

Present status and future directions: Imaging techniques for the detection of periapical lesions

Elisabetta Cotti¹  | Elia Schirru²

¹Department of Conservative Dentistry and Endodontics, University of Cagliari, Cagliari, Italy

²Faculty of Dentistry, Oral & Craniofacial Sciences, King's College London, London, UK

Correspondence

Elisabetta Cotti, Department of Conservative Dentistry and Endodontics, University of Cagliari, Via Roma 149, Cagliari 09124, Italy.
Email: cottiendo@gmail.com

Abstract

Diagnosing and treating apical periodontitis (AP) in an attempt to preserve the natural dentition, and to prevent the direct and indirect systemic effects of this condition, is the major goal in endodontics. Considering that AP is frequently asymptomatic, and is most often associated with a lesion in the periapex of the affected tooth, within the maxillary bones, imaging becomes of paramount importance for the diagnosis of the disease. The aim of this narrative review was to investigate the most relevant classic and current literature to describe which are, to date, the diagnostic imaging systems most reliable and advanced to achieve the early and predictable detection of AP, the best measures of the lesions and the disclosure of the different features of the disease. Dental panoramic tomography (DPT) is a classic exam, considered still useful to provide the basic diagnosis of AP in certain districts of the maxillary bones. Periapical radiographs (PRs) represent a valid routine examination, with few, known limitations. Cone-beam computed tomography (CBCT) is the only system that ensures the early and predictable detection of all periapical lesions in the jaws, with the minor risk of false positives. These techniques can be successfully implemented, with ultrasounds (USI) or magnetic resonance (MRI) imaging, exams that do not use ionising radiations. MRI and USI provide information on specific features of the lesions, like the presence and amount of vascular supply, their content and their relationship with the surrounding soft tissues, leading to differential diagnoses. Further, all the three-dimensional systems (CBCT, USI and MRI) allow the volumetric assessment of AP. Pioneering research on artificial intelligence is slowly progressing in the detection of periapical radiolucencies on DPTs, PRs and CBCTs, however, with promising results. Finally, it is established that all imaging techniques have to be associated with a thorough clinical examination and a good degree of calibration of the operator.

KEYWORDS

apical cysts, apical periodontitis, CBCT, diagnosis, magnetic resonance imaging, ultrasound imaging

INTRODUCTION

Periapical lesions are normally the expression of apical periodontitis (AP), a biofilm-related oral disease, that develops in the periapical region of an infected tooth, as a dynamic encounter between bacteria and other microorganisms infecting the root canal system and reaching the periodontium, and the host defence. The pathogenesis of AP begins with a nonspecific inflammatory reaction, followed by a specific innate, and adaptive immunological response (Siqueira et al., 2020). The complex action of the inflammatory cells with numerous biochemical mediators and the overlapping network between cytokines and chemokines intervening in the process and relating to different bacterial profiles primarily result in the resorption of periapical bone to produce lesions of varying extent (Márton & Kiss, 2014; Siqueira et al., 2020) (Figure 1).

Depending on the specific nature of the infection and host-related factors, AP manifests as acute (symptomatic) or chronic (asymptomatic), and its histopathologic features are mostly represented by a periapical granuloma or a radicular cyst (Nair, 1998; Ricucci et al., 2020). The development of AP into a radicular cyst rather than into a granuloma is associated with the expression of a stronger proinflammatory state that may render healing of the lesion, in response to treatment, less predictable (Weber et al., 2019); thus, it becomes important to make a differential diagnosis between the two conditions.

Apical periodontitis is a highly prevalent disease related to an infected root canal system, and according to the latest systematic review and meta-analysis (Tibúrcio-Machado et al., 2021), its prevalence corresponds to 52% of the adult population worldwide. The scope of endodontic treatment is both to prevent the development of AP or to create adequate conditions to favour the healing of this disease by means of primary and secondary root canal treatment (RCT) (Ng et al., 2011). Interestingly, from the above-mentioned review, it also emerges that AP is more

frequently found in teeth that have received RCT, compared with nontreated teeth. Further, the populations in developing and transitional countries are more often affected by AP, and this awareness brings further concerns on the burden of endodontic disease on the global population (Tibúrcio-Machado et al., 2021).

The presence of untreated or persistent AP leads to important consequences, the most common of which is represented by the loss of teeth, which has a negative impact on the quality of life in a world population who is growing older (Sebring et al., 2022).

Furthermore, the clinical presentation of AP may, on some occasions, lead to direct systemic complications such as cellulitis that may create life-threatening situations (Shemesh et al., 2019).

Finally, the continuous presence of AP constitutes a persistent systemic low-grade inflammation (endodontic burden), which has been strongly associated with cardiovascular diseases and other health conditions (Segura-Egea et al., 2015).

Dental diagnostics and treatment planning rely on imaging, and the assessment of treatment outcome is usually based both on clinical examination and radiographic evaluation (Cotti, 2010; Patel, Dawood, Whaites, & Pitt Ford, 2009).

Given the importance of treating AP, for preserving the natural dentition, and preventing its direct and indirect systemic involvement, and considering that AP is frequently asymptomatic and is most often associated with a lesion in the periapex of the affected tooth, the diagnostic imaging techniques used should have the highest sensitivity and specificity for any given task, while keeping the biologic cost of the exam as low as possible (Cotti, 2010).

To date, the conventional methods to diagnose periapical lesions are represented by periapical radiographs (PR), panoramic radiographs and cone-beam computed tomography (CBCT), supplemented by the use of ultrasound real-time imaging (USI) and magnetic resonance imaging (MRI).

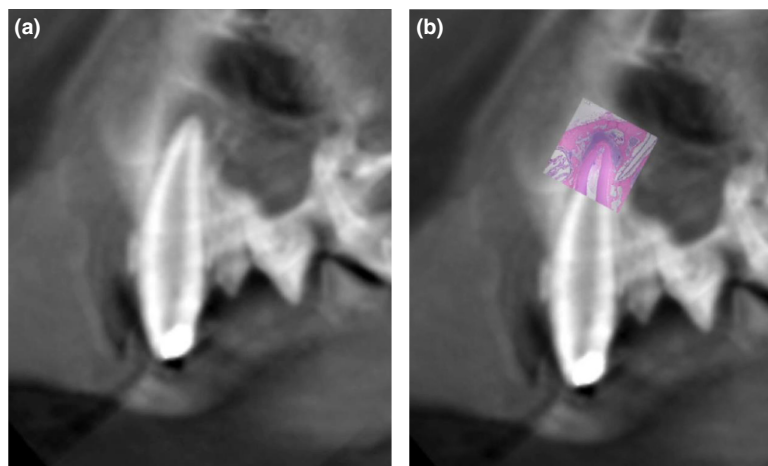


FIGURE 1 (a) Cone-beam computed tomography scan of a periapical lesion in the maxillary bone of an experimental animal. (b) Histopathologic section (haematoxylin and eosin) of the same lesion, superimposed to the corresponding scan

The aim of this narrative review was to investigate the most relevant and current literature on the imaging techniques used to detect AP, to describe which are, to date, the systems most reliable and advanced to achieve: (1) the early and predictable detection of the disease; (2) the most reliable way to measure the lesions in 2D and 3D, for their better assessment and follow-up; and (3) the disclosure of the most important features to differentiate the lesions of AP.

EARLY AND PREDICTABLE DETECTION OF PERIAPICAL LESIONS

Dental panoramic tomography (DPT) analyses a focal trough or section of the lower skull. It is commonly requested by clinicians to obtain an overall view of the teeth and the jaws, less often to assess the periapical status of single teeth. Although being a lower quality choice for fine details, often needed in endodontics, it had increased popularity during the Covid-19 initial outbreak, as a method of reducing the need for intraoral radiograph. However, the evidence of the latest report is limited to caries detection because DPT was used in a sectional bitewing mode (Little et al., 2020).

This radiographic exam has been associated with a high likelihood of underestimating the presence of AP (Estrela et al., 2008), which can be assessed on DPT, with high specificity and positive predictive value, but low sensitivity and negative predictive values. The ability of DPT to provide a true positive finding is dependent on several factors, for an example, the position of teeth with respect to the radiographic (x-ray) beam. When periapical lesions are located in the mandibular canine/premolar area, the x-ray beam is more orthogonal to this section of the jaws, and consequently, AP becomes more identifiable (Nardi et al., 2017). The intra- and interobserver reliability for DMFT score, remaining teeth and root filled teeth, has been reported for DPT (Sebring et al., 2021) to be a valid method, while the assessment of associated periapical lesions on DPTs became predictable only immediately after the calibration of the observers. Importantly, these observations provide an option for using DPT for diagnosing AP even if the overall efficacy of DPT on the early detection of AP is questionable (Figure 2).

Periapical radiographs are the most commonly used radiograph to detect changes in the periapical bones. The conventional wet films have been replaced by digital sensors, with the advantages of reducing radiation dose, processing time, developing issues and storage, which are also helpful in communication with patients. The quality

of radiographic images depends directly on the sensor line pairs and the software used to read them (Nejaim et al., 2016), with digital PRs reported to have a resolution between 15 and 26 line pairs per millimetre (Farman & Farman, 2005; Nejaim et al., 2016) and an effective dose between 1 and 5 μ Sv (Patel et al., 2021).

