Studies on Orthodontic Treatment in Subjects with Periodontal Disease

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To my family,

Povilas,

Paulius, Liepa and Marija

“...the greatest part of a road trip isn’t arriving at your destination. It’s all the wild stuff that happens along the way...” Emma Chase
Abstract

The number of adults with malocclusions and periodontal disease seeking orthodontic treatment is increasing. Therefore, it is important to examine benefits and risks of such treatment.

Periodontal disease is a complex chronic inflammatory disease, affecting tooth-supporting (periodontal) tissues, which results from imbalance between oral biofilm and the host's response. The result of the persisting inflammation and disease progression is the destruction of the periodontal tissues and loss of alveolar bone. Due to reduced periodontal attachment, teeth become mobile and migrate in the dental arch, resulting in malocclusions and further aggravation of the disease. If not treated, periodontal disease may finally result in loss of multiple teeth.

Impaired function and poor dental aesthetics due to the disease lead to poor quality of life in terms of physical as well as psychosocial well-being, and are the primary reasons for seeking treatment.

Treatment of periodontal disease is complex and often includes multidisciplinary teamwork.

Aims: The overall aim of this thesis was to explore the effects, risks and benefits of periodontal – orthodontic treatment on periodontal tissues in subjects with periodontal disease.

Methods: A systematic literature review was conducted which aimed to provide scientific evidence on the effects of orthodontic treatment on periodontal tissues in subjects with periodontal disease (Study 1). The clinical part of the thesis was designed as a randomised clinical trial, which aimed to compare two periodontal treatment timing strategies regarding the effect of orthodontic treatment on periodontal status (Study 2). Fifty subjects with periodontal disease were randomly assigned either to the test (periodontal treatment simultaneous to orthodontic treatment) or control group (periodontal treatment before the start of orthodontic treatment).

Initial treatment included oral hygiene instruction, supra- and sub-gingival debridement and was performed for all study patients. Nonsurgical and subsequent surgical periodontal treatment was performed at different time points for the test and control groups. Orthodontic treatment was performed with a straight-wire appliance. Intrusion and retroclination together with space closure were used for flared cases and were the most used orthodontic movements for
maxillary and/or mandibular anterior teeth. Micro-screws or implants were used for anchorage in the posterior segments where needed. Clinical attachment level (CAL) change was chosen as a primary outcome variable.

All patients were examined by cone beam computed tomography (CBCT) before and after orthodontic treatment to explore the extent of external apical root resorption (EARR) (Study 3) and changes in alveolar bone levels (ABL) (Study 4). EARR and change in ABL of the most proclined maxillary incisor were also studied and related to the orthodontic movements such as intrusion and change in inclination angle.

Results: The findings in the systematic literature review yielded absence of randomized controlled trials or controlled clinical trials on comprehensive orthodontic treatment in patients with periodontal disease. No difference in CAL change, EARR and ABL was found whether orthodontic treatment was performed simultaneously with (test group patients) or after (control group patients) periodontal treatment. Results yielded a median CAL change (sites CAL ≥4 mm) of 0.4 mm (Q1, Q3: 0.19, 0.61). Gain in clinical attachment level was observed in 22 (88%) patients in both treatment groups. CAL remained unchanged in an average of 3/4 of the sites; CAL gain was observed in an average of 1/4 of the sites. Root lengths were shortened in a median of 80.7% (Q1, Q3: 68.0, 90.0) of orthodontically moved teeth with a mean EARR of 1.2 mm (SD 0.44). EARR of <2 mm was observed in 82% of teeth. ABL levels remained unchanged on a mean of 69.3% (SD 8.8) of surfaces, ABL improved on a mean of 15.6% (SD 7.4) of surfaces, more on the mesial and distal, and ABL decreased on a mean of 15.1% (SD 7.5) of surfaces, more on the buccal and lingual.

Amount of intrusion as well as amount of retroclination influenced extent of EARR and ABL changes of the most proclined maxillary incisors.

Conclusions: Based on the results of the present research it can be concluded that periodontal-orthodontic treatment under optimal conditions (experienced clinicians and patients with excellent oral hygiene routines over time), if needed, could be included in the rehabilitation of patients with periodontal disease without deleterious effects. Orthodontic treatment, performed simultaneously with periodontal treatment, could be used in the routine treatment of patients with periodontal disease. However, there are two important prerequisites: meticulous personal oral hygiene of the patient and optimal sub-gingival control of inflammation before and throughout the combined treatment.
Original studies

The thesis is based on the following studies:

**Study 1**


**Study 2**


**Study 3**


**Study 4**


The articles will be printed with the kind permission of the journals.
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### Definitions and abbreviations

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<td>ABL</td>
<td>Alveolar bone level</td>
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<td>B</td>
<td>Buccal</td>
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<td>BoP</td>
<td>Bleeding on probing</td>
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<td>CAL</td>
<td>Clinical attachment level</td>
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<td>CBCT</td>
<td>Cone beam computed tomography</td>
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<td>CCT</td>
<td>Controlled clinical trial</td>
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<td>D</td>
<td>Distal</td>
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<td>EARR</td>
<td>External apical root resorption</td>
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<td>FOV</td>
<td>Field of view</td>
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<td>IA</td>
<td>Inclination angle</td>
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<td>IN</td>
<td>Intrusion</td>
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<td>Lingual</td>
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<td>OHI</td>
<td>Oral hygiene instructions</td>
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<td>OT</td>
<td>Orthodontic treatment</td>
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<td>PAL</td>
<td>Probing attachment level</td>
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<td>PD</td>
<td>Pocket depth</td>
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<td>POH</td>
<td>Professional oral hygiene</td>
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<td>PT</td>
<td>Periodontal treatment</td>
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<td>REC</td>
<td>Gingival recession</td>
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<td>RL</td>
<td>Root length</td>
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<td>RCT</td>
<td>Randomized clinical trial</td>
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<td>VD</td>
<td>Vertical distance</td>
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<td>VPI</td>
<td>Visible plaque index</td>
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Preface

“Can you do orthodontics for this patient?” the periodontologist asked me one day as he was coming out of his operating room. “I can not do any prosthetic work with these spaces, only extract and implant.” This was a periodontal patient with an open bite and wide spaces between her front teeth. She used to hide her mouth with her right hand when she talked. She felt uncomfortable and nearly cried.

I will always remember that patient. We should find the best ways we can to help people like her – but what are they? Should we extract periodontally compromised teeth and insert implants? What is the risk for peri-implantitis? What is the cost for a full mouth implant versus periodontal-orthodontic treatment? Can we promise a result? What are the risks? I opened my computer and started to read.

I read chapters in textbooks about orthodontics and periodontics. I was looking for seminars and conferences, lectures about this topic. Yes, I found some studies and case reports saying that they did interdisciplinary work for a periodontal patient and got favourable results. Yes, the recession became better. Yes, the pocket depths were reduced.

I was inspired and decided to start this project.

The project aims to answer questions about the effects, benefits and risks of orthodontic treatment on periodontal tissues in patients with periodontal disease.
Introduction

The World Health Organization has described oral health as essential to general health and psychosocial wellbeing. Oral health is described as being “free from mouth and facial pain, oral and throat cancer, oral infection and sores, periodontal (gum) disease, tooth decay, tooth loss, and other diseases and disorders that limit an individual’s capacity in biting, chewing, smiling, speaking, and psychosocial wellbeing” (World Health Organization, 2012). Glick and colleagues (2016) summarized the new definition of oral health by the World Dental Federation, which they described as being “multi-faceted, as “without pain, discomfort and disease of the craniofacial complex” (Glick et al., 2016). Furthermore, oral health is described as “the fundamental component of health and physical and mental wellbeing” (Glick et al., 2016).

Behaviours and habits are important factors contributing to oral health status (Bloom et al., 2012). Impaired oral health is related to habits such as smoking, frequent consumption of sugar-containing food, and drinking sweet beverages, and may include serious dental and mouth diseases such as caries, periodontal disease and even oral cancer (Sisson, 2007).

There are number of diseases (e.g. diabetes) and conditions which may be reflected in the oral cavity, primarily in soft tissues of the gums, showing signs of general infection or systemic disease that may affect the entire body (Renvert, 2003, Cullinan and Seymour, 2013, Sanz et al., 2018). On the other hand, research findings show that some oral diseases, such as periodontal disease, may be a potential risk factor for some systemic diseases, such as cardiovascular disease (Buhlin et al., 2015, Ryden et al., 2016).

Oral health is important regardless of age. In recent decades, oral health has improved throughout the world, especially in Sweden. This has been shown in a series of epidemiological studies from Jönköping. The percentage of edentulous individuals has decreased from about 14% to 0.3% over the past 40 years among individuals between 40-70 years of age (Norderyd et al., 2015). This is not the case in other European countries (Konig et al., 2010).
Periodontal disease has been found to be the sixth most prevalent disease among oral conditions globally (Marcenes et al., 2013). The consequences of periodontal disease are impaired function, poor dental aesthetics, fear of tooth loss, which lead to poor quality of life, and impaired physical as well as psychosocial wellbeing (Greenstein et al., 2008, Gerritsen et al., 2010, Araujo et al., 2010, Donos et al., 2012, Jansson et al., 2014).

As the number of adults having compromised periodontal conditions seeking orthodontic treatment is increasing, it is important to understand the aetiology and biology of periodontal disease, as well as benefits and risks related to periodontal-orthodontic treatments.
Background

Healthy periodontium

Armitage (2004) has described a “healthy” periodontium as “comfortable, and free from functional and aesthetic problems” and as an absence of plaque-induced periodontal disease (Armitage, 2004b).

About 150 different species of microorganisms are typically harboured in the mouth; however, most periodontal sites in most individuals do not exhibit attachment loss due to host-microbe homeostasis (Socransky and Haffajee, 2008, Hajishengallis, 2014). “The balance between these organisms and the human host plays a fundamental role in the maintenance of oral health” (Curtis, 2015). Clinically healthy gingiva consist of a keratinized oral epithelium that is continuous with the junctional epithelium that is attached to the tooth surface (Kinane et al., 2008). This is observed in patients with meticulous oral hygiene and host-microbial balance (Kinane et al., 2008).

Plaque-induced gingivitis

Gingivitis is the inflammation of gingiva resulting from accumulation and retention of bacterial plaque, which cause irritation of the gingival tissue and induces “inflammatory response.” The development of gingivitis has been described as “a well-controlled immunologic response” (Kinane et al., 2008), which does not cause loss of connective tissue attachment (Armitage, 1995). Clinical signs of plaque-induced gingivitis include gingival enlargement due to edema, redness and bleeding on probing without attachment loss (Armitage, 2004b, Mariotti, 2015).

Most people are in balance with their biofilm and therefore gingivitis does not result in attachment loss and initiation of periodontal disease (Seymour et al., 2015b). However, in a well-known trial of experimental gingivitis, two different kinds of inflammatory responses have been identified. Gingival inflammation differed even given the same amounts of plaque: in one group of subjects, significantly more severe gingival inflammation was observed than in the other group (Trombelli, 2004). This difference in inflammatory response was related to “increased susceptibility to gingivitis” and
interpreted as a possible risk for development of periodontal disease (Seymour et al., 2015b).

**Periodontal disease**

Periodontal disease is a chronic biofilm-induced inflammatory disease, a consequence of imbalance of the oral microbiota and the host response (Darveau, 2010). The biofilm is a necessary but not sufficient condition for the occurrence of periodontal disease (Hajishengallis, 2014b). The host inflammatory response to microbial challenge is needed to cause the destruction of periodontium (Darveau, 2010).

The host response can be altered by several general and local factors. Inherent genetics, acquired host immunodeficiency, systemic diseases (e.g. diabetes), and behavioural and environmental risk factors such as smoking and diet, were found to predispose to increased susceptibility to the disease (Hajishengallis, 2014b, Nociti et al., 2015). It is scientifically proved that ageing due to declined immune regulation and function increases the susceptibility to periodontal disease (Hajishengallis, 2014a, Kanasi et al., 2016). Local factors, such as poor oral hygiene over “hanging” dental restorations and prosthetic constructions also contribute to disease progression (Broadbent et al., 2011, Broadbent et al., 2006). Occlusal factors such as occlusal trauma were associated with deeper probing depths and poorer periodontal prognosis (Harrel and Nunn, 2009).

**Classification**

**Chronic periodontitis**

The chronic form of the plaque-induced periodontal disease (Figure 1) is more prevalent in adult populations (but may be found in children), where the amount of destruction is consistent with local predisposing factors (especially subgingival calculus) and has a slow degree of progression, although its progression may be exacerbated (Kinane et al., 2015).

The localized form is when <30% of sites are affected and the generalized form is when >30% of sites are affected (Kinane et al., 2008).
On a population basis chronic periodontitis is classified according to number of diseased sites and extent of tissue breakdown (probing attachment loss) at those sites. Low category, when 1–10 sites, medium category when 11–20 sites, and high category >20 sites are affected. The severity is considered mild (PAL = 1–2 mm), moderate (PAL = 3–4 mm) and severe (PAL ≥5 mm) (Kinane et al., 2015).

As a PAL of 1–2 mm at one or several sites can be found in nearly all adults, PAL ≥3 mm has been used to evaluate the severity of the disease (Socransky and Haffajee, 2008).

![Figure 1. Chronic periodontitis and malocclusion in a 50 year old patient.](image)

**Aggressive periodontitis**

Aggressive forms of periodontitis are rare, severe and rapidly progressing forms, often manifesting at an early age, although may be diagnosed in older subjects. The main features of aggressive forms of periodontitis are 1) microbial deposits are inconsistent with the severity of periodontal destruction, 2) rapid attachment loss and bone destruction, 3) familial aggregation of cases, 4) absence of significant systemic conditions, 5) elevated proportions of *Aggregatibacter actinomycetemcomitans* (hyper-responsive macrophage phenotype, including elevated production of prostaglandin E2 and interleukin-1β in response to bacterial endotoxins) (Tonetti and Mombelli, 2015).

Aggressive periodontitis is classified as the localized form when there is pubertal onset and localized first molar/incisor with interproximal attachment loss is found on at least 2 permanent teeth, one of which is molar, and involves ≤2 teeth other than first molars and incisors. A generalized form (Figure 2) classification is made when subjects are 30–35 years of age.
and there is generalized interproximal attachment loss at \( \geq 3 \) teeth other than first molars and incisors (Lindhe et al., 2008).

![Figure 2. Generalized aggressive periodontitis and malocclusion in a 23 year old female patient.](image)

**Aetiology**

An unfavourable alteration of composition in periodontal microbiota, called dysbiosis, has been found to be the primary etiologic factor in periodontal disease (Hajishengallis and Lamont, 2012, Lang and Lindhe, 2015). The detection of specific microorganisms (Porphyromonas gingivalis, Treponema denticola and Tannerella forsythia), called the “red complex,” was strongly associated with periodontal disease (Hajishengallis and Lamont, 2012). Additionally, other periodontal microbiota from the “orange complex” (Fusobacteria, Prevotela, Campylobacter species) have been found to facilitate colonization of dental plaque by red complex bacteria (Curtis, 2015). Aggressive forms of periodontal disease have also been associated with specific microbiota (Aggregatibacter actinomycetemcomitans) (Tonetti and Mombelli, 2015).

**Pathogenesis**

Periodontal inflammation is initiated as a consequence of the imbalance of dysbiotic periodontal microbiota and the host, which is followed by periodontal tissue destruction (Hajishengallis, 2014b). Complex biologic reactions occur between the cells and the extracellular matrix as a result of periodontal inflammation (Seymour et al., 2015a).

Inflammatory reaction begins as a result of dysbiotic microbiota in dental plaque. Polymorphonuclear neutrophils start to migrate into the gingival crevice, where they fail to control the pathologic microorganisms, which
invade the connective periodontal tissue and interact with immune cells, such as macrophages, dendritic cells and lymphocytes, which in turn start to produce bone-resorptive cytokines, such as tumor necrosis factor, prostaglandin and interleukines (Hajishengallis, 2014b). The result of this complex inflammatory response is the breakdown of connective tissue, loss of the connective tissue attachment, apical migration of the junctional epithelium and periodontal pocket formation (Reynolds and Meikle, 1997). The continued production of inflammatory cytokines and perpetuation of the inflammatory process leads to progressive destruction of both connective tissue and alveolar bone through RANKL-dependent mechanisms (Hajishengallis, 2014, Seymour et al., 2015a).

Clinical features of periodontal disease

As a result of microbial challenge, inflammation gradually spreads in the apical direction in the periodontium, causing destruction of the periodontal attachment and loss of alveolar bone.

The clinical features of periodontal disease are 1) color, texture and volume alterations, 2) bleeding on probing (BoP), 3) apical migration of junctional epithelium and the development of periodontal pockets, 4) loss of probing attachment level (PAL), 5) gingival recession, 6) alveolar bone loss, 7) root furcation exposure, 8) drifting and eventual exfoliation of teeth (Figure 3) (Savage et al., 2009, Mariotti, 2015).

Figure 3. Deep bite and over – eruption of maxillary central incisor due to attachment loss.
Consequences of periodontal disease

As marginal tissue breakdown continues, resulting in attachment loss, teeth become mobile and migrate in the dental arch, resulting in rotation, proclination/flaring of the anterior teeth, spacing, over-eruption and finally occlusal collapse, which may cause traumatic contacts between the teeth in opposing dental arches (Johal and Ide, 1999, Greenstein et al., 2008). Decreased posterior occlusion often causes mesial drifting of the posterior teeth and flaring of the anterior segments, which may be aggravated by early loss of teeth that are not replaced (Figure 4) (Dersot and Giovannoli, 1989). If not treated, the disease may finally result in several teeth being lost.

Figure 4. Loss of posterior teeth, decreased posterior occlusion and flaring of the anterior segments.

Prevalence

The prevalence of periodontal disease is high, in some countries reaching up to 50% of the population (Dye, 2012, Eke et al., 2015). Chronic periodontitis has been listed as the sixth most prevalent disease in the global burden of oral conditions (Marcenes et al., 2013).

In a study from the south of Sweden (2013), 20% of individuals had localized and 11% exhibited generalized periodontal bone loss. Periodontal treatment need was found in 53% of cases, defined as probing pocket depth ≥6 mm and bleeding on probing in ≥20% of sites. The percentage of individuals with moderate severity of periodontal disease experience in Sweden decreased from 47% in 1973 to 22% in 2013. Over the 40-year period, the percentage of individuals having no marginal bone loss increased from 8% in 1973 to 45% in 2013 (Norderyd et al., 2015).
Prevalence of periodontal disease varies among European countries (Konig et al., 2010). Data on prevalence of periodontitis in Lithuania is scarce. Data are available from 2001; prevalence of periodontal disease among adults aged 25–64 years was 37.6% in females and 52.3% in males (Globiene, 2001).

**Diagnosis of periodontal disease**

Inflammatory process as a result of infection in periodontal tissues leads to progressive destruction of connective tissue, periodontal pocket formation, bleeding on probing and loss of alveolar bone. Diagnosis of periodontal disease is performed through assessment of attachment loss by clinical (soft tissue) and radiographic (hard tissue) examination.

**Clinical examination**

Clinical examination, including assessment of full-mouth plaque and bleeding on probing (BoP) (Figure 5), followed by assessment of periodontal pocket depth (PD), recession (REC) and clinical attachment level (CAL), has been widely accepted for baseline diagnosis and management of periodontal disease (American Academy of Periodontology, 2011).

