Detection methods of orthodontically induced inflammatory root resorption (OIIRR): a review

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Background: Orthodontically induced inflammatory root resorption (OIIRR) is unwelcome iatrogenic damage associated with orthodontic treatment. Patients with a high risk of developing OIIRR are commonly monitored using radiographic techniques. Alternative, more sensitive methods using biological markers facilitate the early detection of OIIRR, which can minimise root surface damage and allow the timely cessation of orthodontic treatment in order to facilitate a reparative process.
Aim: The present review examines the current use of 2D and 3D radiographic techniques to detect and quantify OIIRR and, further, evaluates the latest literature on alternative detection methods of OIIRR.
Method: Published studies were searched electronically throughout PubMed, Scopus and ScienceDirect using keywords including 'root resorption', 'OIIRR', 'radiograph' and 'biological markers'.
Results: The detection methods for OIIRR were divided into radiographic and biological marker methods. Orthopantomogram (OPG) and periapical radiography are currently the most widely used radiographic methods to detect and monitor OIIRR as they are readily available in most dental clinics, cost effective and have a relatively low radiation dose. However, the radiographic methods are not only subject to standardisation and magnification issues, but also require repeated radiation exposure to patients. Therefore, published research into the potential for biological markers as a safer and more sensitive alternative for the early detection of OIIRR was reviewed.
Conclusion: The result of the review highlights the potential for the use of biological markers in the early detection of OIIRR as a relatively safer and more sensitive alternative to conventional radiographic methods.
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Introduction

Orthodontically-induced inflammatory root resorption (OIIRR) is defined as a complex, sterile, inflammatory process resulting from the application of forces to tooth roots, which involves bone, periodontal cells, surrounding matrix and an extensive tissue response.[1] Root damage is recognised as an inevitable side effect of orthodontic treatment and can be found in up to 91% of cases. Severe OIIRR results in tooth mobility and may subsequently jeopardise the orthodontic outcome. Hence, it may be best to pause treatment to allow root repair when OIIRR is identified. The early detection of root resorption is crucial as this process may be reversible after the removal of the associated orthodontic force.

The commonly used radiographic methods to diagnose OIIRR have their limitations related to the superimposition of structures, magnification issues, exposing patients to ionising radiation and the inability to detect early root resorption. With these constraints of the radiographic methods, researchers have suggested the use of biomarkers as possibly a more sensitive, specific and safer alternative.[2,3] Several biomarkers released during orthodontic tooth movement (OTM) such as inflammatory cytokines, osteoprotegerin (OPG) during bone metabolism and dentine sialophosphoprotein (DSPP) can be used to detect OIIRR. Sampling methods that utilise whole saliva (WS) and gingival crevicular fluid (GCF) are commonly used to isolate and detect the biomarkers.

The aim of the present study is to review the literature over the past 15 years (2004–2019) reporting the different methods used to detect root resorption during orthodontic tooth movement. The published studies were identified electronically through PubMed, Scopus, and ScienceDirect using the keywords 'root resorption', 'OIIRR', 'biological marker' and 'radiograph'. Reference lists of review articles and all included studies were checked to locate additional publications. Only studies that were reported in English and with a completed published status were included. The initial literature search identified 85 potentially relevant studies and, of these, 26 studies were selected after evaluating their titles and abstracts. The publications included 20 observational studies (six prospective; eight cross-sectional and six retrospective), four experimental studies and two review papers. Patients of all age groups were included. The methods of detection were divided into either radiographic or biological marker methods.

Prevalence

Histological studies indicated that the prevalence of OIIRR could be more than 90%[4] and radiographic detection methods varying from 44% to 91%.[5,6] Although there was no reported loss of severely resorbed teeth, longitudinal follow-up studies were few and sample sizes were limited, which may have underestimated the risk of severe root resorption. With age, it is reported that increasing mobility of those teeth with severely resorbed roots can be expected if a root length reduced to less than 10 mm.[7] However, it has also been observed that extensive root resorption does not usually affect the functional capacity or greatly compromise the longevity of the affected teeth, which may be retained for several decades.[8]

Pathophysiology

Proffit et al.[9] described the pathophysiology of root resorption during orthodontic treatment. When a heavy sustained force is applied to a tooth, the periodontal ligament (PDL) will be compressed, leading to occlusion of the blood supply and subsequently resulting in hyalinisation (sterile necrosis). Before orthodontic tooth movement can occur, the hyalinisation needs to be resolved by inflammatory cells. However, during this process, scavanging cells may also remove cementoid and mature collagen from the root surface, leaving exposed cementum that is readily attacked by odontoclastic cells. Usually the cementum will repair itself once the orthodontic force ceases, but, in cases in which the defect is large, the damage will not be replaced and sustained root resorption results.