The ability of PR to detect the presence of periapical lesions has been often a controversial topic. The classic study of Bender and Seltzer in the 60s (Bender & Seltzer, 1961) provided evidence of the inability of PRs to reveal periapical lesions when fully confined to the cancellous bone. AP was believed to be detectable on PRs only if it extended to the cortical plates, or if more than 50% of the bone was lost Shoha et al. (1974) demonstrated that this concept was only partially true, with lesions in the cortical bone located in the pre-molar region being detectable due to the reduced thickness when compared to the molar areas. Several later studies provided contrasting opinions, until a more recent report addressed this issue and created an *ex vivo* model using CBCT images as the reference standard, and comparing them to PRs of the same area of interest. Independently of their location, approximately 94% of all lesions studied were correctly diagnosed, and those confined to the cancellous bone could be identified in 92% of the times with PR. The size of the lesions was an important parameter though, with the larger ones more easily identifiable and more likely to be extended to the cortical bone. Interestingly, when AP was not present, there was a low tendency to misdiagnose the lesion with a false positive. It was then concluded that lesion size could be a better predictor of the ability to detect a periapical lesion on PRs, than its location (Chang et al., 2020).

Despite the location and size of the lesions, PRs images suffer several innate complications such as superimposition of anatomical structures, geometrical distortion, anatomical noise and indeed of their two-dimensional nature (Patel et al., 2019).

Cone-beam computed tomography has been used and introduced in endodontics effectively in the last 20 years and validated by numerous articles. Developed as an evolution of the computerised tomography (CT) scan, it uses a cone or pyramid-shaped beam (instead of a fan-shaped), a single rotation and small volumes to focus attention on a particular area of diagnostic interest. The images thus acquired and processed, reproduce a three-dimensional reconstruction of the targeted region of interest and allow the possibility of analysing it in different spatial planes. The intra- and interobserver agreement, an important factor when considering the diagnosis, the assessment of the outcome, as well as the communication with the patient and the colleagues, has been reported to be higher on CBCT than on PRs (Barnett et al., 2018; Patel, Dawood, Mannocci, et al., 2009).

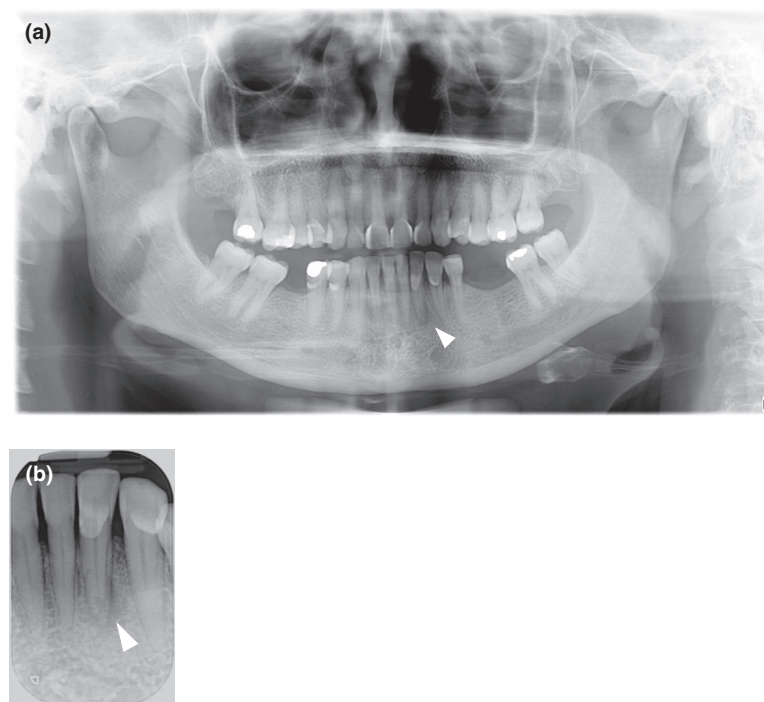


FIGURE 2 (a) Comparison between the panoramic radiograph and (b) the periapical radiograph, for the diagnosis of a periapical lesion (arrows) in the mandibular left lateral incisor

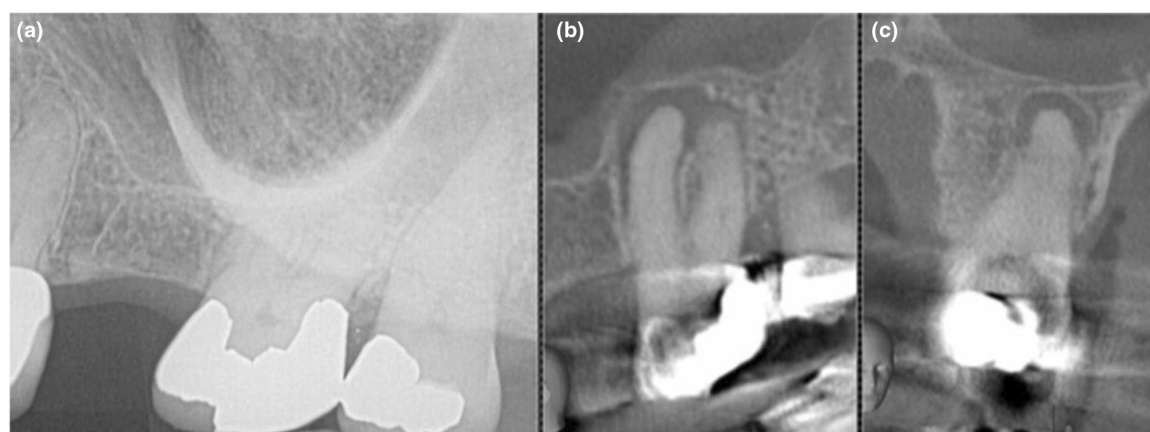


FIGURE 3 Diagnosing more lesions of apical periodontitis (AP). Periapical radiograph of a maxillary left second molar with no apparent evidence of AP (a). Cone-beam computed tomography scans of the same tooth that shows periapical radiolucencies associated with all the roots (b, c). (Courtesy of Prof. A. Azim).

The detection of AP lesions on CBCT images has been studied in several *ex vivo* and *in vivo* studies (Özen et al., 2009; Stavropoulos & Wenzel, 2007; Tsai et al., 2012) that demonstrated higher sensitivity and specificity of the exam when compared to PRs. A recent meta-analysis confirmed this superiority, reporting the sensitivity and specificity to be, respectively, 50% and 83% for PRs, and 95% and 90% for CBCT (Mostafapoor & Hemmatian, 2022). It has been reported that approximately a third of periapical lesions are missed on PRs, when compared to CBCT (Abella et al., 2012; Lofthag-Hansen et al., 2007; Patel et al., 2012), on primary endodontic disease, and similarly on persistent AP (Davies et al., 2015), (Figure 3).

Undoubtedly, CBCT has drastically overcome the limitation of conventional PRs; however, the high level of confidence that CBCT provides in the detection of AP has been recently questioned. A retrospective study approached the hypothesis that CBCT might produce false positives when diagnosing AP (Pope et al., 2014), as when standardised CBCT examinations were conducted on vital, asymptomatic teeth, the presence of an enlargement of the periodontal ligament (PDL), corresponding to 1–2 mm or more, was observed in 20% of the sample studied. Considering that widening of the PDL is an early predictor of AP, these results posed an important question on the possible overdiagnosis of early AP on CBCT, with the

consequent risk of overtreatment. The authors questioned the observer's ability to read the changes in the PDL on a three-dimensional image because they were more familiar with the PRs, and this observation may be realistic. On the other hand, as the authors used the symptoms as the only reference standard to assess the state of the pulp in this study, its methodology has been questioned.

Bone biopsies of periapical tissues would be the ideal diagnostic reference standard for *in vivo* studies; however, this is impractical and ultimately unethical unless the biopsy of the samples is obtained during periapical surgery. Results similar to those described above were found in research where persistent AP post-surgery (5–11 years later), was diagnosed on PRs and CBCT, and the histopathology of the lesions was performed following a secondary surgery (Kruse et al., 2017). In this report, the histology revealed that 42% of the samples did not show signs of inflammation, while a periapical radiolucency was present on CBCT examination but not on PRs. Interestingly, only when the presence of a radiolucency was evident on both PR and CBCT, a correct diagnosis was reached in 63% of cases. The complete statistical analysis was not reported, but the trend for CBCT to overestimate the presence of a periapical radiolucency and the importance of PRs were enforced (Figure 4).

Finally, two consecutive studies on cadavers, with histology as reference, were conducted in an attempt to solve the issue. In one, (Kanagasigam et al., 2017) the authors performed CBCT, PRs and histology in jaw sections of fresh, bodies, reporting the CBCT sensitivity in detecting AP to be very high, a near lack of false positives and

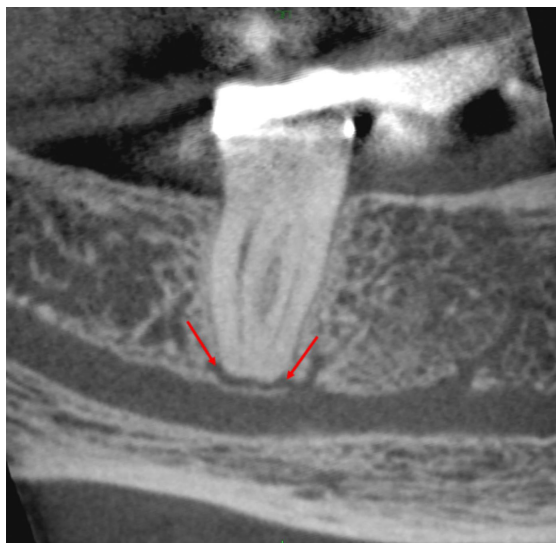


FIGURE 4 Cone-beam computed tomography scan on tooth lower right second molar. The red arrows indicate the presence of a periapical radiolucency, due to nerve branches and blood vessels. The tooth tested positive for sensitivity testing on two separate occasions, 6 months apart.

specificity equal to 1. Using a similar protocol, but with tissues preserved in formalin, the second research showed similar results, a very low risk of overdiagnosis on non-root filled teeth and a more moderate risk for root filled teeth (Kruse et al., 2018).