**Figure 5.** Signs of bleeding after periodontal probing.
Radiographic examination

Radiography is a valuable diagnostic tool supplementing clinical examination, as it provides information on decreased alveolar bone levels and other pathology, where the length of the root(s) with remaining bony support is of major importance (Armitage, 2004a, Corbet et al., 2009). Both two-dimensional (2D) and three-dimensional (3D) radiographic examinations have been used to support clinical diagnosis (Scarfe et al., 2017).

Two-dimensional (2D) radiographic examination

Horizontal and vertical bitewing radiographs have been used for diagnosis of periodontal bone loss (Koong, 2015, Scarfe et al., 2017). Vertical bitewings, supplemented with periapical radiography, have been recommended in cases with pocket depths greater than 5 mm (Royal College of Surgeons, 2013).

Periapical radiographs (Figure 6) performed by the long-cone paralleling technique have also been routinely used to examine mesial and distal interproximal alveolar bone levels for the diagnosis of periodontal disease (Bragger, 2005).

Figure 6. Periapical radiograph showing alveolar bone loss.

Panoramic radiographs (Figure 7) alone have been found to be inadequate to evaluate alveolar bony defects as accurately as periapical radiographs (Kim et al., 2008).
Panoramic radiographs, supplemented by selected intraoral radiographs, were called the “gold standard” for diagnosis of alveolar bone loss in patients with periodontal disease (Molander et al., 1995).

However, these techniques give only a two-dimensional view of complicated three-dimensional (3D) structures (Suomalainen et al., 2015). Panoramic radiographs and periapical radiographs have been found to underestimate bone loss as compared to surgical measurements and also criticized for image distortion as a result of variation in projection (Gröndahl et al., 1984, Hausmann et al., 1989, Eickholz and Hausmann, 2000).

Cone beam computed tomography (CBCT)

The use of 3D imaging such as cone beam computed tomography (CBCT) in periodontology has increased over the last years (du Bois et al., 2012, Fleiner et al., 2013). Even if 2D radiographic imaging in periodontally involved patients is still widely used, it may underestimate the depth and the configuration of the intra-bony defects and furcation involvements (Figure 8) (Walter et al., 2016).
Figure 8. Alveolar bone loss seen in CBCT image in the furcation area of maxillary first molar.

It has been shown that 3D imaging has a significant advantage for the assessment of buccal and lingual alveolar bone defects, which was impossible with conventional 2D radiography (Figure 9) (Misch et al., 2006, de Faria Vasconcelos et al., 2012).

Figure 9. CBCT of anterior teeth showing buccal and lingual alveolar bone loss.
Periodontal treatment

As discussed earlier, the development of periodontal disease results from dysbiosis in the dentogingival area and a destructive host response. Host response cannot be altered on the genetic level (susceptibility); however, actions should be taken to reduce general and local modifying factors, such as treatment of systemic diseases and patient education, including in behavioural change techniques such as smoking cessation (Nociti et al., 2015).

The aim of periodontal treatment is to eliminate factors (inflammation due to bacterial deposits) causing the disease, minimize the clinical symptoms, and restore, where possible, lost periodontal tissue and prevent further disease progression by creating inflammation-free conditions (Graziani et al., 2017). Pocket elimination/closure has been described as being the major goal of periodontal therapy (Graziani et al., 2018).

Individual oral hygiene instructions and development of personal oral hygiene habits to cope with periodontal microbiota prior to any periodontal treatment and compliance of patient has been described to be a key to success (Jonsson et al., 2012, Deas et al., 2016).

Nonsurgical periodontal treatment to reduce microorganisms remains the gold standard for most patients with periodontal disease, despite the advances in technology and development of new periodontal treatment protocols (Sanz et al., 2012, Graziani et al., 2017).

Surgical periodontal treatment is recommended at sites with residual increased probing depths ≥6 mm, angular bone defects, furcation involvement and persistent inflammation, which cannot be accessed by optimal root instrumentation (Heitz-Mayfield and Lang, 2013, Graziani et al., 2018).

The modification of surgical treatment of residual pockets such as the papilla preservation technique and minimally invasive flap technique with or without regenerative materials have also been introduced (Prato et al., 2004, Cortellini and Tonetti, 2009, Cortellini and Tonetti, 2011).

Supportive periodontal treatment has a significant role in maintaining and controlling disease progression (Renvert and Persson, 2004, Graziani et al.,
2017). It has been found that fewer teeth are lost if periodontal maintenance is administered after active periodontal treatment (Chambrone et al., 2010).

Research supporting occlusal interventions as adjunctive treatment of periodontitis in adults is scarce and leads to the conclusion that no evidence is present for or against the use of occlusal interventions in clinical practice (Weston et al., 2008, Weston et al., 2016).

Outcome of periodontal treatment

The outcomes of periodontal treatment are decrease in pocket depth (PD), gain of clinical attachment level (CAL) and gingival recession (REC) (Tomasi and Wennstrom, 2017). It has been described in the literature that PD reduction after initial nonsurgical periodontal treatment usually results in 3 months, although changes in CAL may continue for a period of 6 months or longer after the start of the therapy. Clinical signs of inflammation disappear within a week if optimal mechanical debridement is performed (Badersten et al., 1984, Loos et al., 1988, Claffey et al., 2004).
Orthodontic treatment

Moderate and severe periodontal disease often results in early loss of posterior teeth, loss of integrity of dental arches, and pathological drifting and migration of teeth with attachment loss. This often leads to decreased posterior occlusion, occlusal trauma, and malpositioning of teeth, causing malocclusions and further attachment loss. In these situations, orthodontic therapy is the only possibility to restore the patient’s aesthetics and function (Figure 10) (Sanz and Martin, 2015, Melsen, 2016).

Figure 10. A 50 year old patient before (A and B), during (C) and after (D) orthodontic treatment.

It is recommended that orthodontic treatment should be performed in inflammation free periodontal conditions (Sanz and Martin, 2015). Experimental studies lead to the conclusion that periodontal treatment has to be performed before orthodontic treatment, with elimination of plaque and calculus to arrest clinical inflammation (Melsen et al., 1988, Wennstrom et al., 1993). A six month full healing period has been recommended after periodontal therapy before the start of orthodontic tooth movement (Sanz and Martin, 2015).
Special consideration regarding personal oral hygiene has to be paid when treating patients with periodontal disease. Regular professional oral hygiene monitoring is needed. Depending on a number of circumstances, it is recommended to perform re-evaluation of periodontal status and oral hygiene at six-week to six-month intervals (Sanders, 1999). Repeated re-evaluations are important due to repopulation of subgingival pathogenic microbiota within 6-8 weeks after the pocket has been thoroughly cleansed (Listgarten and Levin, 1981, Rosenberg et al., 1981, Johnson et al., 2008).

An understanding of plaque-induced inflammatory mechanisms and the nature of destructive inflammatory reaction of the host in periodontal tissues are essential prior the orthodontic tooth movement in patients with periodontal disease.

*The biology of tooth movement*

Biological mechanisms of tooth movements in adult patients with stabilized periodontal disease should essentially be similar to those with normal height of periodontium. It is well known that orthodontic tooth movement initiates “aseptic inflammation” in the periodontal tissues. Biologic reactions between the cells and the extracellular matrix, the modelling and remodelling processes in the neighbouring alveolar bone will result in positional changes of a tooth (Sanz and Martin, 2015).

The theory of “pressure” and “tension” zones as well as the “hyalinization” phenomenon was introduced in 1904 by Sandstedt’s studies on dogs (Meikle, 2006). This theory is more or less accepted nowadays.

Application of light mechanical forces (approximately 50–100 g/tooth) on the pressure side results in narrowing of the periodontal ligament, which is not crushed, and therefore the blood flow and the physiology of the cells and tissues is preserved. Light forces are associated with “direct bone resorption” and a direct remodelling process in adjacent alveolar bone and more physiologic tooth movement (Sanz and Martin, 2015).

In contrast, changes in the periodontium after application of stronger orthodontic force include compression of the periodontal ligament space, impeding blood flow and resulting in cell death and a sterile necrotic cell-
free area between periodontal ligament and adjacent alveolar bone (hyalinization) (Meikle, 2006, Sanz and Martin, 2015).

The migration of macrophages, multinuclear giant cells and osteoclasts to the necrotic tissue result in “indirect” resorption of alveolar bone. This hyaline zone has been observed to interfere with the tooth movement and slow the biologic processes.

Inflammatory mediators, cytokines (interleukins, tumor necrosis factor, prostaglandins), have been found to be produced in the periodontal ligament cells as a result of application of mechanical force (Thilander et al., 2018). The up-regulation of the molecule, known as receptor activator of nuclear factor kappa-B ligand (RANKL) in the cells has been found at compression sites. It regulates osteoclast differentiation and function via its receptor (RANK) (Seymour et al., 2015a, Thilander et al., 2018).

The hyalinization process was also related to the external root resorption due to delayed alveolar bone resorption on the compression side, and was associated with cellular activity during the removal of necrotic hyalinized tissue (Meikle, 2006).

The changes in the pressure zone are different from those in the tension zone, where mitotic activity of osteogenic cells, stimulation of osteogenesis at the cortical bone surface and the formation of new bone was observed (Meikle, 2006).

**Orthodontic treatment in subjects with reduced periodontium**

A different approach to orthodontic treatment in patients with reduced bone levels is required concerning force systems, anchorage and retention (Melsen, 2016).

**Force systems**

The center of resistance in teeth with reduced periodontium is displaced apically. Therefore, orthodontic movements result in the expression of greater moments of force and higher risk of tipping instead of bodily movement (Sanz and Martin, 2015).

It is advisable to use the simplest orthodontic mechanics to reduce plaque
accumulation in order to facilitate personal oral hygiene. The self-ligation concept introduced in recent years was claimed to have numerous advantages such as secure archwire engagement, better rotational and torque control, decreased total treatment time, decrease in friction and decreased plaque accumulation (Damon, 1998b, Damon, 1998a, Eberting et al., 2001, Thorstenson and Kusy, 2001, Khambay et al., 2004, Sanz and Martin, 2015). However, recent research has contradicted these claims (Kaklananos et al., 2017, Dehbi et al., 2017, Handem et al., 2016). Despite that, self-ligating systems are advised for more simple oral hygiene (Sanz and Martin, 2015).

**Anchorage**

Orthodontic anchorage in patients with reduced marginal bone support due to periodontitis is often challenging. Difficulties in the usage of conventional anchorage modalities are related to the poor condition of teeth with reduced periodontal support (Melsen and Dalstra, 2017). When orthodontic micro screws were introduced as skeletal anchorage, the new possibilities for more simple mechanics served for everyday work (Xu and Xie, 2017). In the treatment of malocclusions and periodontal pathology, retraction of the entire maxillary dentition can efficiently be achieved by stable and reliable bony anchorage with a mini plate or micro screw (Mavreas, 2006). Mini-implants can provide stable bony anchorage and overcome problems of anchorage loss during extraction space closure, which usually occurs with traditional anchorage preparations (Upadhyay et al., 2009, Mariotti, 2015). However, only case reports have been published on the benefits of mini-implants as orthodontic anchorage in patients with periodontally compromised dentition (Fukunaga et al., 2006, Pinho et al., 2012, Agarwal et al., 2014).

**Retention**

After active orthodontic treatment is finished, permanent retention of the result is usually necessary. Extended retention periods up to 10 years have been recommended for periodontally healthy patients (Zachrisson, 1997, Sadowsky et al., 1994). However, patients with periodontal disease seem to need retention for an unlimited amount of time (Melsen, 2016).
Specific orthodontic tooth movements

To test the effect of orthodontic tooth movement on teeth with an artificially reduced periodontium, experimental animal studies (with varying designs and conclusions) were published.

Animal studies; mesial tipping

Ericsson et al. studied orthodontic tooth movement in dogs and concluded that healthy and inflamed periodontal tissues react differently (Ericsson et al., 1978, Ericsson et al., 1977). Mesial apical (tilting) movement of teeth with experimentally induced periodontal inflammation resulted in the formation of infra-bony pockets, characterized by presence of a pocket epithelium, a large supra- and infra-bony inflammatory cell infiltrate, and angular widening of the marginal periodontal ligament (angular bony defect). Movement of teeth having reduced but healthy periodontium – did not cause additional attachment loss (Ericsson et al., 1978). A study in rats on mesial tipping and displacement of healthy but reduced periodontia found that orthodontic movement stimulated bone apposition (Vardimon et al., 2001). These experimental studies concluded that control of inflammation during orthodontic treatment is considered of significant importance because it helps to avoid additional attachment loss (Melsen et al., 1988).

Animal studies; mesial movement into infra-bony defects

Experimental studies in monkeys assessed orthodontic tooth movement into non-inflamed intra-bony periodontal defects and found no effect on the levels of connective tissue attachment (Polson et al., 1984). Geraci et al. (1990) examined mesial movement of teeth in a monkey with reduced but healthy periodontia and found that a new epithelial attachment coronal to the alveolar crest was created (Geraci et al., 1990). Tooth movement into and through alveolar bone defects – without inflammatory infiltrate – stimulated bone formation (Vardimon et al., 2001, Nemcovsky et al., 2004, Nemcovsky et al., 2007). Nemcovsky et al. (2007) found that (i) orthodontic treatment in rats resulted in restrained epithelial apical down-growth and a decrease in pocket depth and (ii) it was impossible to completely avoid formation of a long junctional epithelium. So they suggested that periodontal reconstructive surgery might be indicated before orthodontic tooth movement (Nemcovsky et al., 2007). But, as found in a dog study, bodily movement of teeth toward
an infra-bony defect with inflamed infra-bony pockets may increase loss of connective tissue attachment (Wennstrom et al., 1993).

Animal studies; intrusion

In monkeys, Melsen et al. found that intrusion of teeth with experimentally induced vertical bony defects improved attachment level – if treatment was performed under healthy conditions (Melsen et al., 1988). Intrusion of teeth with poor oral hygiene resulted in moderate new attachment in some animals while further resorption of marginal bone was found in other animals. In a later monkey study, Melsen found that intrusion of periodontally damaged teeth depended on periodontal status of the teeth. If inflammation occurred, then alveolar bone breakdown was observed. When oral hygiene was good, then intrusion resulted in coronal displacement of attachment level (Melsen, 2001).

Animal studies; extrusion

Ingber mentioned forced eruption as a method of choice in treatment of an osseous defect caused by periodontal disease (Ingber, 1974). Extrusion of experimentally induced periodontitis in dog teeth resulted in shallower periodontal pocket depths, less gingival inflammation, no bleeding on probing, and new bone formation coronal to the original alveolar crest after treatment (van Venrooy and Yukna, 1985).

Animal studies; guided tissue regeneration (GTR) before orthodontic treatment

In foxhounds, Diedrich et al. found that orthodontic tooth movement – particularly intrusion and translatory movement of teeth with periodontally treated infrabony defects – causes no side-effects on periodontal soft tissue healing (Diedrich et al., 2003). In addition, periodontal reconstructive procedures provided better conditions for osteogenesis during orthodontic movement of teeth with attachment loss – provided good oral hygiene was maintained (Diedrich et al., 2003).

In an experimental study of dogs, treatment of class III furcations was performed through combining open flap surgery with intrusion or through GTR surgery with intrusion using microimplants (da Silva et al., 2008). Furcations were closed or reduced to class II or I in the intrusion groups. The
researchers supported the statement of Melsen et al. (1988) that increased mitotic activity of the cells might be induced by the orthodontic stimulation, which results in formation of a new attachment (Melsen et al., 1988).

**Timing of orthodontic treatment in animal studies**

In some experimental studies, orthodontic treatment was initiated 7–10 days after periodontal treatment, assuming that increased cellular mitotic activity appears after surgery (Melsen et al., 1988, Melsen, 2001, Vardimon et al., 2001, Nemcovsky et al., 2004). In other animal studies, tooth movement was delayed up to 1 month and 2–3 months to allow for the complete healing of periodontal tissues after surgery (Geraci et al., 1990, Araujo et al., 2001, Ericsson et al., 1978, Ericsson et al., 1977).

**Human studies**

Findings in animal studies with experimentally induced periodontal disease cannot be easily extrapolated to human conditions because natural periodontal destruction is unknown in monkeys, and it occurs in much older dogs than those used in the studies. Attachment loss in humans occurs relatively slowly over a much longer time and usually has underlying modified host responses (Harrel et al., 2006).

**Radiographic evaluation of orthodontic treatment outcome**

The American Board of Orthodontics has advised six periapical radiographs (maxillary and mandibular periapical as well as bitewing films or a full-mouth series of radiographs) to supplement panoramic radiography for adults for assessment of changes in alveolar bone levels and root lengths (Grubb et al., 2008).

**Alveolar bone level (ABL)**

Anterior periapical radiographs have been used for alveolar bone level (ABL) changes after orthodontic treatment in periodontally healthy adults (Bellamy et al., 2008).
The nature of orthodontic movement, as well as the dentoalveolar complex, is three-dimensional (3D). Therefore, ABL changes have been described as best assessed by means of 3D radiography (Suomalainen et al., 2015). 3D imaging has a significant advantage for the assessment of buccal and lingual alveolar bone defects, which is impossible with conventional 2D radiography (Misch et al., 2006, de Faria Vasconcelos et al., 2012).

It has been found that orthodontic treatment with fixed appliances in periodontally healthy patients results in small amounts of buccal movement of posterior, labial movements of anterior teeth, which are accompanied by significant changes in surrounding ABL assessed on CBCT (Kapila and Nervina, 2015, Cattaneo et al., 2011, Cattaneo et al., 2013). Also, retraction of protrusive but periodontally healthy teeth sometimes results in bony dehiscences after orthodontic treatment (Sarikaya et al., 2002).

Insufficient accuracy of diagnosing dentoalveolar complex has led to recommendation of CBCT examination in cases with pre-existing periodontal disease and thin alveolar biotypes in order to assess alveolar boundary conditions before orthodontic treatment (Kapila and Nervina, 2015).

**External apical root resorption (EARR)**

Intraoral periapical and panoramic radiography have been used for detecting EARR during orthodontic treatment (Sameshima and Asgarifar, 2001, Barros et al., 2017, Jiang et al., 2017, de Freitas et al., 2007). The use of intraoral periapical radiographs for studies of root shortening during orthodontic treatment is well described and the technique has been shown to have a number of shortcomings affecting its validity as well as reproducibility. These shortcomings are related to the technique itself, being a summation of a three-dimensional object, and problems due to projection geometry (Brezniak et al., 2004a, Brezniak et al., 2004b, Brezniak et al., 2004c, Dudic et al., 2008, Yi et al., 2017). Reproducibility is of great importance, especially in longitudinal studies. It is well known that, due to differences in projection geometry, changed inclination of teeth, radiographic follow-up using intraoral techniques reveals a low degree of reproducibility (Katona, 2007). A number of research articles have shown that plain film radiography, due to its two-dimensional nature, underestimates the resorption in buccal and palatal aspects of the roots.
CBCT has been shown to be a more accurate diagnostic tool for detecting EARR than periapical and panoramic radiography (Dudic et al., 2009, Durack et al., 2011, Ren et al., 2013). CBCT has also been shown to be superior in diagnosis of slanted root resorptions on surfaces adjacent to the direction of tooth movement (Lund et al., 2012b, Kapila and Nervina, 2015).