The apical third of the root is particularly susceptible to iatrogenic damage caused by orthodontic treatment because the periapical cementum is more friable and easily injured when subjected to heavy forces and resultant vascular stasis.[10] In addition, the apical region of cementum has reduced hardness and elastic modulus compared with the cervical region, which makes the area more vulnerable to root resorption.[11]

Risk factors

It is important to identify risk factors for OIIRR in patients before commencing treatment. Patients who are identified as high-risk should be informed of the possibility of OIIRR and monitored by periodic radiographic examination. Furthermore, a predisposition to OIIRR could be affected by patient-related and orthodontic treatment-related risk factors. Patient-related risk factors consist of abnormal tooth-root morphology, a previous history of root resorption, previous trauma, and endodontic treatment, while orthodontic-related risk factors include treatment duration, premolar extraction, the magnitude of applied forces and the method of force application.[12] In contrast to patient-related variables, treatment mechanics are more relevant for the clinician as they can modify mechanics by using a lighter force, avoiding extractions when necessary, monitoring with serial radiographs six months after orthodontic treatment commencement, and allowing for a two- to three-month pause in treatment by applying a passive arch wire in selected cases to allow repair.[10]

Methods

1. Radiographic methods

For treatment planning, radiographs provide a clinician with useful information regarding the general condition of the dentition, the presence of pathology, root morphology and bone levels. A panoramic film and lateral cephalogram are considered the standard diagnostic tools required for most patients seeking orthodontic treatment.

Currently, the most commonly used method to monitor root resorption is by the use of radiography, whereby patients at risk of OIIRR are monitored with periapical or a panoramic film. Due to the radiation exposure and costs, a three-dimensional (3D) image such as a Cone Beam Computed Tomographics scan (CBCT) is not routinely advised unless indicated.

An index for the quantitative assessment of radiographically detected root resorption was proposed by Malmgren et al. in 1982.[13] and is presented in Figure 1. The level of root resorption is categorised according to an index grade score of 1–4 in which Grade 1 represents the presence of an irregular root contour, Grade 2 indicates minor root resorption amounting to less than 2 mm of the root apex, Grade 3 reflects severe root resorption from 2 mm to one-third of the original root length, while Grade 4 is extreme root resorption exceeding one-third of the original root length.

Panoramic film

A panoramic film is readily obtainable in most dental clinic settings. It is cost-effective, time-saving, and has a relatively lower radiation dose in comparison with a CBCT scan. Most importantly, a panoramic film is the standard radiograph required prior to commencing orthodontic treatment. However, in quantifying the severity of OIIRR, a panoramic film has its disadvantages. A study conducted by Ahuja et al.[14] considered the accuracy of panoramic films in the evaluation of root resorption in comparison with periapical radiographs of 900 teeth. It was concluded that panoramic films were more challenging in the assessment of root morphology. The overall level of root resorption in the apical region was found to be higher in panoramic films in comparison with periapical films. Patient positioning had a large impact on the quality of the panoramic film, and could cause root apices and palatal structures to be out of focus or even invisible, especially in the anterior regions due to the narrow focal trough in the incisor region.[6] Furthermore, the roots of the anterior teeth can appear either shortened or magnified in cases in which patients have excessively proclined or retroclined teeth as the labial segments cannot fit into the focal trough.[15] This can contribute towards a spurious positive result and promote a false impression of more severe root resorption in the labial segments. Dudic et al.[5] evaluated 275 teeth in 22 patients approaching the end of their orthodontic treatment by using panoramic radiographs, which were found to underestimate root resorption in comparison with a CBCT scan. The conclusions were later confirmed by Alqerban et al.[16] A CBCT was recommended as a more reliable and accurate method for detecting root resorption as it was less affected by patient position and free from the influence of the pattern of superimposition of the anatomical structures, which may significantly affect the measurements.

