



ORIGINAL ARTICLE

# Comparative analysis of prevalence of apical periodontitis in smokers and non-smokers using cone-beam computed tomography

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## KEYWORDS

Apical periodontitis;  
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**Abstract** *Objective:* The aim of this study was to compare the prevalence and size of periapical lesions among smokers and non-smokers using cone-beam computed tomography (CBCT).

*Materials and methods:* Retrievable CBCT datasets for 46 male patients  $\geq 18$  years during a consecutive period from 2008 to 2016 were examined. The medical, smoking history and other clinical findings (signs of previous dental trauma; Decayed Missing Filled Teeth (DMFT) scores; the percentage of root filled teeth; and oral hygiene status) were obtained. Periapical status of all included teeth was assessed by CBCT images. Statistical analysis was conducted using *t*-test, Pearson correlation and multiple regression.

*Results:* The prevalence of apical periodontitis was 13.93% in smokers and 14.26% in non-smokers with no significant difference ( $p = 0.936$ ). The mean of the average size of lesions between the two groups were almost comparable, 3.50 mm in smokers and 2.89 mm in non-smokers

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( $p = 0.567$ ). Pearson correlation and multiple regression analysis showed that the percentage of lesion present and the average lesion size were not correlated to any independent variable.

*Conclusions:* While smoking is considered a risk factor for marginal periodontitis, there was no difference between smokers and non-smokers in terms of apical periodontitis.

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## 1. Introduction

Apical periodontitis (AP) is a function of local factors, systemic factors and host response. Local factors include infection, mechanical and chemical trauma (Graunaite et al., 2012). Periapical status can be affected by systemic diseases; such as diabetes mellitus (Segura-Egea et al., 2015), cardiovascular diseases (Caplan et al., 2006; Caplan et al., 2009; Cotti and Mercurio, 2015; Willershausen et al., 2009), and hypertension (Segura-Egea et al., 2011).

Smoking has been shown to cause an adverse effect on immunity. Tissue destruction occurs due to the effect of smoking on neutrophils and inflammatory mediators (Johnson and Guthmiller, 2007; Krall et al., 2006). Adaptive immunity is impaired by means of reduction of serum immunoglobulin G (IgG) (Graswinckel et al., 2004; Moszczynski et al., 2001), and changes in lymphocytes production and activity (Sopori and Kozak, 1998). Smoking-related effects also include decreased bone healing due to stimulation of osteoclasts (Cesar-Neto et al., 2006), reduced growth factors expression (Theiss et al., 2000), and reduced ability of angiogenesis (Johnson and Hill, 2004; Pinto et al., 2002).

Smoking is considered a risk factor for periodontitis (Bergström, 2006). It has been shown that periodontium is negatively affected by smoking. In addition to the negative impact of smoking on the host's response, it has been shown to alter the microflora (Johnson and Hill, 2004). Current evidence indicates that smoking is a significant factor in inflammation of the marginal periodontium (Johnson and Guthmiller, 2007; Johnson and Hill, 2004; Labriola et al., 2005); therefore, it was hypothesized that it would have a similar effect on apical periodontium.

Prevalence of periapical lesions in smokers compared to non-smokers has been previously investigated. Some studies found increased prevalence among smokers (Correia-Sousaa et al., 2015; Kirkevang and Wenzel, 2003; Lopez-Lopez et al., 2012; Bukmir et al., 2016; Segura-Egea et al., 2011; Segura-Egea et al., 2008), while others found no significant association between smoking and apical periodontitis (Bahammam, 2012; Bergström et al., 2004; Rodriguez et al., 2013). However, all the aforementioned studies examined the periapical status using periapical or panoramic radiographs, which are both two-dimensional radiographs. Cone-beam computed tomography (CBCT), which provides images in the third dimension, has been found to be more accurate in detecting apical periodontitis (Dutra et al., 2016; Liang et al., 2014; Tsai et al., 2012), and able to detect smaller sized lesions compared to periapical radiographs (Tsai et al., 2012). To our knowledge, there is no published study that compares the prevalence of periapical lesions in smokers and non-smokers using CBCT.