Cone beam computed tomography

Dental cone beam computed tomography (CBCT) is a 3D imaging technique, used, when regular dental X-rays are insufficient. A 3D image is created using a cone shaped X-ray beam, rotating 360 degree around the patient’s head. During rotation, a detector on the opposite side collects sequential projection images (Scarfe and Farman, 2008).

Technical characteristics

Depending on the field of view (FOV) used, CBCT generally can be divided into three different types: 1) large (>15 cm scan volume height), usually used for craniofacial imaging, 2) medium (10–15 cm) and 3) small (<10 cm), usually used for dento-alveolar complex. FOV is the most important scanning parameter and affects patient radiation dose and image quality. With larger size of FOV voxel sizes are larger and therefore results in lower spatial resolution (Kiljunen et al., 2015).

Voxel size

Spatial resolution is related to the size of the voxel (the unit element of image volume). Higher spatial resolution can be obtained with smaller voxel sizes (Kiljunen et al., 2015). Beam projection geometry, scatter and patient movements can also affect spatial resolution. Scatter and beam hardening cause image artefacts (resulting from metal fillings, crowns, fixed orthodontic appliances).

Small voxel sizes, as well as small FOVs, have been recommended in order to obtain high-resolution radiographs with relatively low exposure to radiation (Durack et al., 2011). Different voxel sizes (from 0.2 to 0.4 mm) have been used for 3D assessment of alveolar bone level (ABL) changes and
EARR. Smaller voxel sizes improve sensitivity, specificity and accuracy of measurements (Neves et al., 2012, Liedke et al., 2009, Menezes et al., 2016). Sensitivity and accuracy were better with 0.25 mm voxel size in one study; however, 0.3 mm voxel size appeared to be the best protocol in another (Liedke et al., 2009, Neves et al., 2012). For ABL changes, CBCT images have demonstrated good accuracy for both 0.2 mm and 0.3 mm voxel sizes, but 0.2 mm voxel size has shown a decreased number of intraexaminer errors for bone crest level measurements, especially for the mandibular incisor region (Menezes et al., 2016).

The CBCT technique has been described as yielding a high level of reproducibility, despite positional changes during orthodontic tooth movement. Therefore, it has been recommended to use CBCT in orthodontic research (Lund et al., 2010).

Effective radiation doses

CBCT has higher radiation doses than conventional two-dimensional images, such as periapical and panoramic radiographs (Dula et al., 2015). Justification of CBCT examinations has been recommended in clinical practice to weight the benefit of radiographic diagnosis against the potential risk for the patient and to follow the ALARA (as low as reasonably achievable) principal (Carter et al., 2008, Lang and Lindhe, 2015).

Indications for the use of CBCT imaging in periodontics and orthodontics have been presented in the recent “best evidence consensus” meeting of the American Academy of Periodontology, where CBCT was indicated for treatment planning and risk assessment of orthodontic tooth movement in buccal directions for patients with a thin dentoalveolar phenotype and concomitant recessions (McAllister and Eshraghi, 2017, Mandelaris et al., 2017). However, due to higher levels of radiation, routine use of CBCT has not been recommended (Kiljunen et al., 2015, McAllister and Eshraghi, 2017).

A full mouth series of intraoral radiographs has been reported in the literature to result in an effective dose of about 34.9 μSv; panoramic (digital) radiographs in the range of 10.4 to 24.3 μSv (depending on radiographic settings); lateral cephalograms range from 4.5 to 10.4 μSv, and mean adult effective doses of CBCT range from 31.6 to 69.0 μSv for small FOVs.
(Ludlow et al., 2015, Garcia Silva et al., 2008, Gavala et al., 2009, Grunheid et al., 2012, Ludlow et al., 2008, Ludlow and Walker, 2013, Davies et al., 2012) (Table 1). Therefore, the sum of the effective dose for the panoramic radiograph, supplemented by periapical radiographs and lateral cephalogram, may reach an effective dose within the same range as that of small FOV CBCT (Silva et al., 2008).

It has to be emphasized that 2D radiographs will provide less information (as described earlier) and will not be as accurate as 3D imaging.

To minimize CBCT radiation for a patient, the use of small FOV (<10 cm) up to two dental arches, a pulsed exposure mode of acquisition, optimized exposure settings (mA, kVp) and the use of patient protective shielding have been recommended (American Academy of Oral and Maxillofacial Radiology, 2013).

**Table 1.** The median values and/or range of effective dose of different types of dental radiography in adults.

<table>
<thead>
<tr>
<th>Type of radiography</th>
<th>Effective dose (μSv)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraoral</td>
<td>&lt;1.5</td>
<td>Ludlow et al., 2008</td>
</tr>
<tr>
<td>Full mouth series of intraoral radiographs</td>
<td>34.9</td>
<td>Ludlow et al., 2008</td>
</tr>
<tr>
<td>(F-speed film with rectangular collimation)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Panoramic (digital)</td>
<td>10.4–24.3</td>
<td>Ludlow et al., 2008</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Garcia Silva et al., 2008</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gavala et al., 2009</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Grunheid et al., 2012</td>
</tr>
<tr>
<td>Cephalometric</td>
<td>4.5–10.4</td>
<td>Silva et al., 2008</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ludlow et al., 2008</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Grunheid et al., 2012</td>
</tr>
<tr>
<td>i-Cat Next Generation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dentoalveolar CBCT (Large FOV)</td>
<td>84</td>
<td>Pauwels et al., 2012b</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ludlow et al., 2015</td>
</tr>
<tr>
<td>i-Cat Next Generation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dentoalveolar CBCT (Medium FOV)</td>
<td>45</td>
<td>Pauwels et al., 2012a</td>
</tr>
<tr>
<td>i-Cat Next Generation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Small FOV)</td>
<td>31.6–69</td>
<td>Ludlow and Walker, 2013</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Davies et al., 2012</td>
</tr>
</tbody>
</table>

FOV – field of view.
Conceptual framework

As in any medical therapy, orthodontic treatment exposes patients to certain risks. A conceptual framework for evaluating these risks was introduced by Wishney (2017), and it suggests that orthodontic treatment inevitably produces a biological challenge to the stomatognathic system. The outcome of this challenge depends on treatment and patient related factors (Wishney, 2017).

Risks of orthodontic tooth movement in subjects with periodontal disease

Orthodontic treatment for subjects with periodontal disease possesses the same risks as for periodontally healthy subjects: 1) loss of soft tissue attachment, 2) loss of alveolar bone and 3) external root resorption. These risks are important, as they could lead to a reduced amount of root in the remaining alveolar bone, compromised crown-to-root ratio, permanent tooth mobility and risk of tooth loss (Levander and Malmgren, 2000, Bellamy et al., 2008).

Patient related factors

There is no possibility of changing age related or genetic factors (such as patient susceptibility); however, oral hygiene has a huge impact on periodontal health and is modifiable (Wishney, 2017). Animal studies have shown that control of inflammation during orthodontic treatment in patients with reduced periodontium is considered of great importance because it helps to avoid further attachment loss (Melsen et al., 1988).

Treatment related factors

Control of inflammation through removal of sub-gingival plaque and deposits is essential for subjects with plaque-induced periodontal disease (Needleman et al., 2015). Appliance type, the nature of the force systems and mechanics used during the treatment, and the duration of the treatment are important treatment related factors which may affect the outcomes of orthodontic treatment (Wishney, 2017). Certain orthodontic tooth movements have been described as impacting changes in alveolar bone levels, induction of external root resorption and development of gingival
recessions in periodontally healthy patients (Weltman et al., 2010, Lund et al., 2012a, Nayak Krishna et al., 2013, Renkema et al., 2013).

The ideal orthodontic treatment requires the application of forces capable of achieving tooth movement combined with minimum damage to the root, the periodontal ligament, and the alveolar bone (Antoun et al., 2017). Minimizing this damage is particularly important for patients with reduced attachment levels. Forces of low magnitude are less risky for external apical root resorption (Iwasaki et al., 2000, Weltman et al., 2010). Forces of greater magnitude often used in orthodontic treatment do not necessarily produce more efficient tooth movement. They may overload the periodontal tissues and cause biological reactions, such as ischemia and hyalinization of the periodontal ligament that will hinder tooth movement and cause external root resorption (Ren et al., 2004, Melsen, 2001, Harris et al., 2006). However, in a recent review, authors were not able to reach a conclusion about the most appropriate level of force, even though a positive correlation was found between increased force levels and increased root resorption, as well as between increased treatment time and increased root resorption (Roscoe et al., 2015). Light continuous forces have been described as having a better effect on the cell biology of tooth movements, minimizing hyalinization and indirect resorption of alveolar bone, avoiding the repeated interruptions occurring when the blood vessels are occluded and minimizing risk for further bone loss to individuals with decreased osseous support (Mavreas, 2008).
Rationale

As people become older, physiological changes in the body, including changes in the structures of the lower face and oral cavity, occur (Kanasi et al., 2016, Ebersole et al., 2016). One of them is an increased rate of periodontal disease, which affects periodontal structures around the teeth. Periodontal disease aetiology is multifactorial, with the most important factor being bacterial dysbiosis. In susceptible patients, the disease may start at any age and is determined by the host’s immune response to plaque bacteria. Knight et al. (2016) hypothesised that there are cyclic patterns of disease, with periods of disease progression and periods of more stable status of periodontal tissues (Knight et al., 2016).

If not treated, the disease may progress and lead to the loss of attachment and formation of periodontal pockets and finally end in multiple tooth loss.

Instruction in and development of good personal oral hygiene habits are very important for this group of patients. Periodontal treatment following improved oral hygiene is of major importance. However, as a consequence of disease progression, attachment loss and subsequent periodontal treatment, teeth become elongated, the roots of the teeth become disclosed, leading to worsened smile aesthetics (Donos et al., 2012). Occlusal changes, including proclination, overeruption and spacing of anterior teeth are also often encountered (Greenstein et al., 2008). These aesthetic reasons usually lead patients to seek orthodontic help.

In this thesis, the effects, benefits and risks of periodontal-orthodontic treatment on periodontal status in patients with periodontal disease is explored and described in terms of changes in clinical parameters. In addition, radiographic changes of root lengths and alveolar bone levels during orthodontic treatment are presented.

The knowledge presented in this thesis could be applicable in future development of periodontal – orthodontic treatment protocols.
Aims

Overall aim

The overall aim of this thesis was to explore the effects, risks and benefits of periodontal-orthodontic treatment on periodontal tissues in subjects with periodontal disease in terms of clinical and radiographic changes.

Specific aims

I. In a systematic review, to identify data on possible effects of orthodontic treatment on periodontal status in subjects with periodontal disease.

II. To compare the effect of orthodontic tooth movement on periodontal status in periodontitis-susceptible subjects when periodontal treatment was performed before or simultaneous with orthodontic treatment and to evaluate differences in treatment duration.

III. To examine the extent of EARR in periodontitis-susceptible subjects after orthodontic treatment and to analyse how intrusion and change in inclination of the most proclined maxillary incisors influence root resorption.

IV. To examine the alveolar bone level change after orthodontic treatment using CBCT in periodontitis-susceptible subjects and to analyse how intrusion and change in inclination of the most proclined maxillary incisors influence alveolar bone level changes.
Hypotheses

I. No evidence-based studies are available on the effect of orthodontic therapy in patients with chronic periodontitis.

II. No statistically significant difference can be demonstrated between the test and control groups assessing clinical attachment level change after periodontal-orthodontic treatment.

III. The root length of most teeth is reduced after orthodontic treatment in subjects with periodontal disease.

IV. Alveolar bone levels are reduced after orthodontic treatment in subjects with periodontal disease.
Material and methods

The thesis is based on four papers. Study 1 is a systematic literature review. Study 2 is a randomized clinical trial (RCT) on the effect of two periodontal treatment timing strategies in combination with orthodontic treatment on clinical periodontal parameters. Studies 3 and 4 are quantitative radiographic studies on the effect of periodontal-orthodontic treatment on root length and alveolar bone level changes. The methods are described in each paper and briefly summarized in Table 2.

Study 1

In this study, a systematic literature review, based on the PRISMA statement was performed (Liberati et al., 2009). A protocol describing population, intervention, comparison and outcome (PICO) was developed (Richardson et al., 1995). The review was limited to studies on combined periodontal – orthodontic treatment of adult patients with periodontal disease.

Types of participants: Only studies on treatment of adult patients with periodontal disease were included. Types of intervention: We limited the review to studies that assess changes in periodontal tissues when periodontal-orthodontic treatment was administered in patients with periodontitis. Comparison: Outcomes of periodontal parameters in subjects with periodontitis, who received various orthodontic interventions, were compared with that in periodontally healthy subjects. Outcome measures: Changes in periodontal pocket depth (PPD), clinical crown height (CCH), alveolar bone level (ABL), and external apical root resorption (EARR) when periodontal-orthodontic treatment was performed.

Literature search strategy

A librarian at the Lithuanian University of Health Sciences assisted in developing a search strategy. A detailed search (the 1965–June 2014 period) was conducted using the PubMed, MEDLINE, and Cochrane Library Central databases.

Manual searching of reference lists of selected articles was also performed.

*Eligibility criteria:* Randomized controlled trials (RCT), controlled clinical trials (CCT), prospective and retrospective cohort studies and case series with >5 patients and articles written in English.

*Search terms* included: alveolar bone loss, orthodontic, tooth movement, tooth migration, periodontitis, orthodontic intrusion, and orthodontic extrusion.

**Methodological quality assessment**

Methodological quality assessment was performed using *Newcastle-Ottawa quality assessment scale* (NOS scale) for case-control and cohort studies (Wells et al., 2001). The *star* system was applied to each study.

- Selection (i.e. study groups that represented periodontal disease parameters and control groups without periodontally involved adults): maximum of 4 stars.
- Comparability (comparability of cases and controls as per the study design or analysis): maximum of 2 stars.
- Exposure of interest (i.e. changes in periodontal parameters): maximum of 3 stars.
- Statistical analysis: maximum of 2 stars.

Studies with 9–11 stars were considered to have high methodological quality; 6–8 stars, medium quality; and less than 6 stars, low quality.

Methodological quality for RCTs was assessed as described in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins JPT, 2008).
**Table 2.** Design, study sample, data collection and main findings of the studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Sample</th>
<th>Data collection</th>
<th>Main findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A systematic literature review</td>
<td>Adult patients with periodontal disease</td>
<td>PubMed, MEDLINE and Cochrane Library Central; Journal of Periodontology; Periodontology 2000; Journal of Clinical Periodontology; American Journal of Orthodontics and Dentofacial Orthopedics; Angle Orthodontist; International Journal of Periodontics and Restorative Dentistry; European Journal of Orthodontics</td>
<td>RCT n=1, CCT n=1, clinical studies n=12. No evidence from controlled studies and randomized controlled clinical trials which shows that orthodontic treatment improves or aggravates the status of periodontally compromised dentition currently exists.</td>
</tr>
<tr>
<td>2</td>
<td>Randomized clinical trial</td>
<td>Adult patients n=50 with periodontal disease Test (T): n=25 patients (PT simultaneous with OT) Control (C): n=25 patients (PT before OT)</td>
<td>Clinical examination at baseline (T0) Before orthodontic treatment (T1) After orthodontic treatment (T2) Clinical attachment level (CAL) Pocket depth (PD) Recession (REC) Bleeding on probing (BoP) Visible plaque index (VPI)</td>
<td>Both groups showed a gain of CAL and a reduction of sites with PD ≥4mm. Anterior teeth had a greater chance for PD improvement ≥2mm than posterior teeth. Total treatment was significantly longer for the control group. OT simultaneously with the PT could be used in the routine treatment of patients with periodontal disease.</td>
</tr>
<tr>
<td>3</td>
<td>CBCT study</td>
<td>Adult patients n=50 with periodontal disease (same as study 2)</td>
<td>CBCT examination of root lengths at T1 and T2 Intrusion and inclination angle of the most proclined maxillary incisor.</td>
<td>EARR was found in 81% of all single-rooted teeth. In 18%, EARR was &gt;2 mm. Severe EARR was found in 8% of patients and &lt;1% of treated teeth. Intrusion and change in inclination angle of the most proclined maxillary central incisor influenced the extent of EARR, as did longer OT.</td>
</tr>
<tr>
<td>4</td>
<td>CBCT study</td>
<td>Adult patients n=50 with periodontal disease (same as study 2)</td>
<td>CBCT examination of ABL at T1 and T2. Buccal (B), lingual (L), mesial (M) and distal (D) surfaces.</td>
<td>ABL gain was found on 16% of tooth surfaces, more on M and D. ABL loss was found on 15% of tooth surfaces, more on B and L. Bone levels remained unchanged on 69% of surfaces. Intrusion and retroclination influenced ABL changes after OT of the most proclined maxillary incisors.</td>
</tr>
</tbody>
</table>

RCT – randomized clinical trial; CCT – controlled clinical trial; PT – periodontal treatment; OT – orthodontic treatment; EARR – external apical root resorption; ABL – alveolar bone level; T0 – baseline; T1 – before orthodontic treatment, T2 – after orthodontic treatment; M – mesial, D – distal, B – buccal, L – lingual.
Study 2-4

Subjects

Patients with periodontal disease experience who were consecutively attending the Department of Dental and Oral Pathology at Lithuanian University of Health Sciences and two private clinics were assessed for eligibility to undergo periodontal-orthodontic treatment. Occlusion, function and aesthetics were evaluated for all individuals. Patients having malocclusion were offered periodontal-orthodontic treatment and subsequently consulted by the orthodontist. Eligible patients according to inclusion and exclusion criteria were invited for the trial (Table 3). The patient selection period lasted from 2010 to 2015.

All subjects included in the trial were examined by cone beam computed tomography (CBCT) before (T1) and after (T2) orthodontic treatment for external apical root resorption (EARR) and alveolar bone level (ABL) change.

Table 3. Inclusion and exclusion criteria.

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;25 years of age;</td>
<td>systemic disease (e.g. diabetes) or medication that would influence treatment;</td>
</tr>
<tr>
<td>good general health status;</td>
<td>periodontal treatment in the previous 2 years;</td>
</tr>
<tr>
<td>a minimum of 6 anterior teeth present;</td>
<td>pregnant or lactating women;</td>
</tr>
<tr>
<td>periodontitis experience and marginal bone loss at ≥3 teeth and more than 1/3 of the root length (assessed by panoramic radiographs);</td>
<td>smokers (&gt;5 cigarettes/day);</td>
</tr>
<tr>
<td>≥3 teeth with BoP, PD ≥4 mm and CAL ≥4 mm (assessed by clinical examination);</td>
<td>failure to comply to oral hygiene instructions or/and to keep to regular study appointments.</td>
</tr>
<tr>
<td>malocclusion, that needs orthodontic treatment.</td>
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</tbody>
</table>

Settings

The clinical study (Study 2) was conducted at the Faculty of Odontology, Medical Academy, Lithuanian University of Health Sciences (LUHS) and two private clinics in Kaunas, Lithuania.

Periodontal treatment of study patients was performed in the Department of Dental and Oral Pathology at LUHS and different private clinics.
Orthodontic treatment of study patients was performed in the Department of Orthodontics at LUHS and two private clinics.

Radiologic measurements (Study 3 and 4) were performed in the Department of Oral and Maxillofacial Radiology at Sahlgrenska Academy, Institute of Odontology, University of Gothenburg, Gothenburg, Sweden.