The high level of specificity and sensitivity of the CBCT has thus highlighted the importance of this examination when conventional radiography is insufficient to support a correct and confident diagnosis. Several factors should then be considered when requesting a higher dose radiographic investigation such as CBCT: (a) Every image should be justified, optimized and reported (Patel et al., 2019); (b) Two levels of training for the clinicians are recommended for prescribing and interpreting the CBCT images (Brown et al., 2014; Patel & Harvey, 2021); (c) The setting of the scan should be adapted to the area of interest; however, small FOV with high-resolution CBCT should be considered in endodontics, as a coadjuvant to reach the best diagnosis to formulate an adequate treatment planning. The patient should be informed of the risks/benefits associated with the exam, and the quality of images associated with the different machines in the market should be also considered.

2D AND 3D MEASUREMENT OF THE LESIONS

Linear measurements of periapical lesions represent part of the normal routine in endodontic practice. PRs and DPTs have been used initially in analogic, then digital mode to determine the extension of AP radiolucencies and other pathoses. Given the known size of the film or being able to calibrate the radiograph digitally, it is possible to measure with a fair degree of confidence the size of a lesion. The ideal trajectory of the radiographic beam should be orthogonal and the film parallel to the long axis of the tooth, or the root that is intended to be investigated. Multi-rooted teeth represent therefore a challenge in correctly exposing the patient and obtaining reliable radiographs without distortion. Moreover, a magnifying effect occurs due to the distance between focus and film. Software has been used to modify digitally the images, to obtain a standardised projection of the conventional radiographs (Bose et al., 2009; Ideo et al., 2022).

Cone-beam computed tomography has overcome the distortion problem because this exam allows the image to be manipulated on several spatial planes. Linear measurements of periapical lesions on CBCT, however, pose a second issue on where to start and where to end the measurement. Several articles have validated the ability of CBCT to produce accurate linear measurements while establishing the radiographic working length and comparing

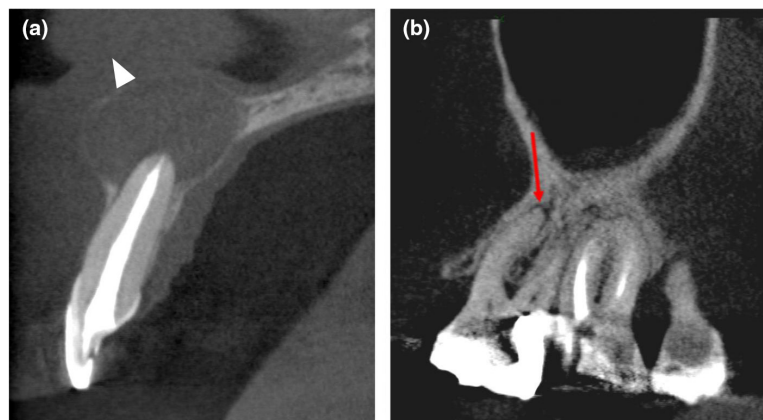


FIGURE 5 Measurements of periapical lesions. Large periapical radiolucency associated with a previously root canal-treated upper incisor, the cortical plates appear thinned, expanded and partially fenestrated (CBCT-PAI 5D) (a). Early stage of bone resorption (arrow), due to pulp necrosis associated with the mesio-buccal root of the upper left first molar (CBCT-ERI 1) (b).

it to apex locator readings and PRs (de Moraes et al., 2016; Segato et al., 2018; Üstün et al., 2016). Amperage, voxel size, field of view (FOV), tube voltage, rotation of the machine and dose reduction mode have a potential influence on the resolution of CBCT images (Yeni et al., 2005). Furthermore, some CBCT appliances do not allow a direct manual set-up of each of these parameters but rely on default settings linked to each other (i.e. selection of a larger FOV = automatic set up of a larger voxel size). The lack of standardisation between manufacturers and the scarce ability to customise each setting, as well as different reconstructive software, has produced a plethora of scientific articles on the topic that is difficult to compare directly. Recent studies have found that the FOVs have a minimal impact on the resolution of the image, as well as the voxel size, as long there were smaller than 0.3 mm^3 when assessing linear measurements (Yilmaz et al., 2017). Considering that the 'endodontic settings' of modern CBCT machines use small voxel size in the range of $0.08\text{--}0.125 \text{ mm}^3$, the standardisation of the CBCT has therefore minimal influence on the images produced.

Since a periapical lesion is a volumetric entity, it is broadly accepted in the scientific literature to measure the largest part of the lesion, in the three planes, however, minimal variations in the angulation of the root might produce errors and false readings. Noticeably, several reports on the quality of volumetric measurements of AP on CBCT have found a high correlation between the sizes measured with the corresponding anatomical samples (Ahlowalia et al., 2013; Da Silveira et al., 2015; Esposito et al., 2013; Liang et al., 2014; Sönmez et al., 2018).

To assess the extent and the alterations of periapical lesions on PRs, a codified scoring system (Periapical Index—PAI) was introduced in 1986 (Ørstavik et al., 1986). Based on previous histological works by Brynolf (1967), and on the amount of bone mineral loss, the PAI index score provides a scale 1–5, ranging from healthy periodontium to the development and exacerbation of AP. The score is used to assess healing and ultimately the outcome of RCTs.

With the introduction of CBCT, an attempt to codify through a reproducible system the complex and increased amount of information was made, introducing a CBCT-PAI (Estrela et al., 2008). The new index was based on a scale of 0–5, from healthy periapical tissue to increasingly larger periapical lesions, assessed by measuring their largest part in millimetres. Two further categories indicated the involvement of the cortical plate in relation with the lesion (expansion and fenestration). The overall approach of the CBCT-PAI is similar to the classic PAI, therefore addressing the periapical lesions still in two dimensions, and without a standardised approach because of the arbitrary positioning of the assessment plane. The following report highlighted this issue and proposed a more accurate assessment of the size of the lesion based on controlling all spatial planes (Esposito et al., 2011). Considering the fine details often present in Endodontics, more accurate measurements were needed. The CBCT-endodontic radiolucency index (CBCT-ERI) (Torabinejad et al., 2018), codified the enlargement of the PDL on a scale 1–6, from 0.5 to 2.5 mm and larger, using minute measurements particularly useful for early stages of AP (Figure 5).

Another index, the COmplex Periapical Index (COPI) was developed as part of a comprehensive model with the purpose to assess more the prognostic factors that affect the outcome of endodontic treatment, than the mere reduction/increase in the size of periapical radiolucencies (Venskutonis et al., 2015). Size of the lesions, the relationship between the root and the lesions and, ultimately, the location of the bone remodelling, were the parameters assessed. In conclusion, when the three CBCT indices were compared, COPI exhibited the best intra- and interobserver agreement, CBCT-PAI the highest interobserver variability and CBCT-ERI the highest intraobserver disagreement (Sisli et al., 2021). The switch between 2D measurements to volumes may overcome the intra-/interobserver variability. Researchers proposed a semiautomated segmentation of the volumes of the periapical radiolucency on CBCT, with the possibility of creating

reproducible volumes. The CBCT-PAVI (periapical volume index), is conceptually similar to CBCT-PAI (scale 0–6), but with progressively larger volumes instead of linear measurements (Boubaris et al., 2021). The overall sensitivity of the CBCT-PAVI was higher than 98%, with a promising increase in its use for the future, although errors may still occur, as the system still relies on small operator-made adjustments to segment the area of interest of the CBCT scan.

DISCLOSE THE MOST IMPORTANT FEATURES TO DIFFERENTIATE THE LESIONS OF AP

Lesions of AP are all inflammatory in origin and manifest prevalently as apical cysts or granulomas, the latter being the most frequent histopathologic feature of AP, as demonstrated in the majority of studies (Ricucci et al., 2020). An apical cyst is a lesion that becomes epithelialized as a consequence of the proliferation of the periodontal epithelial cell rests of Malassez within the granuloma and is characterised by a cavity lined by a stratified squamous epithelium, usually containing a serous fluid, with multiple cholesterol crystals (Nair, 1998). The lumen of the apical cyst in about 8% of the cavity may alternatively be lined by ciliated columnar cells of respiratory origin (Nair et al., 2002; Ricucci et al., 2014). Apical cysts can also be contained within a granuloma and have been distinguished in true and bay cyst forms, depending on their relationship with the root canal that has generated the reaction. A true cyst has no continuity with the root apex, while a bay/pocket cyst has a lumen that includes the tip of the canal responsible for the reaction (Nair, 1998).

The precise pathogenesis of apical granulomas and cysts has not yet been fully explained (Nair et al., 2008), but it is becoming more, and more evident that the development of apical cysts is associated with a higher level of proinflammatory immune reactivity from the host when compared to granulomas, as lately underlined by the significantly increased densities of HLA-DR- and CD83-expressing cells, and by the important shift of macrophages polarisation towards the M1 form in cysts (Weber et al., 2019).

According to the few studies that used strict histopathologic criteria, the prevalence of cysts represents 15%–32% of the AP lesions, with the most recent report concluding that cysts represent 24% of AP, 48% being true and 52% being bay cysts (Ricucci et al., 2020).

Over the years, it has been speculated that the presence of a true cyst may account for one of the reasons for a negative outcome following RCT, the explanation is that the lesion would not be influenced by the RCT because it has

become an independent pathologic entity (Nair, 1998). This hypothesis was recently partially discredited, when it was demonstrated that true cysts actually retain communication with the endodontic system, as bacteria were observed consistently within their lumen, and that they do not differ significantly from bay cysts (Ricucci et al., 2020).

