predisposing risk factors as determinants for the ECRR treatment outcome. However, there is one published study, which examined the treatment outcome based on the Heithersay classification as a local predisposing factor (159). Some similarities and differences between our study and the aforementioned one (159) will be discussed; prior to the results being presented. Both studies had similar size samples: 89 teeth in our study and 101 in the Heithersay study. The minimum follow-up period was one year in our study and three years in the Heithersay study (159). We defined the teeth as functional when there were no clinical findings, regardless of radiographic appearance, while in the other study, success was defined as the absence of resorption and other pathological findings in the radiographs. Our sample included both treated and non-treated teeth, where treatments were provided by different clinicians with different treatment approaches (e.g. multiple different materials were used). On the other hand, the Heithersay's study (159) included only treated cases, treated by one clinician (the author) who followed a specific protocol every time. In our study, a statistically significant difference regarding the treatment outcome was found when the determinant was the "Heithersay classification". More specifically, the failure rate was 0.0% for class 1 cases, and 18.2% for class 2 in our study, while Heithersay presented 100.0% success for both class 1 and class 2 cases. In our study, the failure rate for class 3 cases was 33.3% while in Heithersay's study the failure rate was 22.2%. For class 4 cases the failure rates were 47.8% and 87.5%, respectively. Overall, the third hypothesis is partially accepted, since some but not all potential local predisposing factors were associated with higher failure rates of teeth with ECRR.

An important difference was identified on how the studies by Heithersay (3) and Mavridou et al. (6) were conducted in comparison to the present study. In our study, all data were retrospectively collected from patient charts, whereas in the other two studies the authors collected information by directly interviewing patients. Because of that, the number of local factors we were able to assess was predetermined. For instance, playing of wind music instrument has been described as local predisposing factor in one of those cohort studies (6) and in a case report (95). The fact that in our patients' charts there was no information provided about use of wind music instruments, should not be conclusive evidence of the absence of this predisposing factor. As a result, we assessed fewer local predisposing factors in comparison to the other two studies, namely: trauma, orthodontics, extraction of adjacent tooth, irregular forces (bruxism and eruption disorders) and restoration. In the other two cohort studies (3,6) "orthodontic treatment", followed by "history of trauma" were the two most frequent observed local predisposing factors. In our study, "history of trauma" and "extraction of adjacent tooth" were the predominant ones. Although in our ECRR group, "restoration" was present with a high frequency, it was even more often found in the control group. It is of interest that in our project the number of patients with orthodontic treatment was lower for the ECRR group (n=3) than for the control group (n=5). Although the low numbers of previous orthodontic treatment limit the possibility to draw far reaching conclusions, the 3.1% frequency of orthodontic treatment as a single potential local predisposing factor in the ECRR group is in contrast with the other two cohort studies, where orthodontics overcomes the other factors with frequencies of 21.2% (3) and 45.7% (6) respectively. There are three potential explanations for this notable difference: smaller sample size, the retrospective approach in our study, which could lead to missed information, and the aforementioned difference in the age distribution. For instance, 35.7% of the patients in our study were 60-89 years old at the time of the ECRR diagnosis.

Overall, the number of several predisposing factors simultaneously present was different in the present and two earlier studies (3,6). In our study no predisposing factors were detected in 21.0% of the patients. In Heithersay's study the corresponding frequency was 15.3% (3) and in the study by Mavridou et al. 1.0% (6). An explanation for this difference, could be the number of the local factors examined, which was the lowest in our study and the highest in the Mavridou et al. study. However, there is an agreement between our findings (48.0%) and Mavridou et al. (40.0%) for the presence of a single factor as a determinant of ECRR. More than one factor was present in 28.9% (3), 31.0% (our study), and 59.0% (6) of the ECRR patients. It is noteworthy that in our study, systemic conditions (e.g. viral infections such as herpes) were not included in the analysis of the potential predisposing factors, in contrast with the study of Mavridou et al. (6).

5.2 Novelty and significance

There are no previous cohort studies about the association between systemic determinants and external cervical root resorption (ECRR). In the past, two cohort studies (3,6) have assessed the role of local predisposing factors. The present study suggests that diabetes may be a risk factor for ECRR. This indication is of significance because it may have an impact in early diagnosis of ECRR.

Cohort studies have not been conducted regarding how ECRR treatment-related determinants may be associated with the treatment outcome. The present study showed no statistically significant differences between teeth with and without ECRR treatment. This finding may indicate the potential importance of “no treatment”, as a valid treatment option for some ECRR cases. Also, the presence of root canal treatment and the external cervical root resorption

repair combined with RCT were found to be associated with lower failure rates. These findings are relevant because they may provide some indications for better treatment planning.

Cohort studies have not been conducted regarding how local determinants may be associated with the ECRR treatment outcome, except for one study where one local determinant was examined (159). The present study indicated that posterior teeth with ECRR present higher risk of failure than anterior teeth and that the risk of failure increases as the Heithersay class increases (i.e. Class 1 showed 0.0% and Class 4 showed 47.8% risk of failure). This is of clinical importance because it can provide indications for better treatment planning, and it also highlights the significance of early ECRR diagnosis.

5.3 Limitations

It has been previously mentioned that one of the limitations of the present study is the retrospective approach to collect information from the patients' dental charts. There are local factors (e.g. oral health) that the research team would have preferred to include into the analysis. Due to the retrospective approach, it may also be possible that the MSc candidate was not able to locate all the ECRR cases in the Romexis software, although comprehensive search strategies were used. Another limitation is the relatively small sample size. Because of this, high attention to detail should be paid to the interpretation of the statistical results. For example, 75.0% of teeth with "irregular forces" had a statistically significant high failure rate. However, this percentage represents three of only four teeth with "irregular forces". A third limitation of the study is that some of the patients were not followed up. A fourth limitation is that there may be undetected teeth with ECRR (no full mouth radiographic examination contacted) or undetected patients with ECRR in the Graduate Endodontics clinic of UBC. A fifth limitation is that Heithersay

classification (3) was used, a classification which provides only a two-dimensional description of the resorptive defect. Due to that limitation, during the radiographic assessment; the two examiners had to come to an agreement on how to describe the cases with “well-defined” defects “extending at least at the coronal third of the root”. A sixth limitation is that not all patients had a CBCT taken of the area of interest (46 patients with and 30 patients without CBCT). As a result, we were unable to use the new three-dimensional classification (51) which has been proposed by the most recent “Colleagues for Excellence of the American Association of Endodontists” (180). Also, due to the lack of CBCT, the changes of the resorptive defects during the follow-up years could not quantitatively measured.

5.4 Future directions

In the future, the design of the study should be a prospective cohort study instead of a retrospective cohort study. That would provide the research team with the advantage of collecting all important information by examining the patient directly. Also, a multicenter cohort study would provide a bigger sample size. In addition, use of CBCT could provide a more reliable, three-dimensional evaluation for analysis.

Chapter 6: Conclusions

1. Diabetes may be a potential systemic predisposing factor for external cervical root resorption.
2. Two treatment-related determinants are associated with lower failure rates:
 - External cervical root resorption repair combined with root canal treatment
 - Root canal treatment
3. Two local determinants are associated with higher failure rates:
 - Posterior teeth
 - The higher the class in the Heithersay classification is

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