**Randomization (Study 2)**

After consultation and baseline examination, eligible patients were offered the combined periodontal-orthodontic treatment, including fixed orthodontic appliances. Those who consented to undergo such treatment were randomized according to a computer generated randomization list (SPSS Inc, 20.0, Chicago, IL). Patients were randomly assigned according to the timing of periodontal treatment into either intervention test group (periodontal treatment simultaneous with orthodontic treatment) or control group (periodontal treatment before orthodontic treatment) (Figure 11). All patients were numbered consecutively.

Clinicians and patients were not blinded due to the design of this research.

**Test group**

Twenty-five patients started orthodontic treatment with conventional straight-wire mechanics directly after professional oral hygiene treatment. Micro screws or temporary crowns on implants were used for anchorage if needed (Figure 12). Non-surgical periodontal treatment was performed after orthodontic alignment and levelling phases had been finished. Subsequent modified Widman flap surgery was performed in sites showing probing depth (PD) ≥6 mm that bled on probing.

**Control group**

Twenty-five patients received cause related periodontal treatment including nonsurgical periodontal treatment and subsequent modified Widman flap surgery in sites showing PD ≥6 mm that bled on probing, before orthodontic treatment. Orthodontic treatment was applied as in test group (Figure 12).
Replacement criteria

Patients who dropped out from the study (n=2) were replaced by additional patients, but not later than January 2015.

**Figure 11.** Flow chart of trial subjects.
Randomized (n=50)

**TEST group (n=25)**
- Oral hygiene instruction
- POH (supra- and subgingival debridement)
- Re-evaluation (after 2 weeks)
- Additional POH (if BoP >30%)

**CONTROL group (n=25)**
- Oral hygiene instruction
- POH (supra- and subgingival debridement)
- Re-evaluation (after 2 weeks)

**Periodontal treatment**
- No treatment
- Non-surgical therapy
- Re-evaluation (3 months)
- Modified Widman flap surgery
  (for sites PD > 6mm with BoP)

**Orthodontic treatment**
- Started: directly after POH
- Mechanics: Conventional straight-wire
- Anchorage: Micro-screws or implants (as needed)
- Started: 3-6 months after periodontal treatment.
- Mechanics: Conventional straight-wire
- Anchorage: Micro-screws or implants (as needed)

**Periodontal treatment during orthodontic treatment**
- Non-surgical therapy
- Re-evaluation (3 months)
- Modified Widman flap surgery
  (for sites PD > 6mm with BoP)
- Supportive periodontal treatment: POH 3-6 months
- Supportive periodontal treatment: POH 3-6 months

POH—professional oral hygiene; BoP—bleeding on probing; PD—pocket depth.

**Figure 12.** Flow chart of trial procedures.
**Periodontal treatment**

Initial treatment – Professional oral hygiene

All study patients received oral hygiene instructions (OHI) and professional oral hygiene treatment (POH) following baseline examination by a dental hygienist. POH treatment included supra- and sub-gingival debridement by ultrasonic instrumentation supplemented with hand instruments. The result was assessed after 2 weeks (Figure 12).

For the test group patients, in cases with BoP >30% POH was repeated.

Also, for the test group patients, OHI and POH was repeated during the alignment and leveling phases according to individual needs.

**Periodontal treatment**

Non-surgical periodontal therapy was performed under local anaesthesia by an experienced periodontologist at different time points for test (after alignment and levelling phases) and control (before orthodontic treatment) patients. Treatment was scheduled in four weekly visits. Patients had to rinse with a 0.12% chlorhexidine solution twice daily during this phase.

**Periodontal surgery**

Modified Widman flap surgery was scheduled and performed in sites showing PD \(\geq 6\) mm that bled on probing, following non-surgical treatment at the 3-month follow-up visit. All patients were prescribed mouth rinsing with a 0.12% chlorhexidine solution twice daily during the surgical phase and for two weeks following surgery (American Academy of Periodontology, 2011).

No antibiotics were prescribed for the additional effect of periodontal treatment. However, antibiotics in Lithuania are easily accessible and often used to treat other diseases as in many parts of the world.

The application of active orthodontic forces for the test group was postponed 2–4 weeks after periodontal surgery.
Supportive periodontal treatment

Assessment of periodontal conditions, including periodontal probing and oral hygiene was performed continuously for patients in both groups by the orthodontist (EZ). Thereafter, if needed, oral hygiene was re instructed and nonsurgical periodontal treatment was repeated.

POH was continuously maintained at 3–6 month intervals by a dental hygienist during OT. All treatments are shown in Figure 12.

Orthodontic treatment

Orthodontic treatment (OT) with straight wire appliance was performed in the Orthodontic Department of LUHS and two private clinics by the author.

Good personal oral hygiene with a full-mouth plaque score <25% was assured before the start of OT (Lang and Tonetti, 2003). Monthly to six-week appointments were scheduled throughout the OT course.

After baseline examination and POH treatment, the decision was made about the teeth that needed to be moved in each patient. This depended on the number of teeth present, the severity of malocclusion of each patient, planned/existing neighbouring implants and/or prosthetic restorations.

Self-ligating brackets with MBT (McLaughlin, Bennett, Trevisi), prescription (3M Unitek Orthodontic Products; Monrovia, CA, USA) and 0.022-inch slot were used. Aesthetic brackets (Clarity™ SL) were used for the maxillary anterior teeth to fulfil the aesthetic requirements of the trial patients according to individual needs. Initial levelling and alignment were performed using round, nitinol heat-activated archwires (3M Unitek Orthodontic Products; Monrovia, CA, USA). Space closure was performed using rectangular or round stainless steel wires.

The interdental enamel reduction technique was used in crowded cases where needed (Figure 13: A, B, C). For intrusion, different heights of bracket positioning was used (Figure 13: D, E, F). Intrusion and retroclination of maxillary and/or mandibular anterior teeth was provided in flared incisor cases. Posterior anchorage, where needed, was ensured with micro-screws or temporary crowns on implants (Figure 13: G-L).

Lingual fixed stainless steel soft retainer wire (Bond-a-Braid, Reliance Orthodontic Products, Illinois, USA) for maxillary and mandibular anterior teeth was applied for all patients following active orthodontic treatment (Figure 14). Hawley or vacuum formed retainers were provided for nighttime for unlimited period of time.

Figure 14. A – before orthodontic treatment; B – lingual fixed retainer after orthodontic treatment.
Radiographic evaluation

Study 2

The majority of patients had available panoramic radiographs on referral for orthodontic treatment. The patients who did not have any radiographs were examined with CBCT directly to minimize radiation exposure.

Study 3 and 4

All participants were examined before (T1) and after (T2) orthodontic treatment (T2) using a cone beam computed tomography (CBCT) Next Generation i-CAT scanner (Imaging Sciences International Inc., Hatfield, PA) and the following exposure parameter settings: small field of view (FOV) 6 cm (height) × 16 cm (width), 120 kVp, 3–8 mA, a single 360-degree rotation with acquisition time 26.9s and voxel resolution of 0.2–0.25 mm.

FOV (6 cm) was limited to the area of interest to avoid unnecessary exposure of the patient to radiation (Figure 15).

Primary data reconstructions were made providing tomographic images in axial, sagittal and coronal planes. Contiguous 0.25 mm axial slices were exported using DICOM format for later viewing and reformatting using third-party software. Secondary data reconstruction and reformatting was made using OsiriX MD (Pixmeo® SARL, Bernex, Switzerland). Utilizing a slice thickness and interval of 0.2 mm, reformatting was conducted so that the long axis of the tooth/root became parallel to the axes of the two corresponding perpendicular, vertical image planes, and thus provided optimal visualization of the tooth/root in the axial, coronal, and sagittal planes (Figure 16).

Tomographic images were analysed using a 20-inch flat panel TFT LCD display (Apple Cinema Display, Apple, Cupertino, CA, USA) with screen resolution 1680 × 1050 (Intel Iris Graphics card 6100 1536MB-graphic). Image filters were set to normal and only brightness and contrast were adjusted. The radiographic analyses were made in a dimly lit room and without time restrictions by a maxillofacial radiologist who performed all of the measurements (T1 and T2) in a blinded manner at different time points in order to avoid measurement bias.
Measurement error for assessment of root length and alveolar bone level (ABL) was calculated in an earlier research study by the maxillofacial radiologist (Lund et al., 2010). Measurement errors between repeated measurements for EARR ranged from 0.19–0.32 mm and for distance CEJ-ABL varied between 0.16 and 0.31 mm at baseline and between 0.24 and 0.29 mm at the study end point, depending on the tooth surface.

**Figure 15.** Small field of view (FOV): 6 cm (height) × 16 cm (width) used in the study.

**Figure 16.** Reformatting according to the long axis of the tooth/root, in order to achieve optimal visualization in the corresponding perpendicular axial (A), coronal (B) and sagittal (C) planes.
**Measurements**

**Study 2**

Clinical measurements for every trial patient were performed around each tooth with a manual periodontal probe (Hu-Friedy PCP-UNC 15, Chicago, IL, USA) at four sites per tooth: mesial (M), buccal (B), distal (D) and lingual (L). Periodontal assessments were performed only for teeth that were orthodontically moved.

**Time points:**
- T0: Baseline examination.
- T1: Pre-orthodontic examination.
- T2: Post-orthodontic examination (study end point).

Measurements included: visible plaque index (VPI), bleeding on probing (BoP), pocket depth (PD), gingival recession (REC), clinical attachment level (CAL) (Table 4). Only the deepest measurement was recorded. To decrease measurement bias of the clinical parameters, every clinical examination was recorded on a separate record form at every time point.

Calibration of the examiner (author) for clinical measurements was performed twice (with 1 year interval) during the experimental period.

For inter-class agreement, probing in the same half of the mouth was recorded for 3 patients by the periodontologist and orthodontist. Examiners were blinded to each other. CAL at four sites (B-L-M-D) of 30 teeth was examined. A total of 120 repeated measurements were evaluated.

For intra-class agreement the repeated measurements of the author were made twice at the same visit with 30-minute intervals.

The analysis showed high inter-class agreement (0.95; 95% CI: 0.92, 0.96; \( p = 0.0001 \)) and intra-class agreement (0.93; 95% CI: 0.87, 0.95; \( p = 0.0001 \)).
Study 3 (Root length)

Measurements included: Root length (RL), vertical distance (VD), and inclination angle (IA) (Table 4).

Root length (RL): measurement along the long axis of the root, from the reference line (bucco-palatal/lingual CEJ) to the apex, was performed for every orthodontically treated tooth at T1 and T2 (Figure 17: A). Multi-rooted teeth, and teeth with no clear CEJ reference, were excluded (crowns, cervical fillings or other artefacts).

Vertical distance (VD): measurement from a point on the reference line (bucco–palatal/lingual CEJ) to a point on the reference line between the anterior nasal spine (ANS) and posterior nasal spine (PNS) (Figure 17: B). Assessment was made on the most buccally positioned (proclined) maxillary central incisor.

Inclination angle (IA): measurement of the angle between the ANS–PNS reference line and the long axis of the root, for the most buccally positioned (proclined) maxillary central incisor, before and after orthodontic treatment (Figure 17: C).

Study 4 (Alveolar bone level)

Buccal (B) and palatal/lingual (L) alveolar bone levels (ABL) were measured using the sagittal (for anterior teeth) or frontal image plane (for posterior teeth) (Figure 18: A, C). Measurements of the distance from the reference line (bucco-palatal/lingual CEJ) to the buccal and palatal/lingual ABL crest, respectively, were performed.

Mesial (M) and distal (D) ABL were measured using the frontal (for anterior teeth) or sagittal image plane (for posterior teeth) (Figure 18: B, D). Measurement from the reference line (mesio-distal CEJ) to the mesial and distal ABL crest were performed respectively.

ABL measurements were performed for every orthodontically treated tooth at T1 and T2, excluding teeth with no clear CEJ reference due to artifacts (Table 4).
**Outcome variables**

**Study 2**

Gain in CAL was chosen as the primary response variable to judge the effectiveness of the combined treatment (Page and DeRouen, 1992, Savage et al., 2009). Secondary outcomes included: (i) PD reduction; (ii) REC development, (iii) treatment duration.

**Study 3**

The outcome variable was external apical root resorption (EARR): difference in root length (RL) before and after OT (T1–T2).

Intrusion (IN): difference in vertical distance (VD) (T1–T2).

Change in inclination angle: difference in inclination angle (IA) (T1–T2).

**Study 4**

The outcome variable was the change of ABL in relation to CEJ from before to after the orthodontic treatment (T1-T2).

Measurements and outcomes for Study 2, 3 & 4 are summarized in Table 4.
Table 4. Measurements and outcomes in Study 2, 3 and 4.

<table>
<thead>
<tr>
<th>CLINICAL MEASUREMENTS</th>
<th>CBCT MEASUREMENTS</th>
<th>CBCT MEASUREMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-L-M-D</td>
<td>B-L-M-D</td>
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</table>

<table>
<thead>
<tr>
<th>Visible plaque index (VPI)</th>
<th>Root length (RL)</th>
<th>Alveolar bone level (ABL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding on probing (BoP)</td>
<td>Vertical distance (VD)</td>
<td>ABL buccal (B)</td>
</tr>
<tr>
<td>Pocket depth (PD)</td>
<td>Inclination angle (IA)</td>
<td>ABL palatal/lingual (L)</td>
</tr>
<tr>
<td>Gingival recession (REC)</td>
<td>ABL mesial (M)</td>
<td></td>
</tr>
<tr>
<td>Clinical attachment level (CAL)</td>
<td>ABL distal (D)</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>OUTCOMES</th>
<th>OUTCOMES</th>
<th>OUTCOMES</th>
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<tbody>
<tr>
<td>T0-T1, T1-T2, T0-T2</td>
<td>T1-T2</td>
<td>T1-T2</td>
</tr>
</tbody>
</table>

**Changes:**
- CAL change (sites ≥4 mm)
- PD change (sites ≥4 mm)
- REC development (≥1 mm)

<table>
<thead>
<tr>
<th>Change of CAL and PD class:</th>
<th>Change of ABL group:</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4 mm</td>
<td>&lt;3 mm</td>
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<tr>
<td>4–6 mm</td>
<td>3–6 mm</td>
</tr>
<tr>
<td>&gt;6 mm</td>
<td>&gt;6 mm</td>
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</tbody>
</table>

- Proclined maxillary incisor:
  - External apical root resorption (EARR)
  - Intrusion
  - Change in inclination angle

Figure 17. A: Root length (RL): measurement along the long axis of tooth/root, from the reference line at the buccal–palatal/lingual cementoenamel junction (CEJ) to the apex. Measurement in sagittal plane; B: vertical distance (VD): measurement along the long axis of tooth/root, from the reference line at the buccal–palatal CEJ to the ANS–PNS reference line; C: inclination angle (IA): measurement of the angle between the anterior nasal spine (ANS)–posterior nasal spine (PNS) reference line and the long axis of the root on the most buccally positioned (proclined) maxillary central incisor.

Figure 18. Measurement of buccal and palatal/lingual alveolar bone level (ABL) from reference line at cemento-enamel junction (CEJ) to alveolar bone crest, using a sagital image plane for the anterior teeth (A) and a frontal image plane for posterior teeth (C). Measurement of mesial and distal alveolar bone level (ABL) from reference line at cemento-enamel junction (CEJ) to alveolar bone crest, using a frontal image plane for the anterior teeth (B) and a sagittal image plane for posterior teeth (D).
Statistical analysis

Sample size calculation (Study 2)

Sample size calculation was performed for the clinical part of the study.

The clinical question of this trial was whether periodontal treatment simultaneous with orthodontic treatment will have a mean of 1 mm less effect on CAL change than periodontal treatment prior to orthodontic treatment. This difference was based on the literature where periodontal-orthodontic treatment of periodontally involved teeth resulted in higher amounts of CAL gain (Cardaropoli et al., 2001, Corrente et al., 2003).

Therefore, a difference of CAL of 1.0 mm between the test and control groups was considered to be of clinical importance (Graziani et al., 2017). To be able to detect a clinically meaningful difference in mean CAL of 1.0 mm between groups, standard deviation of 1.0 mm, with a power of 90% and an alpha-level at 0.05, 22 patients were needed in each group (Goodson et al., 2012).

To compensate for dropouts, 25 patients were recruited in each group.

As the original sample size calculation was based on the change of clinical attachment level in two periodontal treatment strategies, the same sample size was also used for data analysis in Studies 3 and 4.
Statistical method

Study 1

Due to high heterogeneity of included studies, no statistical analysis could be performed.

Study 2-4

Statistical data analysis was performed using SPSS 20.0 program package (SPSS Inc, Chicago, IL). The Shapiro-Wilk test was used to test every data set for normality. Statistical analyses to compare two independent variables were conducted using Student’s t test or a Mann-Whitney U test. A Wilcoxon signed-ranks test was used for dependent variables. A chi-square test was used to compare the proportions of categorical variables between the groups. To determine correlation between variables, Spearman’s coefficient was used. Logistic regression analysis was performed to determine odds ratio (OR) predictive values.

For the assessment of reproducibility of measurements (Study 2) the interclass correlation coefficient (ICC) and consistency type was used. Intraclass reproducibility was also calculated based on absolute agreement type. In all analyses a p-value less than 0.05 was considered statistically significant.
Ethical considerations

This study was performed according to the Declaration of Helsinki guidelines (World Medical Association, 2005). Approval by the Regional Ethical Review Board, Kaunas, Lithuania, was obtained (Nr. BE-2-6). All patients signed informed consent to undergo periodontal-orthodontic treatment and radiographic examinations.

A printed letter of information with detailed information about the investigation, as well as benefits and possible risks, was provided to potential participants. The information had additionally been presented by the principal investigator (EZ) at the first visit with the possibility of discussing possible questions before the active periodontal-orthodontic treatment was begun. The principal investigator guaranteed the welfare of the research subjects. The strategy to discontinue orthodontic treatment was discussed in case of development of side effects such as progressive root resorption or loss of soft tissue attachment.

The voluntary basis of participation in the study was emphasized and patients were assured that they could withdraw from the study at any time without any personal consequences and that their individual anonymity was being guaranteed.

Appointments in the evening were offered if daytime was inconvenient in order to ensure fairness in the opportunity to participate.

An attempt was made to ascertain the reason for failure to keep appointments. Patients were informed that their continued cooperation in attending all appointments was necessary. Patients who failed to appear for one or more evaluation visits were rescheduled as early as possible with notation made in the patient records.

The three fundamental ethical principles of respect for persons, distributive justice and beneficence/non-maleficence were applied as far as possible (International Ethical Guidelines for Biomedical Research, 2002). Given the professional responsibility of beneficence “to serve the patient’s best interests”, each radiation exposure was clinically justified. The minimum radiation exposure needed to optimize diagnostic benefit and to follow the “as low as reasonably achievable” (ALARA) principle was used (American Dental Association, 2012).
Results

Study 1

Figure 19 illustrates the search process. The search strategy resulted in 1820 article titles. After screening titles and removing duplicates, 1726 titles were excluded, and 94 studies were selected for further evaluation. Abstracts of the selected 94 studies were evaluated and 13 studies were selected as relevant for the review. Three additional studies were identified after manual search of reference lists. Full texts of the 16 relevant studies were retrieved. After reading these 16 articles, two studies were excluded due to (i) unclear information about applied periodontal and orthodontic therapies and (ii) lack of relevant, measured periodontal parameters. The Khorsand et al. (2013) study was also excluded because only aggressive periodontitis cases were studied (Khorsand et al., 2013, Panwar et al., 2014).