Therefore, the aim of this study is to compare the prevalence, as well as the size of periapical lesions among smokers

and non-smokers using CBCT. The information obtained may help to clarify whether or not smoking is a risk factor for apical periodontitis, and thus is expected to be useful in understanding the immune response in periapical regions.

## 2. Materials and methods

This cross-sectional study was conducted in the College of Dentistry, King Saud University. The ethical committee in the College of Dentistry Research Center approved the study (FR 0219), the study was performed in accordance with the Declaration of Helsinki (2000), and informed consent was obtained from each patient. The CBCT data from the archives of the Radiology Department of King Saud University, College of Dentistry were used to obtain the study sample. The inclusion criteria were male patients  $\geq 18$  years with a retrievable CBCT dataset acquired during a consecutive period from January 2008 to March 2016 which had  $\geq 6$  teeth apices included in the dataset. The reasons for referral and types of treatment requested were not included in the data analysis. Based upon the findings of a pilot study, in order for the study to have a power of 0.9 (based on  $\alpha = 0.05$ ), the required minimum number of teeth in each group was calculated as 262. Patients who fulfilled the inclusion criteria were contacted and informed of the study, its aim, and the procedures to be conducted. Patients who agreed to participate were scheduled for a clinical examination, which was performed after they gave their written consent.

During the clinical examination, medical history, smoking history were obtained and the smoking history of the patient was identified (whether non-smoker, smoker [active, passive]). Patients were considered passive smokers if they were exposed to environmental tobacco smoke (ETS) for at least an hour per week. Because of lack of evidence on a well-established biological limit, this threshold was chosen arbitrary and matches the threshold used in a comparable large population study (Howard et al., 1998). Patients who were found to be smokers, were asked about the number of years of exposure prior to taking the CBCT. Other recorded clinical findings were: any signs of previous dental trauma; number of teeth; Decayed, Missing, and Filled Teeth (DMFT) index scores; and oral hygiene index (OHI) of the patient (Greene and Vermillion, 1964). According to the clinical examination findings, patients who required further dental treatments were referred to the needed specialty.

Patients who reported having any of the following diseases/conditions were excluded: hypertension, heart diseases, diabetes, endocrine diseases, kidney diseases, history of orthodontic surgery, or received any dental trauma. Moreover, the CBCT images used in the study had been obtained by either one of the following CBCT devices: Carestream 9300 (Carestream, Rochester, New York, USA) with a thin-film transistors detector having a size of  $17 \times 13.5$  cm ( $n = 448$

teeth) or ProMax 3D Max (Planmeca, Helsinki, Finland) with a flat panel detector having a size of  $23 \times 26$  cm ( $n = 313$  teeth). Both devices have adjustable field of views (FOV), and the datasets used in the study were acquired with variable FOVs. The reconstructed voxels were isotropic with sizes ranging from 0.09 mm to 0.3 mm, depending on the reason for the acquisition of the CBCT images. The milliampere, Kilovolt Peak (kVp), and exposure time was also variable due to the different quality requirements of the various diagnostic tasks for which the images had been originally requested.

The CBCT datasets were converted to digital imaging and communications in medicine (DICOM) format and imported into a 3D image reformatting software (OnDemand Software, version 1.0, Cybermed Inc., Seoul, South Korea) for reformatting, viewing and recording of measurements. The images were viewed on a 22" flat panel liquid crystal display (LCD) color monitor (Dell P2210, Round Rock Texas, USA) in landscape mode. The specifications of the monitor were as follows: aspect ratio: 16:10; screen resolution  $1680 \times 1050$  (highest, recommended) (calculated pixel size: 0.282 mm); color resolution: 32 bit; luminance  $250 \text{ Cd/m}^2$ ; contrast ratio (Static): 1000:1.