Nevertheless, it is now accepted that apical cysts are the expression of a stronger inflammatory response of the host to root canal infection, than apical granulomas (Weber et al., 2019), thus providing a different explanation of why these lesions may not respond to regular RCT. Further, the formation of true vs pocket cysts may respond to an individual genetic pre-disposition (Ricucci et al., 2020). Even if larger and longer standing lesions are more likely to be cysts, a definitive differential diagnosis between a cyst and a granuloma can only be obtained by performing the histopathologic examination that includes the entire lesion with the apical portion of the involved root and using serial sectioning (Ricucci et al., 2020).

Other anatomical and clinical presentations of AP lesions are represented by a sinus tract, a pathway moving throughout the bone from the enclosed area of infection within the root canal, to an epithelial surface, where it opens to drain (Cotti et al., 2019). The epithelial opening of the sinus tract can be intraoral or extraoral (Abbott, 2004). This condition has a prevalence ranging from 7.4% to 30.75% (Gupta & Hasselgren, 2003; Sutzky-Goldberg et al., 2009). Clinically, patients with a sinus tract (also classified as chronic apical abscess) are asymptomatic, with the draining stoma as the only discomfort (Abbott, 2004). The sinus tract is expected to heal, following treatment of the infected tooth (Abbott, 2004), yet its presence, seems to lower the odds of treatment success by 48%, increasing the risk of tooth loss by 120% (Ng et al., 2011). Moreover, when a sinus tract opens in the skin, it is often misdiagnosed as a dermatological problem (Gupta et al., 2011). Therefore, detecting the infected tooth and also the pathway of the sinus tract is important.

The persistence of chronic apical abscesses with sinus tracts has been attributed to the epithelial lining of the tract, which would impede its closure, but more probably, it is due to the complexity of the infection, which characterised those cases. Infection in sinus tracts involves the intraradicular biofilm within the root, in the periapical lesion and in the external-radicular fraction of the tooth (Ricucci et al., 2018).

Defining the characteristic of the bone lesions of AP, when diagnosed, including the sinus tract pathways, may help in planning endodontic treatment and addressing the healing probabilities of the lesions.

Digital PRs have been used to measure grayscale values to differentiate cysts from granulomas with uncertain results (Shrout et al., 1993). Later it was reported that

granulomas could be distinguished from cysts by density using CT, in a single pilot study with a reduced sample size, followed by few other reports that paved the ground for a more detailed diagnosis of AP (Trope et al., 1989). Following the introduction of CBCT, CT imaging started to be no longer recommended for the pre-operative diagnosis of radiolucent lesions, due to their higher radiation exposure (Bornstein et al., 2015). Despite the fact that, over the last 15 years, CBCT has become the most important diagnostic tool for dental and endodontic indications, the exam does not seem to entail the best characteristics for the pre-operative descriptive or differential diagnosis of AP. Classic studies have used cone-beam CBCT for the differential diagnosis of apical lesions, using histology as the gold standard. Attempts were conducted by defining negative and positive grey-scale values, belonging respectfully either to liquids and air, or to the bone, soft tissue and dental materials, to distinguish extensive cavities by their content (Simon et al., 2006). In alternative complex scoring systems, based on various criteria were used to discriminate between the different entities of AP, validated with histology (Guo et al., 2013; Rosenberg et al., 2010). Later researchers evaluated the dimensions and predictive values of PRs and CBCT regarding the histologic evaluation of lesions of different sizes (Bornstein et al., 2015). Interestingly, irrespective of the method used, the correlation between the radiographic analysis and the histopathological diagnosis of cysts and granulomas using CBCT was weak. To date, there has been concordance in considering USI as the most reliable imaging system to define the content of lesions in the maxillary bones, hence to address the differentiation between cysts and granulomas in comparison with histopathology, the gold standard (Cotti et al., 2003). Ultrasounds have exhibited a high degree of sensitivity and specificity for differentiating periapical cysts and granulomas (Musu et al., 2016; Natanasabapathy et al., 2021).

Ultrasound real-time imaging, also called *echography*, or ultrasonography is based on the reflection of the ultrasound (US) waves that are directed towards the biological tissues of the body using an ultrasonic probe. Depending on the mechanical and acoustic properties of the selected tissues, the ultrasounds are reflected and generate echoes of different intensities that are transformed into an image on the computer screen (Auer & Van Velthoven, 1990).

Echography is a dynamic exam, because the movement of the probe on the chosen area, produces a sequence of moving images (average of 30 images/second) in the monitor, and the continuous changes in the sector plane create a real-time three-dimensional representation of that space. The strength of the echo signals, directly related to the different acoustic properties of two adjacent tissue, is represented as high: bright/white spots or low signals:

dark spots, defined, respectively, as hyperechoic and hypoechoic. Bone exhibits total reflection of the US waves and is therefore hyperechoic, while areas filled with fluid do not reflect the waves, and are anechoic. Areas characterised by different types of tissues show what is called a dishomogeneous echo (Auer & Van Velthoven, 1990).

Most important, ultrasound examination is supplemented by the use of colour-power Doppler (CPD) for the presence, direction and intensity of the blood flow, with its changes in real time (*Doppler*), in the format of colour spots superimposed on the images of blood vessels (colour), and with very high sensitivity for the minor vascularity (*power*) (Auer & Van Velthoven, 1990; Ghorayeb et al., 2008; Hofer, 2005).

Ultrasonic imaging has been used to document lesions in the maxillary bones since the late nineties (Lauria et al., 1996) and further directed to the study of AP (Cotti et al., 2002, 2003), with the purpose to distinguish cavities containing soft tissues, fluids or mixed components, and to disclose, via the CPD, the vascularity within and around the lesions, as a unique characteristic of this technique (Musu et al., 2016; Natanasabapathy et al., 2021).

Solid lesions presenting various intensities of echoes appear as different shades of grey (described as echogenic or hypoechoic), while cavities appear dark (anechoic or transonic) if filled with clear fluids and exhibit various degrees of darkness if filled with liquids containing inclusions.

Within this context, cystic lesions of endodontic origin were described as basically well-contoured cavities, limited by reinforced bony walls, filled with fluids, anechoic and with no evidence of internal vascularity on CPD. Granulomas, on the other hand, appeared as lesions either *echogenic or mixed in content*, with nonprecisely defined contours and the presence of blood vessels based on CPD (Cotti et al., 2003) (Figure 5). The results from the histopathologic examination have confirmed the tentative US diagnosis in the numerous studies performed in the last 15 years (Musu et al., 2016; Natanasabapathy et al., 2021).

The US exam has shown a specificity with respect to the content of the studied bone pathosis when it has displayed the different appearances of cystic lesions contained within a granuloma (mixed lesions) or the peculiar transonic appearance (fluid with scattered echogenic particles) of lesions, which corresponded to the secretion from cells belonging to the ciliated columnar epithelium lining the cyst wall (Cotti et al., 2003; Nair et al., 2002).

Last, a feasibility study has recently shown that sinus tracts of endodontic origin can be detected, and their route traced starting from the abscessed bone cavity, all the way to the opening of the tract, by means of USI, by direct observation of their bone pathways and their vascularity in three dimensions (Cotti et al., 2019). Previously the path

of sinus tracts was obtained by navigating a gutta-percha cone or metallic wire, from their orifice to their origin, corresponding to the infected root, and taking a periapical radiograph (Cotti et al., 2019), (Figure 6).

A more recent alternative, or adjunct, to the potential of ultrasounds to provide a fine diagnosis of periapical lesions is represented by MRI, another exam able to provide structural information for nonmineralized tissue, because it enhances soft tissue contrast and high-resolution imaging, distinguishing the amount of solid versus liquid material within a lesion, (Fujita et al., 2013; Geibel et al., 2015) and its vascular density on contrast examinations (Minami et al., 1996; Unetsubo et al., 2009).

Magnetic resonance imaging is based on the creation of a strong, magnetic field around the body of the patient, that causes the protons in the atoms of water, contained in the tissues, to line up. Then, high-frequency pulses of radio waves are sent towards the tissues examined, perpendicular to the magnetic field, disrupting the alignment of protons, which then start returning to their original position (relaxation), releasing a radio signal of the same frequency (resonance) (Whaites, 2007). The signals

captured by a radio antenna are, at one point, received and measured from a computer system and converted into an image of the tissue of interest. The relaxation time is tissue-specific and mostly responsible for the great soft tissue contrast provided by the MRI, whose images are tomograms (Whaites, 2007). The strength of the MRI system magnetic field is measured in metric units called Tesla (Mendes et al., 2020).

Magnetic resonance imaging performs best on soft tissues and vessels, whereas it does not represent specifically the bony structures, well visualised by CBCT. In MRI, bright images correspond to high signal intensity (SI) and dark images to low SI. Bone and air are dark as they exhibit low SI, while fat and soft tissues appear bright (strong signal). In addition, MRI signal enhancement is possible, when contrast agents are used (Mendes et al., 2020).