Fourteen full-text articles were included for final evaluation (Figure 20).

One of the 14 studies described periodontal changes when treating patients with removable orthodontic appliances. The remaining 13 studies used fixed orthodontic appliances. Eleven of the 14 studies investigated periodontal and orthodontic treatment of anterior teeth for pathologic migration and marginal bone loss.

**Timing of periodontal interventions**

Periodontal surgery was performed before orthodontic treatment (three of these studies used GTR) in 10 clinical studies. In two studies corrective periodontal surgery was performed after orthodontic treatment. No description of periodontal interventions was found in one study.

**Orthodontic movements**

Intrusion of maxillary incisors was the most common orthodontic movement (investigated in 8 of the 14 studies). Figure 20 illustrates all kinds of orthodontic movements analysed in included studies.
Figure 19. Search-and-analysis process and results (n) from each stage.
Figure 20. Description of studies included in the review and orthodontic movements used.

Table 5. Methodological quality of studies included in the review.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Selection</th>
<th>Comparability</th>
<th>Exposure</th>
<th>Statistics</th>
<th>Sum</th>
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<tbody>
<tr>
<td>Eliasson et al., 1982</td>
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<tr>
<td>Artun et al., 1988</td>
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<td>Melsen et al., 1989</td>
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<td>Melsen, 2001</td>
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<tr>
<td>Cardaropoli et al., 2001</td>
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<td>4</td>
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<tr>
<td>Corrente et al., 2003</td>
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<td>Ghezzi et al., 2008</td>
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<tr>
<td>Attia et al., 2012</td>
<td>**</td>
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<td>4</td>
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</table>
Outcomes (clinical parameters)

Significant improvement in periodontal status was found in 11 of the 14 studies. Two studies reported both, deterioration and improvement of periodontal status in different sites.

Orthodontic uprighting of periodontally involved molars (one study) resulted in 50% worsening of furcation defects, which was associated with extrusion, heavy forces and periodontal inflammation.

Outcomes (mesial and distal alveolar bone level)

Nine studies reported changes in alveolar bone level (ABL) on mesial and distal surfaces. ABL gain was found in eight studies (two of them also reported ABL loss), while one study reported ABL loss (molars).

ABL improvement was reported differently: sites in treated teeth, teeth in patients, bone fill in particular bone defects. Reported deterioration in ABL ranged from 10% to 35% per site.

Adverse effects

Adverse effects of orthodontic treatment such as EARR were reported in only two studies; one of them used intrusion, the other bodily movement (Artun and Urbye, 1988, Melsen et al., 1989).

Assessment of included studies

All 13 clinical studies were judged to have low methodological quality (Table 5).

Due to the level of heterogeneity of methodology of the included studies, it was impossible to run a meta-analysis.
Study 2, 3 and 4

Of 117 patients originally referred and consulted for eligibility for the study, 38 individuals declined to participate, while 26 were not eligible for the study due to exclusion criteria (no periodontitis, smoking, systemic diseases), and three for other reasons (living abroad) (See Figure 11).

Finally, the 50 patients eligible for the study were randomly assigned to the two treatment groups.

The prerequisite for participation to the study was development of meticulous personal oral hygiene.

Baseline data

Fifty patients with periodontal disease, 15 men (30%) and 35 women (70%), with a mean age of 45.4 years (95% CI: 42.6–48.22) were enrolled in the study and started combined periodontal-orthodontic treatment.

The majority of included patients showed reduced posterior height of the occlusion with proclined anterior teeth. Most of them had spacing in the upper and/or lower teeth and/or over-eruption of incisors. Nineteen (38%) patients had flared maxillary incisors.

Root length measurements were performed on 742 (74.3%) of the 999 teeth; 257 (25.7%) teeth were excluded: 195 (19.5%) were multi-rooted, and 62 (6.2%) had artifacts, crowns, fillings or other reasons why it was not possible to identify the cement-enamel junction (CEJ). Finally, root lengths of 742 (74.3%) single-rooted teeth were analysed.

For ABL measurements one patient (control group) was excluded due to artifacts in the CBCT examination. 999 teeth and 3996 (100%) surfaces were analysed; 175 (4.4%) surfaces were excluded due to difficulties in detecting the cemento-enamel junction (CEJ). The following reasons for exclusion were registered: 54 (1.4%) due to crowns, and 121 (3.0%) due to artifacts, fillings, abfractions or other reasons. Finally, alveolar bone measurements were performed on 3821 (95.6%) surfaces.

There were no significant differences at baseline between the test and control treatment groups (p>0.05) (Table 6).
Table 6. Comparison of the patients in the test and control groups for registered variables at baseline.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Test n=25</th>
<th>Control n=25</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) Mean (SE)</td>
<td>47.3 (1.62)</td>
<td>43.5 (2.27)</td>
<td>0.2</td>
</tr>
<tr>
<td>Sex n (%)</td>
<td>16 (64%) women 9 (36%) men</td>
<td>19 (76%) women 6 (24%) men</td>
<td>0.4</td>
</tr>
<tr>
<td>Smokers ≤5 cig/day n (%)</td>
<td>1 (0.04)</td>
<td>1 (0.04)</td>
<td></td>
</tr>
<tr>
<td>Orthodontic treatment time (months) Mean (SD)</td>
<td>20.3 (6.12)</td>
<td>21.2 (4.39)</td>
<td>0.6</td>
</tr>
<tr>
<td>Teeth for ortho tx (n) Mean (SD)</td>
<td>19.2 (5.48)</td>
<td>20.8 (5.76)</td>
<td>0.3</td>
</tr>
<tr>
<td>Teeth for ortho tx. Total (n)</td>
<td>479</td>
<td>520</td>
<td></td>
</tr>
<tr>
<td>Maxillary incisors (n)</td>
<td>90</td>
<td>95</td>
<td></td>
</tr>
<tr>
<td>Maxillary canines (n)</td>
<td>45</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>Maxillary premolars (n)</td>
<td>59</td>
<td>66</td>
<td></td>
</tr>
<tr>
<td>Maxillary molars (n)</td>
<td>41</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>Mandibular incisors (n)</td>
<td>87</td>
<td>94</td>
<td></td>
</tr>
<tr>
<td>Mandibular canines (n)</td>
<td>46</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>Mandibular premolars (n)</td>
<td>72</td>
<td>83</td>
<td></td>
</tr>
<tr>
<td>Mandibular molars (n)</td>
<td>39</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>Teeth with PD ≥4 mm (n) Mean (SD)</td>
<td>13.2 (5.70)</td>
<td>15.8 (5.96)</td>
<td>0.1</td>
</tr>
<tr>
<td>Treated both arches: n (%)</td>
<td>21 (84)</td>
<td>23 (92)</td>
<td></td>
</tr>
<tr>
<td>Treated mandibular arch: n (%)</td>
<td>2 (8)</td>
<td>1 (4)</td>
<td>0.4</td>
</tr>
<tr>
<td>Treated maxillary arch: n (%)</td>
<td>2 (8)</td>
<td>1 (4)</td>
<td></td>
</tr>
<tr>
<td>Dental malocclusion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angle I</td>
<td>11</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Angle II</td>
<td>10</td>
<td>10</td>
<td>0.7</td>
</tr>
<tr>
<td>Angle III</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Normal overbite^ (n)</td>
<td>14</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Deep overbite (n)</td>
<td>9</td>
<td>11</td>
<td>0.1</td>
</tr>
<tr>
<td>Open/edge-to-edge bite (n)</td>
<td>2</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Posterior tooth loss, patients (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No loss</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Lost 1</td>
<td>3</td>
<td>3</td>
<td>0.2</td>
</tr>
<tr>
<td>Lost 2</td>
<td>1</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Lost &gt;2</td>
<td>18</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Patients with prosthetic bridges (n)</td>
<td>6</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>1 Quadrant</td>
<td>0</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>2 Quadrants</td>
<td>2</td>
<td>2</td>
<td>0.4</td>
</tr>
<tr>
<td>3 Quadrants</td>
<td>4</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>4 Quadrants</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>% sites PD &lt;4 mm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>69.4 (54.8, 76.4)</td>
<td>51.8 (40.7, 66.5)</td>
<td>0.1</td>
</tr>
<tr>
<td>Min–Max</td>
<td>22.9–85.5</td>
<td>17.9–90.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Median (Q1, Q3)</td>
<td>Min–Max</td>
<td></td>
</tr>
<tr>
<td>----------------------</td>
<td>----------------</td>
<td>----------</td>
<td>-----</td>
</tr>
<tr>
<td><strong>% sites PD 4–6mm</strong></td>
<td></td>
<td></td>
<td>0.1</td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>26.4 (19.8, 33.7)</td>
<td>13.2 – 70.2</td>
<td>40.9 (26.8, 50.0)</td>
</tr>
<tr>
<td>Min–Max</td>
<td>13.2 – 70.2</td>
<td></td>
<td>40.9 – 73.8</td>
</tr>
<tr>
<td><strong>% sites PD &gt;6 mm</strong></td>
<td></td>
<td></td>
<td>0.8</td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>3.6 (1.1, 6.7)</td>
<td>0 – 22.0</td>
<td>4.0 (1.0, 8.7)</td>
</tr>
<tr>
<td>Min–Max</td>
<td>0 – 22.0</td>
<td></td>
<td>4.0 – 33.9</td>
</tr>
</tbody>
</table>

PD of sites ≥4 mm (mm)
Mean (95% CI) 4.99 (4.77, 5.22) 4.97 (4.80, 5.15) 0.9
CAL of sites ≥4 mm (mm)
Mean (95% CI) 5.28 (5.07, 5.49) 5.24 (5.02, 5.47) 0.6
REC of sites ≥1mm (mm)
Mean (95% CI) 1.57 (1.27, 1.86) 1.53 (1.24, 1.82) 0.9

Patients (n) with % sites PD ≥4 mm
<10 0 1
10–20 3 2
20–30 6 2 0.6
>30 16 20

CBCT analyzed teeth for EARR (n)
Maxillary incisors (n) 355 93
Maxillary canines (n) 43 39
Maxillary premolars (n) 34 42
Maxillary molars (n) 0 1
Mandibular incisors (n) 84 93
Mandibular canines (n) 40 45
Mandibular premolars (n) 66 74
Mandibular molars (n) 0 0

CBCT analyzed surfaces for ABL
Total (n) 1853 1968
Buccal (n) 462 495
Lingual (n) 465 495
Mesial (n) 463 490
Distal (n) 463 488

Surfaces excluded ABL (n) 63 112

% sites ABL <3 mm
Mean (SD) 23.1 (13.2) 22.1 (16.0) 0.5
Median (Q1, Q3) 23.9 (12.5, 32.7) 17.6 (8.8, 30.6)
Min–Max 0–52.2 1.6–58.3

% sites ABL 3–6 mm
Mean (SD) 55.0 (9.7) 54.0 (12.5) 0.9
Median (Q1, Q3) 54.0 (47.6, 63.2) 55.2 (44.7, 64.4)
Min–Max 38.1–70.5 25.0–73.9

% sites ABL >6 mm
Mean (SD) 22.0 (12.8) 24.0 (14.5) 0.8
Median (Q1, Q3) 20.0 (11.6, 29.9) 17.9 (15.1, 32.0)
Min–Max 6.5–59.5 9.9–59.4

Ortho tx – orthodontic treatment CAL – clinical attachment level; PD – probing depth; Q1, Q3 – interquartile range; EARR – external apical root resorption; ABL – alveolar bone level; CBCT – cone beam computed tomography; p – value by Mann-Whitney U test or Chi Square test. ^ Normal overbite – vertical overbite up to 50% of lower incisors.
Study 2

Clinical attachment level (CAL)

Median CAL change was 0.4 mm (Q1, Q3: 0.19, 0.61). No difference in CAL change was found between the group in which orthodontic treatment (OT) was performed simultaneously with periodontal treatment (test group patients) or after it (control group patients). Twenty-two (88%) patients in every group resulted in CAL gain (Table 7).

No difference in percentage of sites with CAL gain was found between test and control groups. The values are presented in Table 7.

Pocket depth (PD)

A significant difference between the test and control group patients was found in median percentage of sites that changed to the lower disease group for PD (p=0.03). This difference was observed in sites with baseline PD of 4-6 mm, which after combined treatment became <4 mm (Table 8).

Tooth level analysis of PD change from T0 to T2 showed no significant difference between different teeth and was mean 2.72 mm (SD 1.25 mm).

Univariate binary logistic regression analysis revealed a statistically significant association between PD improvement ≥2 mm and tooth group (anterior/posterior) [OR 2.6; 95% CI: 2.03, 3.21, p=0.001], sex [OR 1.7; 95% CI: 1.29, 2.12, p=0.001], and age group (≤35 / >35 yrs) [OR 1.4; 95% CI: 1.03, 1.78, p=0.03]. Analysis showed multicollinearity between sex and age group (r=0.33, p<0.001).

Multivariate binary logistic regression analysis (overall percentage of the model 72.8%) revealed a higher odds ratio for PD improvement by ≥2 mm for anterior teeth [OR 2.5; 95% CI: 1.97, 3.11, p=0.0001] and teeth in male patients [OR 1.6; 95% CI: 1.18, 1.97, p=0.001].
**Gingival recession (REC)**

No difference in percentage of sites with recession >1 mm (REC) was found between patients in whom OT was performed simultaneously with PT (test patients) (median 10.9%, Q1, Q3: 1.3, 20.5) or after PT (control patients) (median 20.2, Q1, Q3: 5.3, 40.0) (p = 0.2).

**Treatment duration**

(T0-T2)

Total periodontal-orthodontic treatment duration was significantly longer for the control group with mean time difference found of 4.05 (SD 1.59) months (p=0.01).

(T0-T1)

There was a significant difference in mean duration of the pre-orthodontic treatment phase between the test (1.4 months (SD 0.88) and control (4.6 months (SD 1.75)) groups (p<0.0001).

(T1-T2)

Mean orthodontic treatment duration was 20.7 months (SD 5.29). No significant difference was found between mean treatment time in the test (20.3 months; SD 6.12) and control (21.2 months; SD 4.39) groups (p = 0.57).

**Study 3-4**

**External apical root resorption (EARR)**

EARR after orthodontic treatment (OT) was observed in a median of 80.7% (Q1, Q3: 68.0, 90.0, range 40–100%) of all CBCT-measured single-rooted teeth in the 50 patients, with a mean value of 1.2 mm (95% CI: 1.06, 1.31). There was no difference in mean value of EARR between test (1.1 mm, 95% CI: 0.94, 1.27) and control groups (1.3 mm, 95% CI: 1.07, 1.46) (p=0.19). Also no difference was found between median percentage of teeth with EARR between test and control patients (Table 7).
Tooth level analysis yielded that 82.3% of teeth had EARR ≤2 mm and 17.7% of teeth had EARR of >2 mm.

A positive correlation was found between mean EARR per subject and OT duration \( (r = 0.33, p = 0.02) \). Mean EARR was significantly higher \( (1.3 \text{ mm}; 95\% \text{ CI}: 1.13, 1.41) \) in subjects where OT lasted >18 months in comparison with treatment lasting ≤18 months \( (1.0 \text{ mm}; 95\% \text{ CI}: 0.70, 1.21) \) \( (p = 0.02) \).

**Alveolar bone level (ABL)**

No difference between mean ABL at T1 \( (4.66 \text{ mm, CI: } 4.41, 4.90) \) and at T2 \( (4.60 \text{ mm, CI: } 4.38, 4.82) \) was observed and no significant mean ABL change \( (0.06 \text{ mm, CI: } -0.07, 0.19) \) could be found after OT \( (p=0.35) \).

Mean ABL for test patients \( (n = 25) \) at T1 was 4.60 mm \( (\text{CI: } 4.26, 4.94) \), and at T2 was 4.58 mm \( (\text{CI: } 4.30, 4.86) \) \( (p = 0.87) \). Mean ABL at T1 for the control group \( (n = 24) \) was 4.72 mm \( (95\% \text{ CI: } 4.34, 5.10) \), and at T2 was 4.61 mm \( (\text{CI: } 4.25, 4.97) \) \( (p = 0.22) \). No significant difference in mean ABL change was observed between the test \( (\text{mean } 0.02 \text{ mm, } 95\% \text{ CI: } -0.19, 0.22) \) and control \( (0.11 \text{ mm, } 95\% \text{ CI: } -0.07, 0.28) \) group patients \( (p = 0.49) \).

A mean 15.6 % \( (\text{SD 7.4, median 13.9, IQR: 10.2, 22.7 mm}) \) of surfaces with ABL gain was observed after OT. However a similar mean percentage of surfaces \( (15.1 \%, \text{SD 7.5, median 13.8, IQR: 8.8, 21.4 mm}) \) was found with ABL loss. ABL remained unchanged in a mean of 69.3 % \( (\text{SD 8.8, median 69.3, IQR: 64.2, 75.0 mm}) \) of surfaces. These changes were similar in test and control group patients (Table 7).

Significant ABL change was observed on mesial \( (\text{mean } 0.26 \text{ mm, SD 0.50, median 0.16, IQR: -0.09 to 0.42}) \) and distal \( (\text{mean } 0.26 \text{ mm, SD 0.45, median 0.15, IQR: -0.05 to 0.59}) \), surfaces of orthodontically treated teeth, where slight ABL gain was observed \( (p<0.001) \). In contrast, tendency to ABL loss on buccal \( (-0.16 \text{ mm, SD 0.89, median 0.02, IQR: -0.43 to 0.37}) \) and lingual \( (-0.11 \text{ mm, SD 0.70, median -0.06, IQR: -0.57 to 0.34}) \) surfaces was found, but the change was not statistically significant \( (p>0.05) \).

Patient and tooth level analysis of changes of surfaces with different ABL after orthodontic treatment, are presented in Tables 9 and 10.
**Adverse effects**

Five (0.9%) of 585 teeth in four (8%) patients, three maxillary central and two lateral incisors (2.8% of all incisors), ended with severe apical root resorption of >4 mm after OT.

External root resorption in the middle third of the root was observed in 3 (6%) of 50 patients, and in 3 (0.4%) of 742 teeth analysed with CBCT. Of those, a severe external defect towards the pulp was found in one maxillary central incisor (Figure 4, Study 3).