The 3D module of the OnDemand software was used to reformat the images, and the examiners were permitted to adjust the image zoom level, contrast, and density for optimal clarity. The examiners were an Oral and Maxillofacial Radiologist (OMFR) with 8 years experience in reformatting and interpreting CBCT images and a consultant endodontist calibrated with the OMFR in interpretation of the CBCT images. The examiners were blinded to the patients' smoking status.

Each tooth root was examined individually by obtaining transverse cross-sectional images and parasagittal images parallel to the long axis of the root. The thinnest CBCT slice thickness possible was used. All transverse cross-sectional images through the mesio-distal thickness, and parasagittal sections throughout the bucco-lingual width of the tooth were examined for each root, and the images were examined for the presence of apical periodontitis. A periapical lesion was diagnosed when disruption of the lamina dura was detected and the hypodense area associated with the radiographic apex was  $\geq 0.5$  mm or approximately twice the width of the periodontal ligament space and not parallel to the root outline (Abella et al., 2012; Zhang et al., 2015), on 1 or more root(s) on at least 2 planes of the CBCT images.

In the presence of a periapical lesion, the maximum diameter of the lesion was recorded. Each examiner interpreted the images independently and evaluated each tooth once. A consensus was reached in the event of any disagreement. Presence of a periapical lesion at any root was considered as presence of a lesion at the tooth, and in cases of multiple lesions being present, the largest diameter of the lesions was recorded for the lesion size at that tooth. The presence or absence of endodontic filling was also determined for each tooth from the CBCT images. Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) software, version 20 (IBM, Chicago, United States). Independent *t*-test was used to test the difference between smokers and non-smokers with regards to the percentage of periapical lesions present, the average size of lesions, DMFT, and OHI scores. Parametric data were expressed as the mean and standard deviation (SD). The level of significance was set at  $P \leq 0.05$ . Pearson correlation analysis and multiple regression analysis (stepwise method and Enter method) were used to test the correlation

between age, DMFT, OHI, and number of years of smoke exposure before CBCT with percentage of lesions present and average lesion size.

### 3. Results

A total of 76 patients were included in the study. However, 30 patients were excluded due to the following reasons; presence of systemic disease ( $n = 15$ ), history of previous trauma ( $n = 12$ ), artifacts in the CBCT images ( $n = 1$ ), and suspected fibro-osseous disease ( $n = 2$ ). Thus, the number of patients in the study were 46; of which 19 were smokers (41.3%) and 27 were non-smokers (58.7%). All permanent teeth visible in the CBCT datasets were included in the study, the exclusion criteria for CBCT datasets or individual teeth are listed in Table 1.

Age, DMFT, the percentage of root filled teeth, and oral hygiene scores were found to be similar between the two groups (Table 2). The mean age was  $30.2 \pm 12.2$  years for smokers, and  $32.8 \pm 14.1$  years for non-smokers.

The CBCT datasets of patients included 761 teeth. After excluding 161 teeth (Table 1), 327 teeth (54.5%) were examined in the smokers' group and 273 (45.5%) teeth in the non-smokers' group. The prevalence of apical periodontitis was 13.9% in smokers and 14.3% in non-smokers with no significant difference ( $p = 0.936$ ). The mean of the average size of lesions between the two groups were almost comparable, 3.50 mm in smokers and 2.89 mm in non-smokers ( $p = 0.567$ ). In addition, the number of smoking years before taking CBCT was not correlated with either the percentage nor the size of the lesions present.

Using Pearson correlation, the percentage of the lesions present and the average lesion size were found to have no correlation with the other independent variables (Tables 3 and 4). In addition, multiple regression analysis (Table 5) showed no significant relationship between percentage of lesions present or average lesion size and number of years of smoke exposure, OHI, and DMFT, with the exception of a significant correlation found between DMFT and percentage of lesions ( $p$ -value = 0.045) no significant model was found (Table 6).