The most common MRI sequences that characterise tissues are T1-weighted and T2-weighted scans, which represent two different relaxation times. T1 determines the rate at which protons realign with the external magnetic field, and T2 measures the time taken for excited protons to lose phase coherence among the nuclei spinning perpendicular

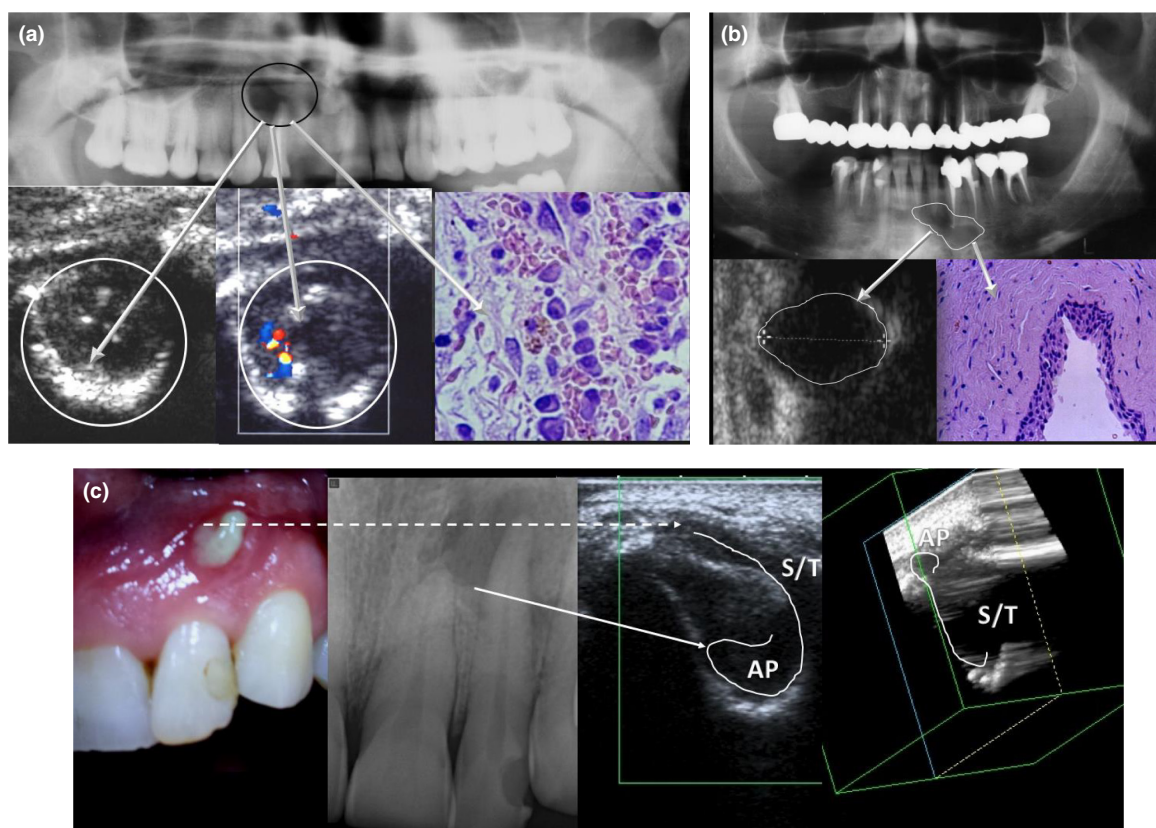


FIGURE 6 Granuloma of the upper jaw in correspondence with upper right central incisor, as seen in the panoramic radiograph, in the US imaging (left arrow), in the US imaging + CPD (centre arrow) and in the histopathologic section (right arrow), (a) Radicular cyst of the lower jaw in correspondence with the left canine, as seen in the panoramic radiograph, in the US imaging (left arrow) and in the histopathologic section (H&E) (right arrow), (b) Representation of a sinus tract (photograph), the corresponding periapical lesion on the periapical radiograph and the echographic representation of the lesion and tracing of the tract (arrows and circles), both in regular and 3-D USI.

to the main field. T1-weighted images are enhanced by injecting, during the scan, gadolinium, a nontoxic contrast agent that brightens signal intensities and is especially useful in looking at vascularity. T1-weighted images are produced by using the short time to echo, the interval between the delivery of the radio pulse and the receipt of the signal, and repetition time (TR), the time between successive pulse sequences on the same slice (Juerchott et al., 2018; Mendes et al., 2020; Whaites, 2007).

Magnetic resonance imaging was shown to be a feasible system for the detection and description of AP, in comparison to CBCT, in a pilot study on 34 periapical lesions, the scans comprised a high-resolution multi-slice acquisition with T1- and T2-weighted contrast, with a scan time ranging from 9:06 min for T1weighted, to 5:43 min for T2 weighted. In detail, T1weighted images provide clear diagnostic information on the same lesions visible on CBCT (Geibel et al., 2015). In MRI the contrast between the lesions and the surrounding bone is inverted: while highly

mineralized structures are bright on CBCT images, they appear as signal voids in the respective MRI scan. When directly compared, AP lesions are more heterogeneous and detailed in MRI images, than in CBCT, without the interference of artefacts. The cortical bone and teeth are identified by contrast with the surrounding soft tissue (mucosa, muscle and salivary glands) and bone marrow (high fat content), (Geibel et al., 2015).

Further, MRI identifies the fluids (hypointense T1-weighted images and hyperintense on T2-weighted images) and the fibrous tissue (isointense on T1- and T2-weighted images) within a lesion. The characterisation of the lesions resulted even superior in the T2-weighted images, with respect to the T1 (Geibel et al., 2015).

Importantly, apical lesions tend to appear larger than in CBCT. Once MRI imaging was shown to be suitable to diagnose periapical lesions in the jaws, and sensible enough to further define their content, it was demonstrated that the exam can be used to differentiate periapical cysts

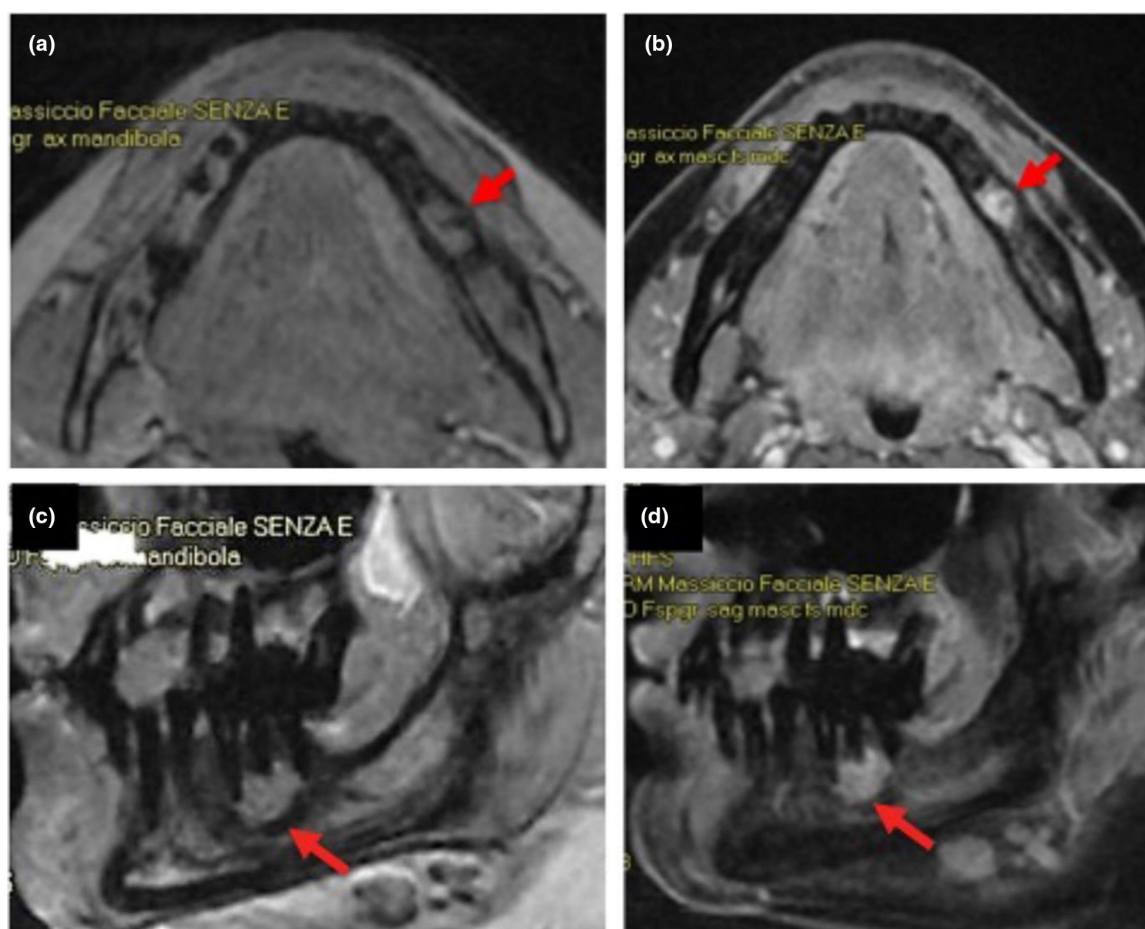


FIGURE 7 Granuloma of the mandible in correspondence with the lower left first molar and the second premolar (arrow). Axial T2-WI with homogeneous low signal intensity (SI) (a); axial T1-WI after contrast agent administration with high homogeneous global enhancement of the lesion (b); sagittal T1-WI with homogeneous low-intermediate SI and absence of low-intensity outline (c); sagittal T1-WI after contrast agent administration with high homogeneous global enhancement of the lesion (d). (Courtesy of Dr. G Lizio & Prof. GA Pelliccioni).