Severe ABL loss (>6 mm) with baseline normal ABL (<3 mm) was observed more on buccal (1.9%) and lingual (1.3%) surfaces than on mesial (0.4%) and distal (0.4%), on different groups of teeth, and only in a mean of 1% of all surfaces (Table 10).
Table 7. Comparison main findings between test and control group patients before (T0) to after (T2) periodontal-orthodontic treatment.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Test patients</th>
<th>Control patients</th>
<th>p* value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=25</td>
<td>n=25</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T0</td>
<td>T2</td>
<td>T0</td>
</tr>
<tr>
<td><strong>CAL (mm) (sites ≥4 mm)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (95% CI)</td>
<td>5.28 (5.07, 5.49)</td>
<td>4.85 (4.67, 5.01)</td>
<td>5.24 (5.02, 5.47)</td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>5.18 (4.85; 5.64)</td>
<td>4.83 (4.49; 5.11)</td>
<td>5.15 (4.84; 5.58)</td>
</tr>
<tr>
<td>Min–Max</td>
<td>4.61–6.39</td>
<td>4.18–5.78</td>
<td>4.51–6.75</td>
</tr>
<tr>
<td>CAL CHANGE (mm) (sites ≥4 mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (95% CI)</td>
<td>0.44 (0.25, 0.62)</td>
<td>0.38 (0.18, 0.58)</td>
<td></td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>0.40 (0.20, 0.59)</td>
<td>0.49 (0.12, 0.62)</td>
<td></td>
</tr>
<tr>
<td>Min–Max</td>
<td>-0.47 to 1.84</td>
<td>-1.34 to 1.02</td>
<td></td>
</tr>
<tr>
<td>CAL LOSS (mm) (sites ≥4 mm)</td>
<td>n=3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>-0.21</td>
<td>-0.58</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>-0.14</td>
<td>-0.35</td>
<td></td>
</tr>
<tr>
<td>Min–Max</td>
<td>-0.47 to 0.02</td>
<td>-1.34 to 0.06</td>
<td></td>
</tr>
<tr>
<td>CAL GAIN (mm) (sites ≥4 mm)</td>
<td>n=22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (95% CI)</td>
<td>0.51 (0.38; 0.64)</td>
<td>0.52 (0.35; 0.70)</td>
<td></td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>0.50 (0.32; 0.66)</td>
<td>0.42 (0.27; 0.67)</td>
<td></td>
</tr>
<tr>
<td>Min–Max</td>
<td>0.08–1.2</td>
<td>0.08–1.84</td>
<td></td>
</tr>
<tr>
<td><strong>CAL NO CHANGE (%) sites</strong></td>
<td>n=22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>76.9 (71.1–82.9)</td>
<td>73.2 (67.9–80.9)</td>
<td></td>
</tr>
<tr>
<td><strong>CAL GAIN (%) sites</strong></td>
<td>n=22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>23.2 (15.3–28.0)</td>
<td>25.0 (18.1–30.7)</td>
<td></td>
</tr>
</tbody>
</table>

*p* values for comparison of test and control group patients before and after periodontal-orthodontic treatment.
<table>
<thead>
<tr>
<th>CAL LOSS (% sites)</th>
<th>Median (Q1, Q3)</th>
<th>0 (0–1.3)</th>
<th>1 (0–2.2)</th>
<th>0.1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teeth with EARR %</td>
<td>Mean (95% CI)</td>
<td>77.8 (72.34, 83.35)</td>
<td>80.2 (73.50, 86.91)</td>
<td>0.4</td>
</tr>
<tr>
<td></td>
<td>Median (Q1, Q3)</td>
<td>80.0 (65.7, 89.5)</td>
<td>84.2 (71.3, 92.8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Min–Max</td>
<td>50–100</td>
<td>40–100</td>
<td></td>
</tr>
<tr>
<td>ABL no change (% sites)</td>
<td>Mean (SD)</td>
<td>68.4 (5.8)</td>
<td>70.2 (11.1)</td>
<td>0.4</td>
</tr>
<tr>
<td></td>
<td>Median (Q1, Q3)</td>
<td>68.5 (64.9, 72.0)</td>
<td>69.6 (63.0, 79.8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Min–Max</td>
<td>57.6–83.3</td>
<td>47.1–86.1</td>
<td></td>
</tr>
<tr>
<td>ABL gain (% sites)</td>
<td>Mean (SD)</td>
<td>16.0 (7.3)</td>
<td>15.2 (7.7)</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>Median (Q1, Q3)</td>
<td>14.3 (11.1, 22.8)</td>
<td>13.0 (9.5, 22.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Min–Max</td>
<td>4.2–29.9</td>
<td>4.3–30.4</td>
<td></td>
</tr>
<tr>
<td>ABL loss (% sites)</td>
<td>Mean (SD)</td>
<td>15.6 (7.1)</td>
<td>14.6 (8.0)</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>Median (Q1, Q3)</td>
<td>15.0 (9.3, 22.0)</td>
<td>13.3 (7.4, 20.7)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Min–Max</td>
<td>6.3–28.6</td>
<td>3.1–31.7</td>
<td></td>
</tr>
</tbody>
</table>

CAL – clinical attachment level; EARR – external apical root resorption; ABL – alveolar bone level; *Mann-Whitney U test; ** Wilcoxon Signed Ranks Test.
Table 8. Distribution of different pocket depth (PD) classes (<4 mm, 4–6 mm, >6 mm) in control (n=25) and test (n=25) patients at registrations before (T0) and after (T2) combined periodontal – orthodontic treatment. Also change of PD class from T0 to T2.

<table>
<thead>
<tr>
<th>PD (mm)</th>
<th>Group</th>
<th>T0 % sites Median (Q1–Q3)</th>
<th>T2 % sites Median (Q1–Q3)</th>
<th>T0 and T2 PD level change (mm)</th>
<th>Group</th>
<th>T0–T2 % sites Median (Q1–Q3)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4</td>
<td>Control</td>
<td>51.8 (40.6–66.5)</td>
<td>90.6 (84.1–95.7)</td>
<td>&lt;4 and &lt;4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Control</td>
<td>51.8 (40.6–66.5)</td>
<td>0.13</td>
</tr>
<tr>
<td></td>
<td>Test</td>
<td>69.4 (54.7–76.4)</td>
<td>93.8 (87.7–95.3)</td>
<td>&lt;4 and &gt;6&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Test</td>
<td>62.5 (50.5–74.0)</td>
<td>0.14</td>
</tr>
<tr>
<td>4–6</td>
<td>Control</td>
<td>40.9 (26.8–50.0)</td>
<td>9.4 (4.3–15)</td>
<td>4–6 and &lt;4&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Control</td>
<td>30.4 (18.8–45.9)</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>Test</td>
<td>26.4 (19.8–33.7)</td>
<td>6.0 (3.9–11.5)</td>
<td>4–6 and &gt;6&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Test</td>
<td>20.5 (13.6–25.5)</td>
<td>0.29</td>
</tr>
<tr>
<td>&gt;6</td>
<td>Control</td>
<td>4.0 (1.0–8.7)</td>
<td>0</td>
<td>&gt;6 and &lt;4&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Control</td>
<td>1.3 (0–5.0)</td>
<td>0.52</td>
</tr>
<tr>
<td></td>
<td>Test</td>
<td>3.6 (1.1–6.7)</td>
<td>0</td>
<td>&gt;6 and &gt;6&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Test</td>
<td>1.1 (0–2.9)</td>
<td>0.69</td>
</tr>
</tbody>
</table>

PD – pocket depth; Q1 – the first quartile; Q3 – the third quartile; Control group n=25; Test group n=25; T0 – baseline; T2 – after total treatment; *p value by Mann-Whitney U test. a – no change, b – increase, c – decrease.
Table 9. Percentage distribution and change in surfaces with different ABL before (T1) and after (T2) orthodontic treatment (patient level for all, control and test).

<table>
<thead>
<tr>
<th>Distance CEJ–ABL</th>
<th>Total n = 49</th>
<th>Control n = 24</th>
<th>Test n = 25</th>
<th>p&lt;sup&gt;i&lt;/sup&gt; value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T1</td>
<td>T2</td>
<td>T1</td>
<td>T2</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Median (Q1, Q3)</td>
<td>Mean (SD)</td>
<td>Median (Q1, Q3)</td>
</tr>
<tr>
<td>&lt;3 mm</td>
<td>22.6 (14.5)</td>
<td>22.1 (16.0)</td>
<td>19.7 (15.7)</td>
<td>23.1 (13.2)</td>
</tr>
<tr>
<td></td>
<td>20.8 (12.4, 31.3)</td>
<td>17.6 (8.8, 30.6)</td>
<td>16.1 (8.3, 24.9)</td>
<td>23.9 (12.5, 32.7)</td>
</tr>
<tr>
<td></td>
<td>0–58.3</td>
<td>2.8–67.7</td>
<td>1.6–58.3</td>
<td>3.3–67.7</td>
</tr>
<tr>
<td>Change T1–T2</td>
<td>1.5 (8.6)</td>
<td>2.4 (7.4)</td>
<td>0.6 (9.7)</td>
<td>0.73</td>
</tr>
<tr>
<td></td>
<td>0.9 (-3.6, 6.6)</td>
<td>2.9 (-3.0, 5.4)</td>
<td>-0.9 to 26.7</td>
<td>-17.9 to 16.7</td>
</tr>
<tr>
<td></td>
<td>-17.9 to 26.7</td>
<td>-9.4 to 26.7</td>
<td>-17.9 to 16.7</td>
<td></td>
</tr>
<tr>
<td>3–6 mm</td>
<td>54.5 (11.1)</td>
<td>57.8 (12.8)</td>
<td>54.0 (12.5)</td>
<td>59.2 (13.7)</td>
</tr>
<tr>
<td></td>
<td>55.6* (46.2, 63.9)</td>
<td>55.2* (44.7, 64.4)</td>
<td>59.8* (50.1, 68.9)</td>
<td>56.0 (47.6, 63.2)</td>
</tr>
<tr>
<td></td>
<td>25.0–73.9</td>
<td>25.0–82.9</td>
<td>25.0–81.3</td>
<td>38.1–70.5</td>
</tr>
<tr>
<td>Change T1–T2</td>
<td>-3.3 (8.3)</td>
<td>-5.2 (8.1)</td>
<td>-1.4 (8.2)</td>
<td>0.17</td>
</tr>
<tr>
<td></td>
<td>-4.4 (-9.1, 3.8)</td>
<td>-5.6 (-9.3, 0)</td>
<td>-1.2 (-8.3, 4.7)</td>
<td>-14.5 to 20</td>
</tr>
<tr>
<td></td>
<td>-30 to 20</td>
<td>-30 to 6.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;6 mm</td>
<td>23.0 (13.5)</td>
<td>21.1 (13.1)</td>
<td>21.2 (14.3)</td>
<td>22.0 (12.8)</td>
</tr>
<tr>
<td></td>
<td>19.3* (13.8, 31.8)</td>
<td>17.9 (15.1, 32.0)</td>
<td>16.2 (10.7, 29.0)</td>
<td>20.0 (11.6, 29.9)</td>
</tr>
<tr>
<td></td>
<td>0.9–59.5</td>
<td>2.6–52.8</td>
<td>2.6–52.8</td>
<td>6.5–59.5</td>
</tr>
<tr>
<td>Change T1–T2</td>
<td>1.8 (7.4)</td>
<td>2.8 (7.4)</td>
<td>0.8 (7.4)</td>
<td>0.50</td>
</tr>
<tr>
<td></td>
<td>1.7 (-4.3, 6.5)</td>
<td>1.3 (-1.4, 6.0)</td>
<td>2.2 (-5.0, 7.3)</td>
<td>-12.6 to 14.6</td>
</tr>
<tr>
<td></td>
<td>-12.6 to 18.5</td>
<td>-9.8 to 18.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p <0.01, T1–T2 by Wilcoxon test; p<sup>i</sup> significance between control and test patients by Mann–Whitney U test; ABL – alveolar bone level; CEJ – cemento-enamel junction.
Table 10. Change of ABL group (<3, 3–6, >6 mm) T1–T2 on buccal (B), lingual (L), mesial (M), distal (D) surfaces. Comparison between bone gain or loss in different surfaces (B, L, M, D).

<table>
<thead>
<tr>
<th>Change T1 to T2</th>
<th>All CBCT measured teeth</th>
<th>B</th>
<th>L</th>
<th>M</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;3 to &lt;3</td>
<td></td>
<td>123 (12.9)</td>
<td>151 (15.7)</td>
<td>174 (18.3)</td>
<td>103 (10.8)</td>
</tr>
<tr>
<td>&lt;3 to 3–6</td>
<td></td>
<td>82 (8.6)</td>
<td>92 (9.6)</td>
<td>68 (7.1)</td>
<td>74 (7.8)</td>
</tr>
<tr>
<td>&lt;3 to &gt;6</td>
<td></td>
<td>18 (1.9)</td>
<td>12 (1.3)</td>
<td>4 (0.4)</td>
<td>4 (0.4)</td>
</tr>
<tr>
<td>3–6 to &lt;3</td>
<td></td>
<td>73 (7.6)</td>
<td>63 (6.6)</td>
<td>63 (6.6)</td>
<td>60 (6.3)</td>
</tr>
<tr>
<td>3–6 to 3–6</td>
<td></td>
<td>441 (46.1)</td>
<td>384 (40.0)</td>
<td>366 (38.4)</td>
<td>418 (44.0)</td>
</tr>
<tr>
<td>3–6 to &gt;6</td>
<td></td>
<td>67 (7.0)</td>
<td>82 (8.5)</td>
<td>34 (3.6)</td>
<td>35 (3.7)</td>
</tr>
<tr>
<td>&gt;6 to &lt;3</td>
<td></td>
<td>8 (0.8)</td>
<td>8 (0.8)</td>
<td>7 (0.7)</td>
<td>6 (0.6)</td>
</tr>
<tr>
<td>&gt;6 to 3–6</td>
<td></td>
<td>61 (6.4)</td>
<td>70 (7.3)</td>
<td>87 (9.1)</td>
<td>74 (7.8)</td>
</tr>
<tr>
<td>&gt;6 to &gt;6</td>
<td></td>
<td>84 (8.8)</td>
<td>98 (10.2)</td>
<td>150 (15.7)</td>
<td>177 (18.6)</td>
</tr>
<tr>
<td>No Change</td>
<td></td>
<td>648 (67.7)</td>
<td>633 (65.9)</td>
<td>690 (72.4)</td>
<td>698 (73.4)</td>
</tr>
<tr>
<td>Bone gain</td>
<td></td>
<td>142 (14.8)</td>
<td>141 (14.7)</td>
<td>157 (16.5)</td>
<td>140 (14.7)</td>
</tr>
<tr>
<td>Bone loss</td>
<td></td>
<td>167 (17.5)\textsuperscript{ab}</td>
<td>186 (19.4)\textsuperscript{cd}</td>
<td>106 (11.1)\textsuperscript{ac}</td>
<td>113 (11.9)\textsuperscript{bd}</td>
</tr>
</tbody>
</table>

\textsuperscript{abcd} \textit{p} <0.001 by chi-square test: \textit{a} = comparison B–M, \textit{b} = comparison B–D, \textit{c} = comparison L–M, \textit{d} = comparison L–D.
Orthodontic movements of the most proclined maxillary incisors (Studies 3-4)

Intrusion

The influence of orthodontic intrusion on EARR of the most proclined maxillary central incisors was analysed. The measurements of 46 maxillary central incisors were evaluated. Three patients were excluded from this analysis because only the lower jaws were treated and one patient was excluded due to difficulties in detecting CEJ following crown restoration.

Intrusion of the most proclined maxillary incisor was performed in 39 of 46 patients with a median intrusion of 1.6 mm (Q1, Q3: 0.8, 2.3, range 0.1–7.3 mm).

External apical root resorption (EARR)

Median EARR of intruded maxillary incisors (n=39) was 1.4 mm (IQR: 0.6, 2.0, range 0–5.1). In comparison the median EARR of non-intruded maxillary incisors (n=7) was 0.4 mm (Q1, Q3: 0.06, 1.30, range 0–1.5) (p=0.04).

A positive correlation was found between EARR of the most proclined maxillary central incisor and intrusion (r = 0.51, p<0.001).

The median value of EARR of maxillary central incisors was increasing with the increasing amount of intrusion. With intrusion of >0–1 mm, mean EARR of the most proclined maxillary central incisors was 0.8 mm; this value was significantly smaller than for the other intrusion groups (Table 11).

Intrusion values of maxillary central incisors (n=39) were grouped by the median value of 1.6 mm. A significant difference was found between mean EARR values in the two intrusion groups (p=0.02), Figure 21.
Alveolar bone level (ABL) change

A significant difference was found in the median value of ABL change of intruded (0.54 mm, IQR: 0.07, 1.01; n=39) versus not intruded (-0.42 mm, IQR -0.85, 0.22, n=7) maxillary incisors (p=0.04).

Surface analysis yielded that ABL was significantly changed on the lingual (median 0.56 mm, IQR: -0.45 to 1.55, p=0.02), on the mesial (median 0.65 mm, IQR: -0.18 to 1.90, p=0.005) and on the distal surface (median 0.34 mm, IQR: -0.31 to 1.16, p=0.01) of the most proclined maxillary incisor, which was intruded (n=39). In contrary no significant ABL change from T1-T2 was found in incisors, which were not intruded (n=7).

Furthermore, if intrusion was >1.6 mm (n=18), significant lingual ABL gain was observed (median 1.38 mm, IQR: 0.01 to 2.12) in comparison to intrusion ≤1.6 mm (n=21) (median -0.02, IQR -0.87 to 0.89, p=0.01). Differences in ABL changes in different surfaces are presented in Figure 22.

Table 11. External apical root resorption (EARR) of the most proclined maxillary central incisor, with different amounts of intrusion.

<table>
<thead>
<tr>
<th>Intrusion group</th>
<th>n</th>
<th>Mean EARR (mm)</th>
<th>SD (mm)</th>
<th>Median EARR (mm)</th>
<th>Min (mm)</th>
<th>Max (mm)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No intrusion</td>
<td>7</td>
<td>0.57</td>
<td>0.59</td>
<td>0.40</td>
<td>0</td>
<td>1.50</td>
<td></td>
</tr>
<tr>
<td>&gt;0–1 mm</td>
<td>14</td>
<td>0.80</td>
<td>0.64</td>
<td>0.75</td>
<td>0</td>
<td>2.10</td>
<td>0.03</td>
</tr>
<tr>
<td>&gt;1–2 mm</td>
<td>15</td>
<td>1.54</td>
<td>1.01</td>
<td>1.50</td>
<td>0</td>
<td>3.20</td>
<td></td>
</tr>
<tr>
<td>&gt;2–3 mm</td>
<td>5</td>
<td>2.19</td>
<td>1.65</td>
<td>1.50</td>
<td>0.90</td>
<td>5.05</td>
<td></td>
</tr>
<tr>
<td>&gt;3–5 mm</td>
<td>3</td>
<td>2.52</td>
<td>2.21</td>
<td>1.80</td>
<td>0.75</td>
<td>5.00</td>
<td></td>
</tr>
<tr>
<td>&gt;5 mm</td>
<td>2</td>
<td>2.75</td>
<td>0.78</td>
<td>2.75</td>
<td>2.20</td>
<td>3.30</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>46</td>
<td>1.35</td>
<td>1.19</td>
<td>1.27</td>
<td>0</td>
<td>5.05</td>
<td></td>
</tr>
</tbody>
</table>

*Significance by Mann-Whitney U test.
Figure 21. Mean values for external apical root resorption (EARR) of the most proclined maxillary central incisor, in different groups of intrusion and change in inclination angle. Grouping was based on the median values of each variable.
Figure 22. Alveolar bone level change (mm) of the most proclined maxillary incisor in different groups of intrusion.

**Change of inclination of maxillary central incisor**

Nineteen (38%) patients had flared maxillary incisors and the need for retraction in pre-treatment evaluation. A positive correlation was found between EARR and change in inclination angle of the most proclined maxillary incisor ($r = 0.35$, $p = 0.017$). Fourteen incisors were retroclined $>8.6^\circ$, 15 incisors were retroclined $\leq 8.6^\circ$ (median value of retroclination) and 17 were proclined.
External apical root resorption (EARR)

A significant difference was found in EARR of the most proclined maxillary incisors in two retroclination groups. A significantly higher mean EARR was observed, if incisors were retroclined >8.6° (n=14) in comparison to retroclination ≤8.6° (n=15), p=0.02, or proclination (p=0.04) (Figure 21). No difference in EARR was found between retroclined ≤8.6° and proclined teeth.