**Table 1** Causes of teeth exclusion.

	Number of teeth excluded
1. Bone dehiscence or fenestration over apex	18
2. Apex enclosed within thick maxillary sinus lining or thick nasal lining	53
3. Apex in contact with screw or degraded image because of screw artifact	2
4. Apex in contact with or within the inferior alveolar canal	8
5. Apex within palatal cleft	3
6. Impacted tooth	31
7. Apex in contact with impacted or unerupted tooth	15
8. Apex in contact with adjacent pericoronal lesion	5
9. Open apex	6
10. External apical root resorption	3
11. Images not clear	9

**Table 2** Mean and std. deviation of the percentage of lesions, average size of lesions, DMFT, and OHI score between smokers and non-smokers.

Variables	Smokers	Non-smokers	P-value
Percentage of lesions (%)	13.93 ± 15.04	14.26 ± 12.96	0.936
Average size of lesions (mm)	3.50 ± 0.75	2.89 ± 3.72	0.567
DMFT	12.32 ± 5.04	14.15 ± 7.40	0.355
OHI score (out of 3)	0.89 ± 0.51	1.04 ± 0.48	0.312
Percentage of root filled teeth	4.14 ± 8.13	5.71 ± 9.72	0.566

**Table 3** Pearson correlation between percentage of lesion present and each of the independent variables.

Percentage of lesions present	Pearson correlation	p-value
Number of smoke exposure years before CBCT	-0.13	0.389
DMFT	0.245	0.101
OHI score	0.165	0.273
Age	0.077	0.611
Percentage of root filled teeth	0.23	0.123

**Table 4** Pearson correlation between average lesion size and each of the independent variables.

Average lesion size	Pearson Correlation	P-Value
Number of smoke exposure years before CBCT	-0.083	0.585
DMFT	0.138	0.362
OHI score	0.262	0.079
Age	-0.092	0.545
Percentage of root filled teeth	0.092	0.542

**Table 5** Multiple regression for the percentage of lesions present and the independent variables (Enter method and Stepwise method).

Percentage of lesions present	B	P-value	Partial correlation	p-value	R	R-Square
Age	0	0.998	0	0.32	0.36	0.132
Number of smoke exposure years before CBCT	-0.265	0.403	-0.132			
OHI score	5.944	0.173	0.214			
DMFT	0.313	0.488	0.11			
Percentage of root filled teeth	0.276	0.375	0.14			

**Table 6** Multiple regression (Enter method) for the average lesion size and the independent variables.

Average lesion size	B	p-value	Partial correlation	p-value	R	R-Square
Age	-0.051	0.463	-0.162	0.336	0.36	0.128
Number of smoke exposure years before CBCT	-0.012	0.306	-0.024			
OHI score	1.996	0.881	0.275			
DMFT	0.094	0.078	0.128			

#### 4. Discussion

The aim of this cross-sectional study was to compare the prevalence and severity of apical periodontitis among smokers and non-smokers using CBCT images. No statistically significant difference between smokers and non-smokers was observed with regards to the presence of apical periodontitis and the average size of the periapical lesions. The present study's findings were in agreement with the findings of Bergström et al. (2004) and Bahammam (2012) who found no significant difference between smokers and nonsmokers with regards to presence of apical periodontitis.

The results of this study, however, were in contrast with those of other studies which found an association between the prevalence of apical periodontitis and smoking status (Correia-Sousaa et al., 2015; Kirkevang and Wenzel, 2003; Lopez-Lopez et al., 2012; Bukmir et al., 2016; Segura-Egea et al., 2011; Segura-Egea et al., 2008). Such difference is due the type of radiographs, panoramic radiographs were used to assess the periapical status by López-López et al. (2012) and Correia-Sousaa et al. (2015), while periapical radiographs were used by Segura-Egea et al. (2011, 2008). Bukmir et al. (2016) examined the periapical status using both panoramic and periapical radiographs. In the present study CBCT was used, which has been shown to be more accurate in detecting apical periodontitis compared to two-dimensional radiographs (Dutra et al., 2016; Liang et al., 2014; Tsai et al., 2012). Moreover, the present study excluded the confounding factors of systemic diseases and dental trauma, whereas previous studies did not, although it has been shown that periapical status can be affected by both (Caplan et al., 2006; Caplan et al., 2009; Cotti and Mercurio, 2015; Graunaite et al., 2012; Willershausen et al., 2009). Furthermore, in the current study, consensus of an oral and maxillofacial radiologist and an endodontist was used for determination of presence or absence of periapical periodontitis because previously published studies reported intra- and inter-observer reliabilities in interpreting CBCT images which were not excellent (Caplan et al., 2009; Correia-Sousaa et al., 2015; Bukmir et al., 2016).