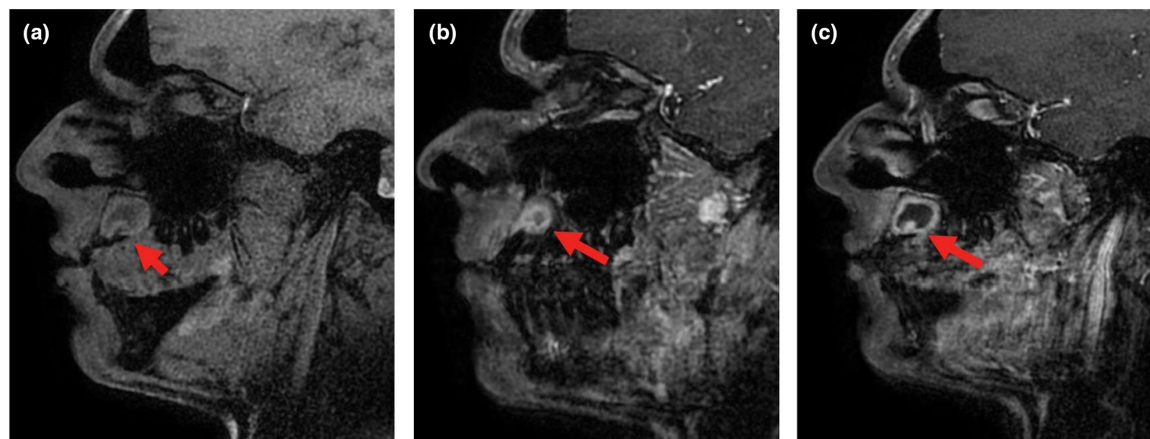


FIGURE 8 Radicular cyst of the maxillary bone in correspondence with the upper right central, lateral incisors and canine (arrow). Sagittal T1-WI with hypointense signal from the core (internal fluid) in comparison with that from the external fibrous-epithelial capsule (a); sagittal T2-WI with inverted contrast with respect to the sagittal T1-WI (b). Both images (a and b) show low-intensity outlines and clear lesion margins; sagittal T1-WI after contrast agent injection with high hyperintensity if the signal from the peripheral wall and hypointensity of the inner part (c). (Courtesy of Dr. G Lizio & Prof. GA Pelliccioni).

from granulomas in three consecutive reports based on the application of fat-saturated T2-weighted images, non-contrast-enhanced T1-weighted images T1wFS with and without fat saturation (T1w/T1wFS) and contrast-enhanced fat-saturated T1-weighted images (Geibel et al., 2017; Juerchott et al., 2018; Lizio et al., 2018).

Using what seem the most reliable MRI parameters, granulomas and cysts can be identified as follows: Granuloma is a lesion with (1) low to intermediate SI, respectively, in T1- and T2-weighted images; (2) absence of a low-intensity outline (LIO); (3) unclear margins; (4) homogeneous signal (SH); (5) global contrast medium distribution pattern. Cysts, on the other hand, are a lesion showing: (1) high to high-intermediate SI on T2-weighted images, (indicative of the presence of internal fluids); (2) presence of LIO, (indicative of the presence of a fibrous capsule); (3) clear margins; (4) nonhomogeneous signal; (5) peripheral thin/peripheral thick contrast agent distribution pattern, indicative of the presence of an epithelial wall (Lizio et al., 2018), (Figures 7 and 8).

When an infective lesion of the jaws spreads out to the bone and the corresponding soft tissues, degenerating into osteomyelitis, MRI becomes an elective diagnostic technique (DelBalso, 1995).

CONCLUSION AND FUTURE DIRECTIONS

Considering the important advances in imaging of periapical lesions and the availability of multiple systems, the key point is the training and the calibration of the operators. A prepared and trained clinician can now use multimodular assessments to obtain the essential data on periapical

lesions. Some information can be achieved using DPT, in certain areas of the mouth, provided a certain degree of calibration has been undertaken. PRs are mostly reliable as a routine examination and can be still used successfully, while CBCT represents, to date, the only system that ensures the early and predictable detection of all periapical lesions in the jaws. The only risk of CBCT examinations is represented by the possible false positives, mostly related to the lack of adequate training and to the tendency for the clinician to read the PDL coordinates with the same attitude used when viewing PRs. Limited FOV CBCT is therefore replacing PR as a good standard and will always be the first move towards a diagnostic approach.

Volume calculation being mostly semiautomated will soon succeed in linear measurements creating a new standardised method for evaluating the size of the lesions and, consequently, endodontic outcomes.

Pioneering research on artificial intelligence is slowly progressing in the detection of periapical radiolucencies on DPTs, PRs and CBCTs, however, with promising results. Deep learning algorithms and convolutional neuronal networks are only few of the tested artificial intelligence systems in the field of Endodontics, that have reached similar or even more accurate results when compared to human evaluations (Ekert et al., 2019; Endres et al., 2020; Li et al., 2022; Pauwels et al., 2021; Setzer et al., 2020). Larger sample sizes are needed to further validate these protocols.

Improving the understanding of the features of AP (vascularity, liquid content, degrees of turbidity, presence of fibrous tissues, abscesses and sinus tracts), that may drive towards a more accurate definition of a lesion, at present time may be obtained either with US imaging and CPD or with MRI, complemented by a contrast

medium. Both exams, in comparison to the clinical standard, may enable pre-interventional tissue characterisation, and incorporating them in the endodontic assessment phase represents an additional value because ultrasonography and MRI can be predictably used when other differential diagnosis of lesions within the maxillary bones become important. Another advantage, coming from these advanced techniques, is that they entail a lower biological risk since USI uses ultrasounds and MRI uses radio waves, and this is an important consideration as they have to be used in conjunction with a CBCT.

Difficulties in using ultrasounds are due to the impossibility to relate a given image to a specific tooth, or group of teeth, once the exam is completed. Disadvantages of MRI are represented by the cost and availability of the device, long acquisition time of the scans and limitations in the use of the exam to patients not carrying metals, last, depending on the apparatuses, claustrophobia of the patient is a strong contraindication. Most importantly, the learning curve required to use and interpret MRI and USI at their best, needs attention.

However, future developments, including dedicated US probes for echography, wireless coils, dental coils and position systems and reduced scan times for MRI may lead to a multimodular diagnostic system that will implement the information necessary to approach the most important clinical questions, when needed.

AUTHOR CONTRIBUTIONS

Elisabetta Cotti: Conceptualization, writing, review and editing (lead). **Elia Schirru:** Writing, review and editing.

CONFLICT OF INTEREST

The authors deny any conflict of interest related to this article.

ETHICAL APPROVAL

The article is a review and did not involve human participants. It therefore complies with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ORCID

Elisabetta Cotti  <https://orcid.org/0000-0002-8314-5410>

REFERENCES

- Abbott, P.V. (2004) Classification, diagnosis and clinical manifestations of apical periodontitis. *Endodontic Topics*, 8, 36–54.
- Abella, F., Patel, S., Duran-Sindreu, F., Mercadé, M., Bueno, R. & Roig, M. (2012) Evaluating the periapical status of teeth with irreversible pulpitis by using cone-beam computed tomography scanning and periapical radiographs. *Journal of Endodontics*, 38, 1588–1591.
- Ahlowalia, M.S., Patel, S., Anwar, H.M.S., Cama, G., Austin, R.S., Wilson, R. et al. (2013) Accuracy of CBCT for volumetric measurement of simulated periapical lesions. *International Endodontic Journal*, 46, 538–546.
- Auer, L.M. & Van Velthoven, V. (1990) *Intraoperative ultrasound imaging in neurosurgery: comparison with CT and MRI*. Berlin; New York: Springer-Verlag.
- Barnett, C.W., Glickman, G.N., Umoren, M. & Jalali, P. (2018) Interobserver and intraobserver reliability of cone-beam computed tomography in identification of apical periodontitis. *Journal of Endodontics*, 44, 938–940.
- Bender, I.B. & Seltzer, S. (1961) Roentgenographic and direct observation of experimental lesions in bone: II. *The Journal of the American Dental Association*, 62, 708–716.
- Bornstein, M.M., Bingisser, A.C., Reichart, P.A., Sendi, P., Bosshardt, D.D. & von Arx, T. (2015) Comparison between radiographic (2-dimensional and 3-dimensional) and histologic findings of periapical lesions treated with apical surgery. *Journal of Endodontics*, 41, 804–808.
- Bose, R., Nummikoski, P. & Hargreaves, K. (2009) A retrospective evaluation of radiographic outcomes in immature teeth with necrotic root canal systems treated with regenerative endodontic procedures. *Journal of Endodontics*, 35, 1343–1349.
- Boubaris, M., Chan, K.L., Zhao, W., Cameron, A., Sun, J., Love, R. et al. (2021) A novel volume-based cone-beam computed tomographic periapical index. *Journal of Endodontics*, 47, 1308–1313.
- Brown, J., Jacobs, R., Levring Jäghagen, E., Lindh, C., Baksi, G., Schulze, D. et al. (2014) Basic training requirements for the use of dental CBCT by dentists: a position paper prepared by the European Academy of DentoMaxilloFacial Radiology. *Dento Maxillo Facial Radiology*, 43, 20130291.
- Brynnolf I. (1967) *A histological and roentgenological study of the periapical region of human upper incisors*. Odontologisk Revy. Suppl.
- Chang, L., Umoren, M., Augsburg, R.A., Glickman, G.N. & Jalali, P. (2020) Periradicular lesions in cancellous bone can be detected radiographically. *Journal of Endodontics*, 46, 496–501.
- Cotti, E. (2010) Advanced techniques for detecting lesions in bone. *Dental Clinics*, 54, 215–235.
- Cotti, E., Campisi, G., Garau, V. & Puddu, G. (2002) A new technique for the study of periapical bone lesions: ultrasound real time imaging. *International Endodontic Journal*, 35, 148–152.
- Cotti, E., Campisi, G., Ambu, R. & Dettori, C. (2003) Ultrasound real-time imaging in the differential diagnosis of periapical lesions. *International Endodontic Journal*, 36, 556–563.
- Cotti, E., Musu, D., Goddi, A., Dettori, C., Campisi, G. & Shemesh, H. (2019) Ultrasound examination to visualize and trace sinus tracts of endodontic origin. *Journal of Endodontics*, 45, 1184–1191.
- Da Silveira, P.F., Fontana, M.P., Oliveira, H.W., Vizzotto, M.B., Montagner, F., Silveira, H.L. et al. (2015) CBCT-based volume of simulated root resorption–influence of FOV and voxel size. *International Endodontic Journal*, 48, 959–965.
- Davies, A., Mannocci, F., Mitchell, P., Andiappan, M. & Patel, S. (2015) The detection of periapical pathoses in root filled teeth