Periapical radiographs

Periapical radiographs are more accurate than panoramic films in quantifying the severity of root resorption as they have a greater precision in assessing

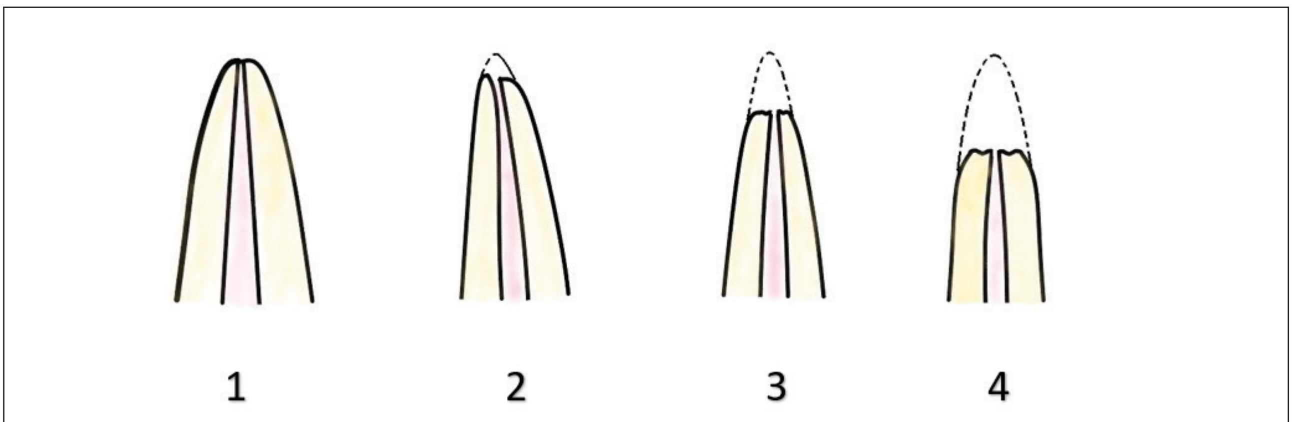

Figure 1. Score system categorising the severity of root resorption by Malmgren et al. (1982)13 based on index score from 1–4. Grade 1 – mild resorption, root with normal length and only displaying an irregular contour, Grade 2 – moderate resorption, small area of root loss with apex exhibiting almost straight contour, Grade 3 – accentuated resorption, loss of almost one-third of root length, Grade 4 – extreme resorption, loss of more than one-third root length.

fine details and reduced distortion compared with a panoramic film.[17] Ideally, a periapical radiograph should have an aspect ratio almost identical to the tooth length; however, images might be foreshortened or magnified as it is difficult to achieve an absolutely perpendicular view with the paralleling-technique.[15] Usually, a film holder is used to protect the film from bending against the palate or other structures and to assist in directing and aligning the X-ray beam at a right angle to the long axis of the tooth.[7] Periodic identical radiographs are not feasible in orthodontics because teeth move during treatment and the changes in angulation contribute to projection error.[6] Numerous studies have used periapical radiographs before and after active orthodontic treatment to evaluate the amount of root resorption induced by orthodontic tooth movement.[17–19] Smale et al.[19] compared the amount of root resorption using periapical radiographs in 290 subjects, three to nine months after a tooth alignment stage, and found that only 4.1% of the 290 subjects showed an average resorption of more than 1.5 mm. An additional 15.5% revealed one or more maxillary incisors with resorption of 2 mm or more. Although this level of root resorption is clinically insignificant, it might be alarming if progression occurs. Maués et al.[17] found severe root resorption in 2.9% of 959 teeth in 129 patients, while Marques et al.[18] reported a higher prevalence of severe root resorption in 14.5% of 1049 Brazilian subjects. The difference may be due to a larger sample size recruited in the Maués et al. study, which allowed more variables, as well as the different evaluation methods reporting the prevalence to be included.

Lateral cephalograms

The radiographic technique used in lateral cephalometry is highly reproducible in the display of the lengths of the upper and lower incisors. However, lateral cephalograms have the disadvantage of the overlapping of the left and right side that makes them a less favourable tool in diagnosing OIIRR. Without correction, they are also subject to a 5–12% enlargement factor because of the radiographic projection.[15] In a retrospective study that assessed the amount of root resorption of upper central incisors using pre- and post-treatment lateral cephalograms, it was reported that the majority of the subjects (84%) exhibited mild root loss after orthodontic treatment.[20] The authors admitted that they faced difficulty in accurately locating worn edges of upper incisors as well as the root apices on the radiograph due to superimposition of the adjacent teeth.