The findings of this study were comparable with those of Rodriguez et al. (2013) who found a significant difference



between smokers and non-smokers with regards to presence of apical periodontitis, but after adjusting for the quality of root canal treatment, the difference was no longer significant. In this study, the percentage of root filled teeth and DMFT was found to be similar between the two groups. It is documented in the literature that the health of apical tissues is significantly affected by tooth-related factors, such as coronal restoration and quality of endodontic treatment (Gomes et al., 2015). Previous investigations, which found a significant difference in the presence of periapical lesions between smokers and non-smokers did not adjust for tooth-related factors, which might be another reason behind the variable results between the present study and other studies.

Smoking has been shown to affect healing (Pinto et al., 2002) and is also considered a risk factor for marginal periodontitis (Bergström, 2006). However, our results indicate that there is no difference in prevalence and size of periapical lesions between smokers and non-smokers. This may indicate different healing processes involved in marginal and apical periodontium.

In the present study, there was no difference between smokers and non-smokers with regard to percentage of root-filled teeth, DMFT, and OHI scores. Although other studies did not use the DMFT index used in this study, they found a correlation between the prevalence of apical periodontitis and variables related to this index's components. Correia-Sousa et al. (2015) and López-López et al. (2012) found increased prevalence of apical periodontitis in root filled teeth, which would be considered as 'Filled' in the DMFT index. Kirkevang and Wenzel (2003) demonstrated an association between apical periodontitis and secondary carious lesions, coronal fillings, and root fillings, which would be all counted in the DMFT index if used.

In the present study, prevalence of apical periodontitis in each group (smokers and non-smokers) was calculated as the percentage of teeth with such lesions, whereas previous studies calculated prevalence of apical periodontitis as the percentage of patients with such lesions (Lopez-Lopez et al., 2012; Segura-Egea et al., 2011; Segura-Egea et al., 2008). The percentage of teeth was considered in the present study, as opposed to the number of the patients, because it was considered that multiple teeth with periapical periodontitis in a single patient should have a higher impact on the statistical calculations than only one tooth. Calculating the prevalence of apical periodontitis as the percentage of patients with such lesions considers all patients with at least one lesion as having periapical periodontitis, and disregards the differences in percentage of lesions within patients, thus effectively disregarding relevant data. Another advantage of calculating the percentage of teeth, as opposed to percentage of patients, was that it allowed analysis of the correlation between presence of periapical periodontitis and tooth related factors, a correlation which was found to be statistically significant.

The present study included only males in the sample population because the prevalence of smoking among males in the Saudi population is ten times greater than females (World Health Organization, 2015). Therefore, it was considered difficult to recruit sufficient number of female smokers to provide the required subsample of females for a powerful statistical analysis. Therefore, to maintain the gender homogeneity of the study sample, only males were included. Also, the images used in the present study were acquired with variable FOVs

and voxel sizes ranging from 0.09 mm to 0.3 mm. The variation in such parameters was found in images of both study groups, and was not expected to be clinically significant because the minimum size of lesion which was considered 0.5 mm, and the parameters used have demonstrated spatial resolution adequate for the detection of objects of such size (Sonya et al., 2016).