Alveolar bone level (ABL) change

Results revealed a difference of lingual ABL between T1 and T2 when teeth were retroclined >8.6 degrees during OT. Mean lingual ABL at T1 was 6.5 mm (SD 1.88, median 6.4 mm, Q1, Q3: 4.80, 7.95) and at T2 was 5.5 mm (SD 2.08, median 5.2 mm, Q1, Q3: 4.54, 5.48) (p=0.01). Significant ABL gain on the lingual surface of most proclined maxillary incisors, which were retroclined >8.6 degrees was found after orthodontic treatment with mean 1.03 mm (SD 1.14, median 1.08, Q1, Q3: -0.10 to 1.83), (Figure 23).

![Figure 23. Alveolar bone level change (mm) of the most proclined maxillary incisor in 3 groups of change of inclination angle.](image-url)
Discussion

This thesis presents a comprehensive evaluation of periodontal-orthodontic treatment outcomes on periodontal tissues in a group of adult patients with periodontal disease. Orthodontic treatment is more often included in the multidisciplinary treatment of patients with periodontal disease due to impaired smile aesthetics, functional problems or as adjunctive treatment prior to prosthetic rehabilitation. These patients have teeth with attachment loss, pathologic migration of anterior teeth, decreased posterior occlusion and worsened smile aesthetics (Johal and Ide, 1999, Brunsvold, 2005). Orthodontic therapy is sometimes the only choice for the conservative rehabilitation of occlusion, function and patients’ aesthetics (Sanz and Martin, 2015, Melsen, 2016). However, for many patients it seems like a long and time-consuming procedure to first undergo periodontal treatment and after that to start orthodontic treatment.

It has to be respected that orthodontic treatment may produce certain biological risks, which have been found to be dependent on patient and treatment related factors (Wishney, 2017).

Therefore, the aim of the present thesis was to evaluate the effects of periodontal-orthodontic treatment, including benefits and adverse events in periodontal tissues in patients with periodontal disease, and to analyse related factors.

Methodological considerations

The strength of evidence was important; therefore it was decided to perform a systematic literature review (Study 1) in order to identify scientific evidence of orthodontic treatment on periodontal status in subjects with periodontal disease prior to the clinical trial (Dhar, 2016). In contrast to earlier reviews (van Gastel et al., 2007, Bollen, 2008), the present review was limited to studies on combined periodontal-orthodontic treatment of adult patients with periodontal disease.
As 12 of the included articles were clinical studies, the methodological quality assessment was performed using the Newcastle-Ottawa quality assessment scale (NOS scale) for case-control and cohort studies (Wells et al., 2001). Low methodological quality of included studies was found.

The clinical project (Studies 2-4) was designed as a randomized controlled trial (RCT), which aimed to evaluate benefits and risks of orthodontic treatment on periodontal tissues when two different timing strategies of periodontal treatment (before or simultaneous) were applied in combination with orthodontic treatment for patients with periodontal disease. The rationale was to shorten overall treatment time for a patient, to start immediate orthodontic treatment after POH due to complains of impaired function and aesthetics and to perform final periodontal treatment under better healing conditions (without traumatic occlusal interferences) (Harrel and Nunn, 2009).

Periodontal inflammation has been found to result as a consequence of the imbalance of dysbiotic periodontal microbiota and the host (Hajishengallis, 2014). Therefore the outcome of both periodontal treatment and orthodontic tooth movement in subjects with periodontal disease is dependent on some treatment related and patient related factors.

**Data collection**

In the beginning of data collection, it was thought to collect patients with Angle class II malocclusions. Even though, all patients, who had periodontal pathology and had a need for orthodontic treatment, were included. After half a year, sample size was evaluated and consisted of patients with all different malocclusions, different numbers of teeth with periodontitis and alveolar bone loss. Therefore, it was decided to proceed including all patients with a need of periodontal-orthodontic rehabilitation of occlusion, despite the numbers of teeth or existing malocclusions. This would represent periodontal patients in an orthodontic practice. Patients were referred by the periodontologists after introduction of the project in the local research conferences and lectures within the university (LUHS) in Kaunas.

The main difficulty in the present project was to collect the adequate number of adult patients who would consent to orthodontic treatment.
Sample

Sample size calculation yielded that 22 patients were needed in each group. It was decided to include 50 patients to compensate for dropouts, if needed. The selection period lasted 5 years. Two patients dropped out from the study and were replaced by the following consulted patients.

From 117 patients originally consulted, 26 were not eligible due to exclusion criteria, 3 lived abroad and were also excluded. Eligible subjects were offered combined periodontal-orthodontic treatment. 38 subjects declined participation mostly due to aesthetic reasons of fixed orthodontic appliances. The other reasons included fear of discomfort and pain.

The random allocation of subjects to test and control groups was performed. Only those, who consented to undergo orthodontic treatment, were included and randomized. Even if differences in baseline data were not significant between the two groups (Table 6), clinically some differences were present in number of sites with pocket depth and number of teeth incorporated in orthodontic appliances.

The sample consisted of selected patients, who were motivated to undergo combined periodontal-orthodontic treatment and were able to develop meticulous personal oral hygiene.

Treatment related factors (Periodontal treatment)

Oral hygiene instructions (OHI) (supra-gingival control) and professional oral hygiene (POH) treatment (sub-gingival control) to reduce microbiota and inflammation (Drisko, 2001, Needleman et al., 2015) were of key importance in the present research studies.

Sub-gingival debridement was chosen as initial periodontal therapy for both groups. It has shown to result in significant reduction in all microbial parameters and therefore reduced signs of inflammation already following 1 week (Loos et al., 1988). Reassessment was performed after 2 weeks to determine the presence of residual deposits, non-responsive areas with gingival redness and bleeding and to decide if additional POH was needed. In cases of persistent inflammation in the test group subjects, sub-gingival debridement was repeated before the start of orthodontic treatment.
Orthodontic treatment was started under controlled supra- and sub-gingival plaque (microbiota) conditions for both groups and therefore inflammation was under control. This is particularly important as both periodontal disease and orthodontic tooth movement have impact on periodontal ligament and alveolar bone (Meikle, 2006, Hajishengallis, 2014).

The main difference between the groups was that for the control subjects periodontal treatment was finished including healing of periodontal pockets. Resultant “healthy” periodontium was obtained. For the test group orthodontic treatment was instituted directly after oral hygiene treatment phase with no aim of pocket healing. It is important to underline that repeated OHI and POH treatment was performed by dental hygienist at initial levelling and alignment phases to ensure inflammation control. Non-surgical and later surgical periodontal treatment of periodontal pockets was postponed and performed after levelling and alignment phases before the active space closure and/or inter-arch mechanics was started.

Non-surgical periodontal treatment was chosen instead of immediate surgical treatment, which was performed before orthodontic treatment in earlier studies in patients with periodontal disease (Cardaropi et al., 2001, Corrente et al., 2003). It has been shown that surgical periodontal therapy had a relatively lower impact on oral health related quality of life than non-surgical periodontal treatment (Shanbhag et al., 2012) and also results with higher extent of gingival recessions. Surgical periodontal treatment in the present project was limited only for sites with residual pockets ≥6 mm (Graziani et al., 2017).

**Treatment related factors (Orthodontic treatment)**

The aim of orthodontic treatment was 1) to improve smile aesthetics through realignment and levelling of anterior teeth (especially previously migrated teeth), 2) rehabilitate posterior occlusion through realignment of migrated posterior teeth and creation of adequate spaces for restorative (implant, prosthetic) treatment where needed, 3) to reach functionally stable occlusion, however not ultimately Angle class I sagittal relationship.

Orthodontic treatment (OT) was performed with straight wire appliance, self-ligating brackets and a simple orthodontic mechanics in order to reduce plaque accumulation and facilitate personal oral hygiene (Sanz and Martin,
Round, heat-activated nitinol archwires producing low levels of force were used for levelling and alignment phases. Light forces have been associated with “direct bone resorption” and direct remodeling process in adjacent alveolar bone and more physiologic tooth movement (Sanz and Martin, 2015). However, due to reduced alveolar bone levels even light forces could result in some kind of hyalinization and external root resorption due to delayed alveolar bone resorption on the compression side and cellular activity during the removal of necrotic hyalinized tissue (Meikle, 2006).

The center of resistance of teeth with attachment loss is displaced apically, which increases risk for tipping instead of bodily movement (Sanz and Martin, 2015). In cases of posterior anchorage need micro-screws or temporary crowns on implants were used. As a result less extensive movements of posterior teeth with reduced periodontal support were needed and minimized risk for their tipping.

All patients were informed that they would need permanent fixed retention ant night-time removable retainers for unlimited period of time.

**Patient related factors**

The risks for progressive loss of soft tissue attachment and alveolar bone are very important for patients with plaque-induced periodontal disease.

To avoid patient related factors such as systemic diseases and medications, we included only subjects who were clinically healthy (Cullinan and Seymour, 2013).

There is a high prevalence of smokers in Lithuania. It is well known, that smoking (behavioural factor) has a huge impact on the progression of periodontal disease and also treatment success (Nociti et al., 2015). Therefore, smokers ≥5 cigarettes per day were excluded from the study.

However, two subjects who declared smoking up to 5 cigarettes per day were included, as association of smoking and periodontitis has been described in the literature to be dose dependent (Lang and Tonetti, 2003). This decision was done after the discussion with the subjects and their positive response to smoking-cessation, as well as motivation for the orthodontic treatment (both patients were positive to stop smoking and they managed that quickly after consultation) (Nociti et al., 2015).
There was not possible to change patient related factors, such as age and genetics (patient susceptibility), however oral hygiene has shown to have a huge impact on periodontal health and could be modifiable (Wishney, 2017). The development of self-performed personal oral hygiene has been found to be of key importance for outcomes of both nonsurgical and surgical periodontal treatments (Graziani et al., 2017, Melsen et al., 1988). Therefore patients were continuously re instructed for oral hygiene through the monthly orthodontic appointments.

**CBCT for changes in root length and ABL levels**

The length of the root(s) with remaining bony support is of major importance when studying treatment effect in dentitions with reduced alveolar bone levels (Armitage, 2004a, Corbet et al., 2009). CBCT enabled us to study changes not only in mesial and distal, but also in buccal and lingual bone. Also we were able to relate ABL changes and EARR to orthodontic movements, such as intrusion and change in inclination of maxillary incisors during orthodontic treatment.

CBCT was used for research purpose to gain knowledge about hard tissue changes during orthodontic tooth movements. All patients consented to undergo CBCT examination as a part of the project. Otherwise multiple radiographic examinations, including orthopantomograms, lateral cephalograms, supplemented with periapical radiographs should be performed as recommended in the literature (Grubb et al., 2008).

The advanced imaging technique was used due to superiority over conventional radiography in obtaining data with a high level of validity and reproducibility of the measurements (Yi et al., 2017). It is well known that intraoral periapical radiographs suffer from shortcomings related to the technique itself as a summation of an object (Brezniak et al., 2004a). Further it is well known that, due to differences in projection geometry, changed inclination of teeth, radiographic follow-up using intraoral technique reveals a low degree of reproducibility (Lund et al., 2010). Assessment of marginal bone level at buccal and/or palatal/lingual surfaces with the intraoral technique would have been impossible (de Faria Vasconcelos et al., 2012). CBCT imaging was recently recommended by American Academy of Periodontology for planning of orthodontic movements and risk assessment prior to orthodontic treatment (Mandelaris et al., 2017).
Small field of view (6 cm height and 16 cm width) for the field of interest was used to reduce the radiation and follow the ALARA principal (American Academy of Oral and Maxillofacial Radiology, 2013).

Main findings

Despite the increasing number of periodontal patients in daily orthodontic practices, the findings of systematic literature review yielded that there were no randomized controlled trials or controlled clinical trials on comprehensive orthodontic treatment in patients with periodontal disease. This led to the conclusion that no evidence exists about the effects of periodontal-orthodontic treatment on periodontal tissues in patients with periodontal disease.

The scarcity of evidence was a good rationale for the clinical studies.

The key finding of the present clinical studies was similar changes in soft and hard tissues independent of timing of periodontal treatment. In 50 patients, CAL was unchanged in majority of sites, CAL gain was observed in an average of 1/4 of sites. Similarly ABLs remained unchanged in an average of 69% of surfaces, ABL improved more in proximal surfaces (16%), ABL decreased more in buccal and lingual surfaces (15%). Root lengths were shortened in an average of 81% of orthodontically moved teeth within 50 subjects. However, majority had EARR <2 mm (82%). 18% of teeth, mostly anterior, resulted in EARR of >2 mm because of greater orthodontic movements.

One has to pay attention that the combined treatment was performed under special conditions and strict oral hygiene protocol. The close cooperation of the team of experienced oral hygienists, periodontologists and orthodontist ensured meticulous personal oral hygiene, control of sub-gingival inflammation and orthodontic movements throughout the course of combined treatment.
**Adverse effects**


In the present study severe EARR (>1/3 root) were observed only in 8% of patients and less than 1% of all teeth, mostly maxillary incisors (2.8% of all incisors) (Figure 4, Study 3). Prevalence of severe EARR in the literature has been reported to be up to 14.5% (range 1–14.5%) of orthodontically treated patients depending on calculation per tooth or per patient (Marques et al., 2010, Maues et al., 2015, Martins et al., 2012, Levander and Malmgren, 1988, Lund et al., 2012b, Levander et al., 1998, Lupi et al., 1996, Remington et al., 1989).

The results of the present study are in line with the findings in the CBCT study, where 7% of patients had ≥1 tooth with severe EARR and in total 2.6% of incisors with EARR >4mm was found (Lund et al., 2012b). The number of teeth with EARR found in the present study are less than in the study with periodontally healthy patients (Motokawa et al., 2012).

Severe ABL loss (>6 mm) with baseline normal ABL (<3 mm) was observed more on lingual and buccal sites and on 1% of all surfaces (Table 10). This phenomena could be related to orthodontic movements “out of the bone” which was also found in periodontally healthy adolescents. Severe ABL loss was observed mostly on lingual surfaces of mandibular incisors due to retroclination in premolar extraction cases (Lund et al., 2012a).

**Treatment duration**

Orthodontists and periodontologists are quite used to hear the questions of adult patients “how long the treatment will last” and discussion about long treatments. Treatment duration, especially treatment with fixed orthodontic appliances, is usually important for the adult patients. The Study 2 aimed to answer the question, if it’s possible to perform periodontal treatment simultaneous to orthodontic tooth movement and to shorten overall treatment time for a patient.

As two periodontal treatment strategies were used it is quite natural that there were differences in total periodontal–orthodontic treatment duration. Whole treatment was significantly longer for the control group with mean
time difference of 4 months. It seems to be rather short time, however for some patients it is important to initiate orthodontic treatment as soon as possible. Correction of migrated teeth is sometimes a major concern. It is interesting that patients in the control group were also eager to start orthodontic tooth movement as soon as possible due to the same reasons. Orthodontic treatment time (20.7 months) was similar for both groups and is in agreement with the findings in the literature (Tsichlaki et al., 2016). So, if treatment time is important for the patient, periodontal treatment may be performed simultaneous to orthodontic tooth movement. However, a prerequisite is subgingival control of inflammation and optimal personal plaque control over a long period of time.

**EARR and orthodontic treatment duration**

Orthodontic treatment duration was found to have influence on the amount of mean EARR. Our findings are in line with other studies where longer treatment duration was found to result in more EARR (Roscoe et al., 2015, Segal et al., 2004, Sharab et al., 2015, Apajalahti and Peltola, 2007, Maues et al., 2015). EARR is important for periodontal patients due to reduced ABL, therefore shorter orthodontic treatment should be considered.

**Orthodontic movement of the most proclined maxillary incisors**

Due to flaring and over-eruption of periodontally involved anterior teeth, intrusion and retroclination were mostly used orthodontic movements in the present study. To be able to relate these orthodontic movements to EARR and ABL changes, the values of the variables were examined on the most proclined maxillary incisor. The values of intrusion and change in inclination angle after orthodontic treatment were evaluated on CBCT images.

Intrusion and change of inclination angle were possible to measure on CBCT examinations due to identification of such anatomical landmarks as anterior (ANS) and posterior nasal spine (PNS). This was possible due to the field of view used (6×16 cm) (Figure 15). CEJ was used as a reference line to avoid influence of incisal wear or restorations during orthodontic treatment in some patients. The EARR was the measurement difference of root length before and after orthodontic treatment (Figure 17: A). Intrusion was the subtraction of T1-T2 measurements of the vertical distance (Figure 17: B).
Change of inclination angle was also subtraction of pre-treatment (T1) and post-treatment values of inclination angles (Figure 17: C).

Generally the results revealed that higher extent of incisor movements resulted in positive changes of ABL and higher amounts of EARR.

**Intrusion**

Intrusion of the most proclined maxillary incisor was performed in 39 patients. A positive correlation was found between intrusion and EARR of the most proclined maxillary central incisor. Intrusion influenced both development of EARR and improvement of ABL. It is logical that the EARR of intruded maxillary incisors was significantly higher vs. those not intruded. The values of EARR of maxillary central incisors were increasing with the increasing amount of intrusion. These results are similar to those found by Melsen et al. (1989) where all periodontally involved maxillary incisors which were intruded had EARR (Melsen et al., 1989). However, wide ranges of EARR in the present study were observed, which may be the result of combined intrusion and retroclination movements (Table 11).

When intrusion values of maxillary central incisors were grouped by the median value of 1.6 mm significant difference was found between mean EARR values in the two intrusion groups (Figure 21), suggesting that intrusion >1.6 mm results in double amount of EARR.

Intrusion was also found to influence ABL changes around the most proclined maxillary incisors. A significant difference was found in ABL change of intruded (n=39) versus not intruded teeth (n=7). More bone was gained around the incisors, which were intruded. ABL change of 0.5 mm was found after intrusion of the most proclined maxillary incisors (n=39). The surface analysis yielded that ABL level was significantly gained on the lingual, mesial and distal surfaces of the most proclined maxillary incisor, which was intruded in comparison to ABL change of the non-intruded incisor; however, a wide range was observed. These findings are contradictory to the studies where reduction of mesial and distal bone levels was found following orthodontic treatment, mainly intrusion, in periodontally healthy adults (Bellamy et al., 2008, Nelson and Artun, 1997). The authors found increased distance from CEJ to ABL of incisors and explained this by apical movement of marginal alveolar bone during
intrusion movements. The difference in changes could be explained by differences in periodontal health. There is no possibility for ABL improvement for healthy periodontal tissues; however, this is possible in teeth with previously lost alveolar bone, especially when this loss is related to previous malposition and occlusal trauma. Therefore it could be expected that periodontal treatment and repositioning of teeth in a more favourable place in the alveolar bone in some cases may result in ABL gain. However, a wide range of effects was observed (Figure 23).

It’s also interesting that >1.6 mm of intrusion in the present findings resulted in significant bone gain on the lingual surface. It may be hypothesized that alveolar bone is gained where it was mostly resorbed before. Orthodontic treatment eliminates heavy occlusal contacts, replaces migrated tooth and therefore enables bone regeneration. The illustration of this process may be seen in Figure 24.