3D imaging techniques

In general, two-dimension (2D) imaging is more readily available in most dental clinics and has a lower radiation dose. However, it has the limitations of a lack of standardisation in conventional film and X-ray tube orientation, which could contribute to incorrect projection and magnification, further complicated by anatomic variations. In conventional 2D imaging, surface resorption detection is only possible when a film is mesiodistally placed, at a right angles to the focal beam, or when the damage has advanced to a severe stage.[15]

CBCT 3D imaging is superior to 2D imaging in the detection of root resorption because of its advantages in eliminating overlapping structures and better visualisation of structure volume in all three planes.[6,21,22] CBCT images are superior in the detection and linear quantification of root resorption to periapical radiographs as CBCT scans are able to produce a distortion free and reproducible image especially for single rooted teeth.[6,23] Ponder et al.[22] compared the low and high resolution of a CBCT in quantifying simulated external apical and lateral root resorption defects, in comparison with periapical radiographs. Both low- and high-resolution CBCT images were found to be significantly more accurate in the detection of root resorption. A high-resolution CBCT showed significantly more accuracy than a low-resolution CBCT. Lund et al.,[21] in a prospective study, investigated the incidence and severity of OIIRR in all roots from incisors to molars using CBCT. Out of 152 patients, 91% revealed some level of root shortening and up to 15% of the palatal root surfaces showed slanted root resorption, which could only be evaluated using 3D imaging. Large resorptive areas were easily interpreted by all techniques, while low resorption grades, especially Grade 1, could be interpreted only on CBCT images. A study by Alamadi et al.[24] compared the accuracy of 2D (periapical radiographs, panoramic film) and 3D (CBCT) radiographic techniques using a histologically analysed extracted deciduous canine as a standard. All techniques were able to diagnose large defects, but a low resorption grade could only be detected using a CBCT scan. However, the disadvantages of a CBCT include a higher cost and radiation dosage compared with conventional 2D radiographs. In addition, the detection of minor resorption defects might not be clinically significant, which is why a justification of the risk and benefits is required before obtaining a CBCT and may only be indicated for higher risk patients.

Although 3D imaging can overcome the drawbacks of conventional 2D imaging in diagnosing root resorption, the monitoring of OIIRR still requires repeated radiation exposure for patients. This is particularly concerning in children and adolescents because their tissue metabolism makes them more sensitive to radiation-induced carcinogenesis.[25]

In conclusion, radiographic methods have several drawbacks and limitations in monitoring the progress of OIIRR. Repeated radiation exposure is required, and accuracy is an issue. In addition, early root resorption is not detected until 60–70% of mineralised tissue is lost and radiographic methods are unable to indicate whether the process of root resorption is still active.[26] The disadvantages related to a lack of standardisation and magnification issues in conventional 2D radiography have encouraged researchers to seek an alternative method to evaluate OIIRR.

2. *Methods using biological markers*

A biological marker is defined as a substance that can be measured and objectively evaluated as an indicator of normal biologic processes, pathogenic processes and pharmacologic responses to a therapeutic intervention.[27] The use of biomarkers is a more sensitive, specific and safer alternative compared with conventional radiographs to detect early root resorption. Orthodontic force applied during treatment induces an inflammatory process, alveolar bone remodelling (formation and resorption), and subsequently root resorption. This sequence of events following orthodontic tooth movement can be represented and identified using suitable biomarkers. Recent research has used blood, saliva and gingival crevicular fluid (GCF) as a medium to detect OIIRR during active orthodontic treatment.

The inflammatory markers

The levels of inflammatory cytokines such as IL-1β, IL-6, IL-8 and tumour necrosis factor-alpha (TNF-α) are increased in the GCF during orthodontic tooth movement.[28] The review by Ren and Vissink focused on cytokines in the GCF during orthodontic tooth movement and it was suggested that light continuous force is preferred in orthodontics as it can induce relatively longer lasting levels of cytokines that are needed for continuous periodontal remodelling.[28]

Rody et al.[3] evaluated the levels of GCF proteins such as interleukin-1 beta (IL-1b), IL-1RA, nuclear factor kappa β ligand (RANKL), osteoprotegerin (OPG), matrix metalloproteinase-9 (MMP-9), and dentin sialoprotein (DSP) from resorbing deciduous teeth and non-resorbing controls of a group of 11 patients in the mixed dentition. IL-1RA, which is an inhibitor of bone remodelling, was down-regulated in the GCF from resorbing teeth, which suggests its potential as a biomarker.[28]