One of the limitations of this study was the sample of patients which is confined to those attending dental clinics and who had a CBCT examination carried out rather than a random sample of the general population. It is conceivable that smokers in the general population who did not attend dental clinics may have different disease status than those attending dental clinics, and, thus, different prevalence of apical periodontitis. However, exposing randomly members of the general population to ionizing radiation for research purposes was considered unethical by the authors. Thus, this limitation is inherent in most studies utilizing ionizing radiation. Another limitation is that the sample was limited to males, for the reasons stated above. It is conceivable that hormonal differences between males and females may yield different results. A third limitation of this study was that, active and passive smokers were considered as one group in this study. Passive smokers should be considered as a separate group from active smokers because it is possible that the prevalence of apical periodontitis would be different between these groups. Further studies are needed to investigate the association between apical periodontitis and smoking on a larger and sub-grouped sample. Smokers can be further divided into heavy and light smokers. Furthermore, Hookah users can be considered as an independent group and compared to cigarette smokers' results.

The results of this study conclude that there is no significant difference between smokers and non-smokers with regard to the prevalence and size of apical periodontitis. Further studies are needed to compare the prevalence and severity in terms of size using CBCT after adjusting for tooth-related factors.

#### Conflict of Interest

We have no conflict of interest to declare.

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#### References

- 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. *J. Endod.* 38 (12), 1588–1591.