- using single and parallax periapical radiographs versus cone beam computed tomography—a clinical study. *International Endodontic Journal*, 48, 582–592.
- de Moraes, A.L.G., de Alencar, A.H.G., de Araújo Estrela, C.R., Decurcio, D.A. & Estrela, C. (2016) Working length determination using cone-beam computed tomography, periapical radiography and electronic apex locator in teeth with apical periodontitis: a clinical study. *Iranian Endodontic Journal*, 11, 164–168.
- DelBalso, A.M. (1995) Lesions of the jaws. *Seminars in Ultrasound, CT and MRI*, 16(6), 487–512.
- Ekert, T., Krois, J., Meinhold, L., Elhennawy, K., Emara, R., Golla, T. et al. (2019) Deep learning for the radiographic detection of apical lesions. *Journal of Endodontics*, 45, 917–922.
- Endres, M.G., Hillen, F., Salloumis, M., Sedaghat, A.R., Niehues, S.M., Quatela, O. et al. (2020) Development of a deep learning algorithm for periapical disease detection in dental radiographs. *Diagnostics*, 10, 430.
- Esposito, S., Cardaropoli, M. & Cotti, E. (2011) A suggested technique for the application of the cone beam computed tomography periapical index. *Dento Maxillo Facial Radiology*, 40, 506–512.
- Esposito, S.A., Huybrechts, B., Slagmolen, P., Cotti, E., Coucke, W., Pauwels, R. et al. (2013) A novel method to estimate the volume of bone defects using cone-beam computed tomography: an in vitro study. *Journal of Endodontics*, 39, 1111–1115.
- Estrela, C., Bueno, M.R., Azevedo, B.C., Azevedo, J.R. & Pécora, J.D. (2008) A new periapical index based on cone beam computed tomography. *Journal of Endodontics*, 34, 1325–1331.
- Farman, A.G. & Farman, T.T. (2005) A comparison of 18 different x-ray detectors currently used in dentistry. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontology*, 99, 485–489.
- Fujita, M., Matsuzaki, H., Yanagi, Y., Hara, M., Katase, N., Hisatomi, M. et al. (2013) Diagnostic value of MRI for odontogenic tumours. *Dento Maxillo Facial Radiology*, 42, 20120265.
- Geibel, M.A., Schreiber, E.S., Bracher, A.K., Hell, E., Ulrici, J., Sailer, L.K. et al. (2015) Assessment of apical periodontitis by MRI: a feasibility study. *Röfo*, 187, 269–275.
- Geibel, M.A., Schreiber, E., Bracher, A.K., Hell, E., Ulrici, J., Sailer, L.K. et al. (2017) Characterisation of apical bone lesions: comparison of MRI and CBCT with histological findings—a case series. *European Journal of Oral Implantology*, 10, 197–211.
- Ghorayeb, S.R., Bertoncini, C.A. & Hinders, M.K. (2008) Ultrasonography in dentistry. *IEEE Transactions on Ultrasonics, Ferroelectrics, & Frequency Control*, 55, 1256–1266.
- Guo, J., Simon, J.H., Sedghizadeh, P., Soliman, O.N., Chapman, T. & Enciso, R. (2013) Evaluation of the reliability and accuracy of using cone-beam computed tomography for diagnosing periapical cysts from granulomas. *Journal of Endodontics*, 39, 1485–1490.
- Gupta, R. & Hasselgren, G. (2003) Prevalence of odontogenic sinus tracts in patients referred for endodontic therapy. *Journal of Endodontics*, 29, 798–800.
- Gupta, M., Das, D., Kapur, R. & Sibal, N. (2011) A clinical predicament—diagnosis and differential diagnosis of cutaneous facial sinus tracts of dental origin: a series of case reports. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*, 112, 132–136.
- Hofer, M. (2005) *Teaching manual of color duplex sonography*. Bern: Medidak Publishing GmbH, pp. 8–16.
- Ideo, F., Niazi, S., Mezzena, S., Mannocci, F. & Cotti, E. (2022) Prevalence of apical periodontitis in patients with autoimmune diseases under immunomodulators: a retrospective cohort study. *Journal of Endodontics*, 48, 722–729.
- Juerchott, A., Pfefferle, T., Flechtenmacher, C., Mente, J., Bendszus, M., Heiland, S. et al. (2018) Differentiation of periapical granulomas and cysts by using dental MRI: a pilot study. *International Journal of Oral Science*, 10, 17.
- Kanagasingam, S., Lim, C.X., Yong, C.P., Mannocci, F. & Patel, S. (2017) Diagnostic accuracy of periapical radiography and cone beam computed tomography in detecting apical periodontitis using histopathological findings as a reference standard. *International Endodontic Journal*, 50, 417–426.
- Kruse, C., Spin-Neto, R., Reibel, J., Wenzel, A. & Kirkevang, L.L. (2017) Diagnostic validity of periapical radiography and CBCT for assessing periapical lesions that persist after endodontic surgery. *Dento Maxillo Facial Radiology*, 46, 20170210.
- Kruse, C., Spin-Neto, R., Wenzel, A., Vaeth, M. & Kirkevang, L.L. (2018) Impact of cone beam computed tomography on periapical assessment and treatment planning five to eleven years after surgical endodontic retreatment. *International Endodontic Journal*, 51, 729–737.
- Lauria, L.L., Curi, M.M., Chammas, M.C., Pinto, D.S. & Torloni, H. (1996) Ultrasonography evaluation of bone lesions of the jaw. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontology*, 82, 351–357.
- Li, S., Liu, J., Zhou, Z., Zhou, Z., Wu, X., Li, Y. et al. (2022) Artificial intelligence for caries and periapical periodontitis detection. *Journal of Dentistry*, 122, 104107.
- Liang, Y.H., Jiang, L., Gao, X.J., Shemesh, H., Wesselink, P.R. & Wu, M.K. (2014) Detection and measurement of artificial periapical lesions by cone-beam computed tomography. *International Endodontic Journal*, 47, 332–338.
- Little, R., Howell, J. & Nixon, P. (2020) COVID-19 and beyond: implications for dental radiography. *British Dental Journal*, 229, 105–109.
- Lizio, G., Salizzoni, E., Coe, M., Gatto, M.R., Asioli, S., Balbi, T. et al. (2018) Differential diagnosis between a granuloma and radicular cyst: effectiveness of magnetic resonance imaging. *International Endodontic Journal*, 51, 1077–1087.
- Lofthag-Hansen, S., Huuonen, S., Gröndahl, K. & Gröndahl, H.G. (2007) Limited cone-beam CT and intraoral radiography for the diagnosis of periapical pathology. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontology*, 103, 114–119.
- Márton, I.J. & Kiss, C. (2014) Overlapping protective and destructive regulatory pathways in apical periodontitis. *Journal of Endodontics*, 40, 155–163.
- Mendes, S., Rinne, C.A., Schmidt, J.C., Dagassan-Berndt, D. & Walter, C. (2020) Evaluation of magnetic resonance imaging for diagnostic purposes in operative dentistry—a systematic review. *Clinical Oral Investigations*, 24, 547–557.
- Minami, M., Kaneda, T., Ozawa, K., Yamamoto, H., Itai, Y., Ozawa, M. et al. (1996) Cystic lesions of the maxillomandibular region: MR imaging distinction of odontogenic keratocysts and ameloblastomas from other cysts. *AJR. American Journal of Roentgenology*, 166, 943–949.