Interleukin-6 (IL-6) plays an important role in bone resorption and osteoclastic cell recruitment during orthodontic tooth movement. Kunii et al.[29] found that IL-6 could be a potential biomarker for OTM as its levels increased significantly in a resorption group compared to a control group. Furthermore, the authors also investigated the effects of different static compressive forces (CFs) on IL-6 production by human periodontal ligament (hPDL) cells and the influence of IL-6 on osteoclastic activation from human osteoclastic precursor (hOCP) cells in vitro. it was found that the release of IL-6 protein increased in a time- and magnitude-dependent manner. Heavy compressive force induced IL-6 production and stimulated osteoclastogenesis, indicating that IL-6 may induce or facilitate OIIRR. Kawashima-Ichinomiya et al.[30] reported that the levels of IL-6 increased significantly in patients with severe root resorption after neuropeptide stimulation.[31] However, the expression of cytokines may also be affected by other inflammatory processes in the body, making them less specific to OIIRR.

The bone remodelling markers

Osteoclastogenesis is induced by receptor activator of nuclear factor kappa β (RANK) and its ligand RANKL. It is inhibited by OPG through competing with the binding of RANKL to RANKL receptor, thus regulating the bone remodelling process.

According to George and Evans,[32] OPG was locally present in excess amounts over RANKL and an increased RANKL/OPG in the group with root resorption, which could be correlated with increased bone resorption activity during OTM. Later studies showed that RANKL plays an important role in facilitating OIIRR.[31,33,34]

Dentine matrix protein markers

Released dentine matrix proteins are derived from the proteolysis of dentine sialophosphoprotein (DSPP) and dentine matrix protein 1 (DMP-1). The DSPP proteins are the major component of the non-collagenous protein in dentine. DSPP includes dentine sialoprotein (DSP), dentine glycoprotein (DGP) and dentine phosphoprotein (DPP). The DSPPs are considered highly dentine specific as they are not present in bone, cartilage, soft tissues or other components of the oral tissues. Dentine matrix proteins are not routinely released into surrounding space as dentine does not undergo the process of bone-like remodelling. It is only in the presence of active external root resorption that these proteins are freed into the periodontal ligament space.[2] Thus, the increase in concentration of dentine matrix proteins may reflect the level of root resorption.

Several studies have reported the potential for using dentine matrix protein as a specific biological marker for OIIRR[2,35–38] Balducci et al.[2] compared upper permanent incisors under active orthodontic treatment and experiencing different levels of resorption with a control group of untreated teeth. It was noted that the concentration of DSP and DPP were statistically significantly higher in severe OIIRR (>2 mm root shortening) than in mild OIIRR (<2 mm root shortening) cases.

Using ELISA methods, Mah and Prasad[39] compared the DPP levels in GCF of 20 untreated subjects in whom 20 primary second molars had half of the root resorbed and mildly resorbed upper permanent central incisors of patients undergoing active orthodontic treatment. It was found that the highest DPP level was noted in the severely resorbed deciduous second molars. The orthodontic group showed an elevated level of DPP compared with a control group. In this cross-sectional observational study, the authors assumed that physiological resorption of deciduous teeth was comparable to pathological root resorption during orthodontic tooth movement as both processes are largely similar in their biochemical processes and the composition of non-collagenous protein in dentine.[35]

The potential to use DSP as a biomarker for OIIRR was also confirmed by Kereshanan et al.[35] A rise in DSP levels in GCF was detected as early as 12 weeks after fixed appliance treatment. The result agreed with a radiographic study by Smale et al.,[19] in which the initiation of root resorption was noted as early as the tooth alignment stage. Also found was the presence of DSP in untreated subjects, which was similar to the findings of Mah and Prasad in 2004.[39] It was hypothesised that cementum matrix might contain DSP which was released into the tissue surroundings as a natural consequence of the resorption/repair process during physiological root resorption and during orthodontic tooth movement.[35]

Sha et al. found a significant elevation of DSPP level of GCF in 10 subjects two months after the intrusion of upper central and lateral incisors.[36] Intrusive tooth movement is more likely to cause root resorption according to a review of treatment mechanic risk factors by Wahab et al.[12]

Conclusion

The present paper examined the current literature with respect to the use of 2D and 3D radiographic techniques to evaluate OIIRR and discussed the disadvantages with respect to their accuracy, reproducibility, costs and safety. The review further highlighted the potential to use biological markers as a safer and more sensitive alternative for the early detection of OIIRR compared with conventional radiographic methods. Hence, prolonged longitudinal studies to assess the changes in the concentration of different biological markers in GCF and saliva at different stages of root resorption, and the practicality of the approach, are recommended.

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