The results of mesial bone gain in the present study could be compared to the findings observed in periapical radiographs of intruded maxillary incisors (Cardaropoli et al., 2001, Corrente et al., 2003, Melsen, 2001). The studies on segmented orthodontic treatment, mainly intrusion, in maxillary anterior teeth have been found with bone fill mesial to central incisors (Cardaropoli et al., 2001, Corrente et al., 2003). Similarly, the results in a CBCT study in periodontal patients revealed significant gain of ABL of intruded maxillary incisors. The authors studied 14 subjects with chronic periodontitis before and after orthodontic intrusion of incisors in combination with circumferential supracrestal fiberotomy.

It could be concluded that intrusion presents a risk for EARR, but may initiate gain of ABL. This would equalize the amount of the root in the alveolar bone.
Figure 24. Intraoral photographs and sagittal and frontal CBCT image views of a patient (tooth 11) that reveals reattachment of soft and hard tissues between T1 (A,C,D) and T2 (B,E,F) examinations, respectively. Note: external apical root resorption of 1.2 mm (C-E, D-F).

Change of inclination of maxillary central incisor

A positive correlation was found between EARR and change in inclination angle of the most proclined maxillary incisor

ABL gain on the lingual surface of most proclined maxillary incisors, which were retroclined >8.6 degrees, was found after orthodontic treatment with the median value of 1.08 mm. However, higher values of EARR were also observed, with the change of inclination of >8.6 degrees (Figures 21 and 22).

Intrusion and retroclination of the most proclined anterior incisors were measured in our study patients, as they were proclined and over-erupted as a result of periodontal pathology. The severity of periodontal disease and the presence of antagonistic forces were found to induce radicular resorption without history of orthodontic treatment (Crespo Vazquez et al., 2011). Periodontally healthy teeth, which have been exposed to traumatic occlusal contacts, were also described to aggravate root resorption during orthodontic treatment (Cakmak et al., 2014).
It is logical that during intrusion and retroclination of anterior teeth the highest stress is located at the apices of the root. The nature of orthodontic treatment is well known to cause sterile inflammation in the periodontium due to pressure zones in the periodontal ligament and was in the literature called “orthodontitis”. The inflammation causes surface cemental remodeling and resorption of alveolar bone. But sometimes, cemental resorption is initiated, causing shortening of the root (Brezniak and Wasserstein, 2014). The resorption of thin apex of the root usually does not significantly reduce the surface of root facing the alveolar bone. Resorbed apex has been found to have almost the same area of surface in the bone (Consolaro and Furquim, 2014). Therefore, teeth usually remain stable for long periods after orthodontic treatment (Marques et al., 2011, Brezniak and Wasserstein, 2014).

It is quite difficult to control amounts of forces, especially in periodontal patients, where tooth movements are usually very quick due to reduced resistance of pathologically resorbed supporting bone. Therefore, it should be taken into consideration when treating such patients.

In comparison to the aforementioned results in the present study, similar results of EARR were found in a study with periodontally healthy adult patients, where retraction and intrusion of anterior teeth with skeletal anchorage ended up in more pronounced EARR (Liou and Chang, 2010). Increased overjet, Class II-1 malocclusion before treatment, and retraction of maxillary anterior teeth in periodontally healthy adolescents and adults have been also described to influence the extent of EARR due to increased movement of the apex of maxillary incisor roots and the need for longer treatment (Sameshima and Sinclair, 2001, Marques et al., 2010, Tieu et al., 2014, Martins et al., 2012).

In contrast to EARR in the present study, higher degree of intrusion caused remodeling of lingual alveolar bone of the most proclined maxillary incisor. The soft tissue change on lingual surfaces of maxillary incisors was described in the study by Melsen et al. (1989) after orthodontic intrusion. In the aforementioned study, pockets of about 3 mm were found to develop in all cases localized to the lingual surface following by improvement of recession. However due to the 2D radiography, it was not possible to evaluate lingual bone level changes in that study. Results of ABL gain on the
lingual surfaces of intruded and retroclined maxillary incisors in the present study highly support the theory of “new attachment” introduced in 2001 (Melsen, 2001).

Based on the results of the present study, remodelling and regeneration of alveolar bone could be expected, mostly on mesial, distal and lingual aspects of intruded and retroclined maxillary incisors with initially reduced periodontium, caused by periodontal disease (Figure 25). The main prerequisite is healthy even if reduced periodontal tissues and excellent personal oral hygiene, which has to be monitored throughout the treatment.

As EARR of periodontally involved teeth was correlated with the extent of orthodontic movements in the present study, one should be aware of the risks of EARR before starting orthodontic treatment. This is particularly important for patients with reduced bone levels.
Figure 25. Illustration of ABL changes before and after intrusion and retraction of tooth 11 in a patient with periodontal disease: A, B – change on mesial and distal surface; C, D – change on buccal and lingual surface; G, H – change in vertical distance; J, K – change in inclination; E, F and I, L – change of occlusion and soft tissues; C, D – EARR development.
General discussion of the results

In the previous studies, surgical periodontal treatment was instituted 7–10 days before orthodontic tooth movement and it was explained that this induces cellular mitotic activity in the periodontal tissues earlier studied histologically in animals (Melsen et al., 1988, Corrente et al., 2003, Melsen, 2001). The present study resulted in CAL gain and PD reduction in both periodontal treatment strategies and suggested that final periodontal treatment may be postponed and performed during orthodontic treatment. The main clinical finding was CAL gain of 0.4 mm observed in 88% of patients in spite of periodontal treatment timing.

Favourable periodontal outcomes which were found in the present study were mostly influenced by patient cooperation with personal oral hygiene, monthly appointments, repeated sub-gingival debridgements and close cooperation between orthodontist, oral hygienist and periodontologist.

Pocket depth (PD) improvement

PD reduction of sites ≥4 mm was also observed in both treatment groups in every treatment phase. In previous studies that were performed in periodontal patients, CAL gain and PD reduction was also observed (Cardaropoli et al., 2001, Melsen et al., 1989, Re et al., 2004, Re et al., 2000).

The difference we found between the two treatment strategies was healing of sites with PD ≥4 mm (Table 4, Study 2). A higher percentage of sites healed in the control group, when periodontal treatment was performed before orthodontic tooth movements. In order to understand this phenomenon, PD was classified in three levels (<4 mm, 4–6 mm, >6 mm). The analysis showed that the difference in PD improvement was mainly in sites with baseline PD of 4–6 mm, which after combined treatment became <4mm (Table 8). A higher percentage of sites with PD 4–6 mm at T0 in the control group explained the difference in PD improvement between the test and control groups. We also think that this difference could be influenced by the method we used to classify pockets.
The pockets that initially were 6 mm could heal to 4 mm, but we could not see the improvement, as they remained in the limits of the same class. However, deep periodontal pockets (>6 mm) at T0 showed similar improvement in both groups (Table 8). Nearly half of them healed to the “healthy” status (<4 mm).

The multivariate binary logistic regression analysis on tooth level showed greater chance for PD improvement by ≥2 mm in anterior teeth. This could be explained by the fact that single rooted teeth respond better to periodontal-orthodontic treatment. It was described in earlier literature that single rooted teeth respond better to periodontal treatment alone (Tomasi et al., 2007).

Biologic mechanisms of orthodontic tooth movement in patients with periodontal disease

Professional subgingival control of inflammation, as well as meticulous personal hygiene, was ensured before and throughout the orthodontic treatment for all patients in the present study.

Orthodontic tooth movements under conditions of uncontrolled inflammation have been found to result in further loss of the connective tissue attachment and progressive resorption of alveolar bone in experimental study (Wennstrom et al., 1993). The explanation is the following: cytokines responsible for activation of osteoclasts and bone resorption (due to “sterile inflammation”) have been found to be produced in the periodontal ligament cells as a result of application of mechanical force (Thilander et al., 2018). The production of cytokines is also initiated due to periodontal inflammation in susceptible subjects (Hajishengallis, 2014). The continued inflammatory process and production of inflammatory cytokines leads to progressive loss of soft tissue attachment and alveolar bone (Hajishengallis, 2014, Mariotti, 2015).

It could be speculated that active inflammation in the periodontal tissues, as a result of the presence of plaque microbiota, in susceptible subjects may impede bone formation and/or remodelling in the pressure and tension zones during orthodontic tooth movement. This would result in progressive loss of soft tissue attachment and alveolar bone.
Radiographic findings

External apical root resorption (EARR)

EARR is described as an inevitable, well-known side effect of orthodontic treatment (Roscoe et al., 2015). The importance of studying EARR in subjects with periodontal disease is due to crown-to-root ratio changes, which may lead to unfavourable bone support of a root and permanent tooth mobility (Levander and Malmgren, 2000).

Eighty one percent of CBCT analysed teeth in 50 patients with periodontal disease were found to have some amount of EARR after orthodontic treatment. However, wide individual variation (40–100%) of EARR was observed. Root lengths of resorbed teeth were reduced by a mean of 1.3mm, which comprised approximately 10% of the mean root length. The wide range of EARR in the present study may be explained by individual genetic susceptibility to EARR (Al-Qawasmi et al., 2003). As we did not perform genetic evaluation of the study patients, we were not able to confirm this theory.

Due to scarcity of literature on 3D analysis of EARR in patients with periodontal disease, we were not able to compare our results to previous findings from studies using similar methodology. Therefore, our results were compared with periodontally healthy adults and adolescents.

EARR in the present study was not higher than in the CBCT study on adolescents without periodontal disease, where up to 91% of teeth after orthodontic treatment showed some degree of root shortening (Lund et al., 2012b). Eighteen percent of teeth were found to result in EARR >2 mm in the present study. This prevalence was counted on all CBCT analysed teeth, including upper/lower incisors, canines and premolars (n=585) and is slightly higher in comparison to the EARR >2 mm in children, which was reported to range between 11–14% of maxillary incisors on periapical radiographs (Brin et al., 2003).

The greater amount of EARR can probably be explained by the greater tooth movements (especially in anterior teeth) in periodontal patients, where flaring, over-eruption and extrusion of teeth is the main factor of malocclusion (Figure 24).
Alveolar bone level (ABL) change

Small mesial and distal ABL gain found after orthodontic treatment could be related to remodelling of bone. This bone was lost in the interproximal surfaces of previously flared teeth, which were exposed to occlusal trauma due to malpositions in the dental arches. It could be speculated that periodontal treatment and space closure creates conditions of bone regeneration due to positioning of tooth roots closer to each other in the alveolar bone.

The use of CBCT enabled us to study ABL on buccal and lingual surfaces of orthodontically treated teeth. We found that small and not significant ABL loss was present on these surfaces. These findings are in line with the studies in periodontally healthy adolescents (Lund et al., 2012a, Castro et al., 2016). Slight reduction of ABL levels on buccal and lingual surfaces during orthodontic treatment could be explained by anatomically thin alveolar bone. Buccal dehiscences and fenestrations of untreated patients have been analyzed on CBCT. It has been found that these are more prevalent in the buccal regions of mandibular anterior teeth (Patcas et al., 2012, Evangelista et al., 2010).

A significant difference in the present study was found between mean ABL levels at T1 and T2 in maxillary posterior teeth, with the tendency of ABL loss. This could be related to naturally thin alveolar bone, which has been found to be present also in maxillary posterior regions (Garib DG, 2010, Yagci et al., 2012). It was found in an earlier CBCT study on periodontally healthy patients that orthodontic treatment results in slight expansion of maxillary posterior regions and reduced bone levels on buccal surfaces (Cattaneo et al., 2011).

ABL in the present study was classified into three groups, where ABL <3 mm was considered to be physiologic for adult patients (Persson et al., 1998). ABL loss 3–6 mm was classified as moderate bone loss, and >6 mm as severe bone loss (Koong, 2015). Our results were presented as change to the lower respectively higher ABL group.

On the tooth level, the percentage of sites with bone gain was similar on each surface; however, significantly higher percentage of sites with bone loss was observed on lingual and buccal in comparison to mesial and distal
surfaces (Table 10). More than 6% of all surfaces which had moderate bone loss (3–6 mm) changed the group to normal ABL height (<3 mm) after orthodontic treatment. The results on the tooth level explain the results found in the patient level with the change of sites of different levels of ABL (Table 9).

The findings of the present studies suggest that comprehensive orthodontic treatment in combination to periodontal therapy in patients with periodontal disease results in clinical attachment level gain and pocket depth reduction. Changes in alveolar bone levels are small and not deleterious. However, development of EARR should be expected. The main prerequisite is inflammation control and meticulous personal oral hygiene, which has to be monitored throughout the treatment.

Therefore, orthodontic treatment should be carefully planned for every patient and performed by an experienced team of dental hygienist, periodontologist and orthodontist. Benefits and risks should be discussed with every patient.
Conclusions

Based on the results of this trial, it can be concluded that periodontal-orthodontic treatment under optimal conditions (experienced clinician and patient with excellent oral hygiene routines over time), if needed, could be included in the rehabilitation of patients with periodontal disease without deleterious effects.

Orthodontic treatment simultaneous with periodontal treatment could be used in the routine treatment of patients with periodontal disease. However, there are two important prerequisites: meticulous personal oral hygiene performed by the patient over time and optimal subgingival control of inflammation before the start of the combined treatment performed by an experienced clinician.

Specific conclusions

I. No evidence was found from controlled studies and RCTs that orthodontic treatment improves or aggravates the status of periodontally compromised dentitions.

II. Both treatment groups, test group (periodontal treatment simultaneous with orthodontic treatment) and control group (periodontal treatment before orthodontic treatment) of the present RCT showed gain of clinical attachment level and reduction of sites with probing depth ≥4 mm. Total periodontal–orthodontic treatment time was significantly longer for the control group.

III. Orthodontic treatment in conjunction with periodontal treatment in patients with periodontal disease resulted in external apical root resorption (EARR) in 81% of all single-rooted teeth. EARR >2 mm was found in 18% of teeth. Severe EARR (>4 mm) was found in four (8%) patients and in 5 maxillary incisors (<1% of all examined teeth).

The amount of intrusion, and change in inclination angle of the most proclined maxillary central incisor influenced the extent of EARR.
IV. Alveolar bone level (ABL) gain was found on 16% of tooth surfaces, mainly on mesial and distal, after orthodontic treatment in patients with periodontal disease. ABL loss was found on 15% of tooth surfaces, mainly on lingual and buccal. ABL remained unchanged on 69% of surfaces. Intrusion and retroclination influenced the ABL changes of the most proclined maxillary incisors.
Practical implications

As many adult patients with periodontal disease have aesthetic and functional consequences caused by malocclusions due to migration of teeth, some of them need rehabilitation of occlusion, including orthodontic treatment. This thesis has shown that orthodontic treatment, in combination with periodontal treatment, results in favourable outcomes, including soft and hard tissue changes.

Therefore, combined periodontal-orthodontic treatment may be included in the overall treatment plan of rehabilitation of the occlusion, provided periodontal health is obtained during the course of the treatment and maintained throughout the treatment.

It is safe to perform periodontal treatment simultaneous with orthodontic treatment and by this reduce the total treatment time, which is appreciated by many patients.

Follow up of the outcome needs to be studied to ensure the long-term prognosis.
Future research

Issues of interest in subjects with periodontal disease

Soft tissue as well as alveolar bone level change for particular teeth in both dental arches.

Intrusion of posterior teeth, its effect on soft tissues and alveolar bone level changes.

Change of alveolar bone in vertical bone defects.

Impact of interdental enamel reduction on soft and hard tissue changes.

Follow up of the periodontal-orthodontic treatment outcome to prove the long-term prognosis.

Patients’ experience of orthodontic treatment as a part of combined treatment of periodontal disease.
Antalet vuxna med malocklusioner och parodontal sjukdom, som söker ortodontisk behandling ökar. Därför är det viktigt att undersöka för- och nackdelar vid handläggning av individer med omfattande parodontalt och ortodontiskt behandlingsbehov.

Avhandlingen fokuserar på ortodontibehandling av vuxna individer med parodontal sjukdom.


Behandlingen av parodontal sjukdom är komplex och innefattar ofta teamarbete mellan olika professioner i tandvården.

Det övergripande syftet med denna avhandling var att undersöka effekter, risker och fördelar med parodontal-ortodontisk behandling på parodontala vävnader hos patienter med parodontal sjukdom.

En systematisk litteraturöversyn genomfördes som syftade till att utvärdera befintliga vetenskapliga evidens avseende effekterna av ortodontisk behandling på parodontala vävnader hos individer med parodontal sjukdom.

Den kliniska delen av avhandlingen utformades som en prospektiv randomiserad klinisk studie. Den syftade till att jämföra två parodontala behandlingstidsstrategier avseende effekten på parodontala vävnader av ortodontisk behandling. Femtio personer med parodontal sjukdom randomiserades antingen till test- (parodontal behandling samtidigt med ortodontisk behandling) eller kontrollgrupp (parodontal behandling före starten av ortodontisk behandling).

Initial behandling inkluderade supra- och sub-gingival hygienbehandling och utfördes på alla studiepatienter. Icke-kirurgisk och eventuell efterföljande kirurgisk parodontal behandling utfördes vid olika tidpunkter för test- och

Förändring i klinisk fästenivå (CAL) valdes som en primär utfallsvariabel.

 Alla patienter undersöks före och efter ortodontisk behandling med röntgentomografi (CBCT) för att undersöka förekomsten av extern apikal rotresorption (EARR) och förändringar i alveolära bennivåer (ABL).

Resultaten av den systematiska litteraturgranskningen visade inga randomiserade kontrollerade kliniska prövningar eller kontrollerade studier vid omfattande ortodontisk behandling hos patienter med parodontal sjukdom.

Ingen skillnad i CAL-förändring, EARR och ABL upptäcktes om ortodontisk behandling utfördes samtidigt med (testgruppssjukdom) eller efter (kontrollgrupportation) parodontal behandling. Resultaten gav en median CAL-förändring av 0.4 mm (Q1, Q3: 0.19, 0.61). Tjugo-två (88%) patienter i båda behandlingsgrupperna resulterade i CAL-vinst. CAL förblev oförändrad på i genomsnitt 3/4, CAL-vinst observerades på i genomsnitt 1/4 av tandytor.

Rotlängderna förkortades på en median av 80.7% (Q1, Q3: 68.0, 90.0) av ortodontiskt förflyttade tänder med genomsnitt EARR på 1.2 mm (SD 0.44). På dessa observerades EARR<2 mm på 82% av tänderna. Arton procent av tänderna resulterade i EARR>2 mm.

ABL-nivåer var oförändrade på ett genomsnitt av 69.3% (SD 8.8) av ytorna, ABL förbättrades på 15.6% (SD 7.4) av ytorna, mer på mesial- och distalytor. ABL minskade på 15.1% (SD 7.5) av ytorna, mer på buccal- och lingualytör.

Baserat på resultaten från denna kliniska studie kan man dra slutsatsen att parodontal-ortodontisk behandling under optimala förhållanden (erfarna tandläkare och patienter med goda munhygienrutiner över tid) kan utan skadliga effekter ingå i rehabilitering av patienter med parodontal sjukdom. Ortodontisk behandling, samtidigt med parodontal behandling, kan användas vid rutinbehandling av patienter med parodontal sjukdom. Det finns dock två viktiga förutsättningar: noggrann personlig munhygien hos patienten och optimal subgingival kontroll av inflammation före och under den kombinerade behandlingen.
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