- Mostafapoor, M. & Hemmatian, S. (2022) Evaluation of the accuracy values of cone-beam CT regarding apical periodontitis: a systematic review and meta-analysis. *Oral Radiology*, 38, 309–314.
- Musu, D., Rossi-Fedele, G., Campisi, G. & Cotti, E. (2016) Ultrasonography in the diagnosis of bone lesions in the jaws: a systematic review. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology*, 122, 19–29.
- Nair, P.N. (1998) New perspectives on radicular cysts: do they heal? *International Endodontic Journal*, 31, 155–160.
- Nair, P.N., Pajarola, G. & Luder, H.U. (2002) Ciliated epithelium-lined radicular cysts. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontology*, 94, 485–493.
- Nair, P.N., Sundqvist, G. & Sjögren, U. (2008) Experimental evidence supports the abscess theory of development of radicular cysts. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontology*, 106, 294–303.
- Nardi, C., Calistri, L., Pradella, S., Desideri, I., Lorini, C. & Colagrande, S. (2017) Accuracy of orthopantomography for apical periodontitis without endodontic treatment. *Journal of Endodontics*, 43, 1640–1646.
- Natanasabapathy, V., Arul, B., Mishra, A., Varghese, A., Padmanaban, S., Elango, S. et al. (2021) Ultrasound imaging for the differential diagnosis of periapical lesions of endodontic origin in comparison with histopathology – a systematic review and meta-analysis. *International Endodontic Journal*, 54(5), 693–711.
- Nejaim, Y., Gomes, A.F., Silva, E.J.N.L.D., Groppo, F.C. & Haiter Neto, F. (2016) The influence of number of line pairs in digital intra-oral radiography on the detection accuracy of horizontal root fractures. *Dental Traumatology*, 32, 180–184.
- Ng, Y.L., Mann, V. & Gulabivala, K. (2011) A prospective study of the factors affecting outcomes of nonsurgical root canal treatment: part 1: periapical health. *International Endodontic Journal*, 44, 583–609.
- Ørstavik, D., Kerekes, K. & Eriksen, H.M. (1986) The periapical index: a scoring system for radiographic assessment of apical periodontitis. *Dental Traumatology*, 2(1), 20–34.
- Özen, T., Kamburoğlu, K., Cebeci, A.R.I., Yüksel, S.P. & Paksoy, C.S. (2009) Interpretation of chemically created periapical lesions using 2 different dental cone-beam computerized tomography units, an intraoral digital sensor, and conventional film. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontology*, 107, 426–432.
- Patel, S. & Harvey, S. (2021) Guidelines for reporting on CBCT scans. *International Endodontic Journal*, 54, 628–633.
- Patel, S., Dawood, A., Mannocci, F., Wilson, R. & Pitt Ford, T. (2009) Detection of periapical bone defects in human jaws using cone beam computed tomography and intraoral radiography. *International Endodontic Journal*, 42, 507–515.
- Patel, S., Dawood, A., Whaites, E. & Pitt Ford, T. (2009) New dimensions in endodontic imaging: part 1. Conventional and alternative radiographic systems. *International Endodontic Journal*, 42, 447–462.
- Patel, S., Wilson, R., Dawood, A. & Mannocci, F. (2012) The detection of periapical pathosis using periapical radiography and cone beam computed tomography—Part 1: pre-operative status. *International Endodontic Journal*, 45, 702–710.
- Patel, S., Brown, J., Semper, M., Abella, F. & Mannocci, F. (2019) European Society of Endodontology position statement: use of cone beam computed tomography in Endodontics: European Society of Endodontology (ESE) developed by. *International Endodontic Journal*, 52, 1675–1678.
- Patel, S., Puri, T., Mannocci, F. & Navai, A. (2021) Diagnosis and management of traumatic dental injuries using intraoral radiography and cone-beam computed tomography: an in vivo investigation. *Journal of Endodontics*, 47, 914–923.
- Pauwels, R., Brasil, D.M., Yamasaki, M.C., Jacobs, R., Bosmans, H., Freitas, D.Q. et al. (2021) Artificial intelligence for detection of periapical lesions on intraoral radiographs: comparison between convolutional neural networks and human observers. *Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology*, 131, 610–616.
- Pope, O., Sathorn, C. & Parashos, P. (2014) A comparative investigation of cone-beam computed tomography and periapical radiography in the diagnosis of a healthy periapex. *Journal of Endodontics*, 40, 360–365.
- Ricucci, D., Loghin, S., Siqueira, J.F., Jr. & Abdelsayed, R.A. (2014) Prevalence of ciliated epithelium in apical periodontitis lesions. *Journal of Endodontics*, 40, 476–483.
- Ricucci, D., Loghin, S., Gonçalves, L.S., Rôças, I.N. & Siqueira, J.F., Jr. (2018) Histobacteriologic conditions of the apical root canal system and periapical tissues in teeth associated with sinus tracts. *Journal of Endodontics*, 44, 405–413.
- Ricucci, D., Rôças, I.N., Hernández, S. & Siqueira, J.F., Jr. (2020) “True” Versus “Bay” apical cysts: clinical, radiographic, histopathologic, and histobacteriologic features. *Journal of Endodontics*, 46, 1217–1227.
- Rosenberg, P.A., Frisbie, J., Lee, J., Lee, K., Frommer, H., Kottal, S. et al. (2010) Evaluation of pathologists (histopathology) and radiologists (cone beam computed tomography) differentiating radicular cysts from granulomas. *Journal of Endodontics*, 36, 423–428.
- Sebring, D., Kvist, T., Buhlin, K., Jonasson, P., EndoReCo & Lund, H. (2021) Calibration improves observer reliability in detecting periapical pathology on panoramic radiographs. *Acta Odontologica Scandinavica*, 79, 554–561.
- Sebring, D., Buhlin, K., Norhammar, A., Rydén, L., Jonasson, P., EndoReCo et al. (2022) Endodontic inflammatory disease: a risk indicator for a first myocardial infarction. *International Endodontic Journal*, 55, 6–17.
- Segato, A.V.K., Piasecki, L., Nuñovero, M.F.I., da Silva Neto, U.X., Westphalen, V.P.D., Gambarini, G. et al. (2018) The accuracy of a new cone-beam computed tomographic software in the preoperative working length determination ex vivo. *Journal of Endodontics*, 44, 1024–1029.
- Segura-Egea, J.J., Martín-González, J. & Castellanos-Cosano, L. (2015) Endodontic medicine: connections between apical periodontitis and systemic diseases. *International Endodontic Journal*, 48, 933–951.
- Setzer, F.C., Shi, K.J., Zhang, Z., Yan, H., Yoon, H., Mupparapu, M. et al. (2020) Artificial intelligence for the computer-aided detection of periapical lesions in cone-beam computed tomographic images. *Journal of Endodontics*, 46, 987–993.
- Shemesh, A., Yitzhak, A., Itzhak, J.B., Azizi, H. & Solomonov, M. (2019) Ludwig angina after first aid treatment: possible etiologies and prevention—case report. *Journal of Endodontics*, 45, 79–82.
- Shoha, R.R., Dowson, J. & Richards, A.G. (1974) Radiographic interpretation of experimentally produced bony lesions. *Oral Surgery, Oral Medicine, and Oral Pathology*, 38, 294–303.

- Shrout, M.K., Hall, J.M. & Hildebolt, C.E. (1993) Differentiation of periapical granulomas and radicular cysts by digital radiometric analysis. *Oral Surgery, Oral Medicine, and Oral Pathology*, 76, 356–361.
- Simon, J.H., Enciso, R., Malfaz, J.M., Roges, R., Bailey-Perry, M. & Patel, A. (2006) Differential diagnosis of large periapical lesions using cone-beam computed tomography measurements and biopsy. *Journal of Endodontics*, 32, 833–837.
- Siqueira, J.F., Antunes, H.S., Perez, A.R., Alvez, F.R.F., Midala, I., Silva, E.J.N.L. et al. (2020) The apical root canal system of teeth with posttreatment apical periodontitis: correlating microbiologic, tomographic and histopathologic findings. *Journal of Endodontics*, 46, 1195–1203.
- Sisli, S.N., Yilmaz, B., Özpolat, Z. & Gülşahi, K. (2021) Comparative analysis of different periapical index systems used in cone-beam computed tomography. *Australian Endodontic Journal*, 47, 401–407.
- Slutzky-Goldberg, I., Tsisis, I., Slutzky, H. & Heling, I. (2009) Odontogenic sinus tracts: a cohort study. *Quintessence International*, 40, 13–18.
- Sönmez, G., Koç, C. & Kamburoğlu, K. (2018) Accuracy of linear and volumetric measurements of artificial ERR cavities by using CBCT images obtained at 4 different voxel sizes and measured by using 4 different software: an ex vivo research. *Dento Maxillo Facial Radiology*, 47, 20170325.
- Stavropoulos, A. & Wenzel, A. (2007) Accuracy of cone beam dental CT, intraoral digital and conventional film radiography for the detection of periapical lesions. An ex vivo study in pig jaws. *Clinical Oral Investigations*, 11, 101–106.
- Tibúrcio-Machado, C.S., Michelon, C., Zanatta, F.B., Gomes, M.S., Marin, J.A. & Bier, C.A. (2021) The global prevalence of apical periodontitis: a systematic review and meta-analysis. *International Endodontic Journal*, 54, 712–735.
- Torabinejad, M., Rice, D.D., Maktabi, O., Oyoyo, U. & Abramovitch, K. (2018) Prevalence and size of periapical radiolucencies using cone-beam computed tomography in teeth without apparent intraoral radiographic lesions: a new periapical index with a clinical recommendation. *Journal of Endodontics*, 44, 389–394.
- Trope, M., Pettigrew, J., Petras, J., Barnett, F. & Tronstad, L. (1989) Differentiation of radicular cyst and granulomas using computerized tomography. *Dental Traumatology*, 5, 69–72.
- Tsai, P., Torabinejad, M., Rice, D. & Azevedo, B. (2012) Accuracy of cone-beam computed tomography and periapical radiography in detecting small periapical lesions. *Journal of Endodontics*, 38, 965–970.
- Unetsubo, T.H., Konouchi, Y., Yanagi, J., Murakami, M., Fujii, H.M. et al. (2009) Dynamic contrast-enhanced magnetic resonance imaging for estimating tumor proliferation and microvessel density of oral squamous cell carcinomas. *Oral Oncology*, 45, 621–626.
- Üstün, Y., Aslan, T., Şekerci, A.E. & Sağsen, B. (2016) Evaluation of the reliability of cone-beam computed tomography scanning and electronic apex locator measurements in working length determination of teeth with large periapical lesions. *Journal of Endodontics*, 42, 1334–1337.
- Venskutonis, T., Plotino, G., Tocci, L., Gambarini, G., Maminkas, J. & Juodzbals, G. (2015) Periapical and endodontic status scale based on periapical bone lesions and endodontic treatment quality evaluation using cone-beam computed tomography. *Journal of Endodontics*, 41, 190–196.
- Weber, M., Ries, J., Büttner-Herold, M., Geppert, C.I., Kesting, M. & Wehrhan, F. (2019) Differences in inflammation and bone resorption between apical granulomas, radicular cysts, and dentigerous cysts. *Journal of Endodontics*, 45, 1200–1208.
- Whaites, E. (2007) *Essentials of dental radiology and radiography*, 4th edition. Oxford, UK: Elsevier.
- Yeni, Y.N., Christopherson, G.T., Neil Dong, X., Kim, D.G. & Fyhrie, D.P. (2005) Effect of microcomputed tomography voxel size on the finite element model accuracy for human cancellous bone. *Journal of Biomechanical Engineering*, 127, 1–8.
- Yilmaz, F., Kamburoğlu, K. & Şenel, B. (2017) Endodontic working length measurement using cone-beam computed tomographic images obtained at different voxel sizes and field of views, periapical radiography, and apex locator: a comparative ex vivo study. *Journal of Endodontics*, 43, 152–156.

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