- Bahammam, L., 2012. Tobacco smoking and dental periapical condition in a sample of Saudi Arabian sub-population. *J. King Abdulaziz Univ.: Med. Sci.* 98 (285), 1–14.
- Bergström, J., Babcan, J., Eliasson, S., 2004. Tobacco smoking and dental periapical condition. *Eur J Oral Sci* 112 (2), 115–120.
- Bergström, J., 2006. Periodontitis and smoking: an evidence-based appraisal. *J. Evid. Based Dent. Pract.* 6 (1), 33–41.
- Bukmir, R.P., Grgic, J.M., Brumini, G., Spalj, S., Pezelj-Ribaric, S., Brekalo Prso, I., 2016. Influence of tobacco smoking on dental periapical condition in a sample of Croatian adults. *Wien. Klin. Wochenschr.* 128 (7–8), 260–265.
- Caplan, D.J., Chasen, J.B., Krall, E.A., et al, 2006. Lesions of endodontic origin and risk of coronary heart disease. *J. Dent. Res.* 85 (11), 996–1000.
- Caplan, D.J., Pankow, J.S., Cai, J., Offenbacher, S., Beck, J.D., 2009. The relationship between self-reported history of endodontic therapy and coronary heart disease in the Atherosclerosis Risk in Communities Study. *J. Am. Dent. Assoc.* 140 (8), 1004–1012.
- Cesar-Neto, J.B., Benatti, B.B., Sallum, E.A., et al, 2006. The influence of cigarette smoke inhalation and its cessation on the tooth-supporting alveolar bone: a histometric study in rats. *J. Periodontal Res.* 41 (2), 118–123.
- Correia-Sousaa, J., Madureira, A.R., Carvalho, M.F., Teles, A.M., Pina-Vaz, I., 2015. Apical periodontitis and related risk factors: Cross-sectional study. *Rev. Port. Estomatol. Med. Dent. Cir. Maxilofac.* 56 (4), 226–232.
- Cotti, E., Mercurio, G., 2015. Apical periodontitis and cardiovascular diseases: previous findings and ongoing research. *Int. Endod. J.* 48 (10), 926–932.
- Dutra, K.L., Haas, L., Porporatti, A.L., et al, 2016. Diagnostic accuracy of cone-beam computed tomography and conventional radiography on apical periodontitis: a systematic review and meta-analysis. *J. Endod.* 42 (3), 356–364.
- Gomes, A.C., Nejaim, Y., Silva, A.I., et al, 2015. Influence of endodontic treatment and coronal restoration on status of periapical tissues: a cone-beam computed tomographic study. *J. Endod.* 41 (10), 1614–1618.
- Graswinckel, J.E., Van Der Velden, U., Van Winkelhoff, A.J., Hoek, F.J., Loos, B.G., 2004. Plasma antibody levels in periodontitis patients and controls. *J. Clin. Periodontol.* 31 (7), 562–568.
- Graunaite, I., Lodiene, G., Maciulskiene, V., 2012. Pathogenesis of apical periodontitis: A literature review. *J. Oral. Maxillofac. Res.* 2 (4), e1.
- Greene, J.C., Vermillion, J.R., 1964. The simplified oral hygiene index. *J. Am. Dent. Assoc.* 68, 7–13.
- Howard, G., Wagenknecht, L.E., Burke, G.L., et al, 1998. Cigarette smoking and progression of atherosclerosis: The Atherosclerosis Risk in Communities (ARIC) Study. *JAMA* 279 (2), 119–124.
- Johnson, G.K., Guthmiller, J.M., 2007. The impact of cigarette smoking on periodontal disease and treatment. *Periodontol* 2000 (44), 178–194.
- Johnson, G.K., Hill, M., 2004. Cigarette smoking and the periodontal patient. *J. Periodontol.* 75 (2), 196–209.
- Kirkevang, L.L., Wenzel, A., 2003. Risk indicators for apical periodontitis. *Commun. Dent. Oral. Epidemiol.* 31 (1), 59–67.
- Krall, E.A., Abreu Sosa, C., Garcia, C., Nunn, M.E., Caplan, D.J., Garcia, R.I., 2006. Cigarette smoking increases the risk of root canal treatment. *J. Dent. Res.* 85 (4), 313–317.
- Labriola, A., Needleman, I., Moles, D.R., 2005. Systematic review of the effect of smoking on nonsurgical periodontal therapy. *Periodontol* 2000 (37), 124–137.
- 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. *Int. Endod. J.* 47 (4), 332–338.
- Lopez-Lopez, J., Jané-Salas, E., Martín-González, J., et al, 2012. Tobacco smoking and radiographic periapical status: a retrospective case-control study. *J. Endod.* 38 (5), 584–588.
- Moszczyński, P., Żabiński, Z., Rutowski, J., Słowiński, S., Tabarowski, Z., 2001. Immunological findings in cigarette smokers. *Toxicol. Lett.* 118 (3), 121–127.
- Pinto, J.R., Bosco, A.F., Okamoto, T., Guerra, J.B., Piza, I.G., 2002. Effects of nicotine on the healing of extraction sockets in rats. A histological study. *Braz. Dent. J.* 13 (1), 3–9.
- Rodriguez, F.R., Taner, B., Weiger, R., Walter, C., 2013. Is smoking a predictor of apical periodontitis? *Clin. Oral. Investig.* 17 (8), 1947–1955.
- Segura-Egea, J.J., Castellanos-Cosano, L., Velasco-Ortega, E., 2011. Relationship between smoking and endodontic variables in hypertensive patients. *J. Endod.* 37 (6), 764–767.
- Segura-Egea, J.J., Jiménez-Pinzón, A., Ríos-Santos, J.V., Velasco-Ortega, E., Cisneros-Cabello, R., Poyato-Ferrera, M.M., 2008. High prevalence of apical periodontitis amongst smokers in a sample of Spanish adults. *Int. Endod. J.* 41 (4), 310–316.
- Segura-Egea, J.J., Martín-González, J., Castellanos-Cosano, L., 2015. Endodontic medicine: connections between apical periodontitis and systemic diseases. *Int. Endod. J.* 48 (10), 933–951.
- Sonya, D., Davies, J., Lee Ford, N., 2016. A comparison of cone-beam computed tomography image quality obtained in phantoms with different fields of view, voxel size, and angular rotation for iCAT NG. *J. Oral Maxillofac. Radiol.* 4 (2), 31–39.
- Sopori, M.L., Kozak, W., 1998. Immunomodulatory effects of cigarette smoke. *J. Neuroimmunol.* 83 (1–2), 148–156.
- Theiss, S.M., Boden, S.D., Hair, G., Titus, L., Morone, M.A., Ugbo, J., 2000. The effect of nicotine on gene expression during spine fusion. *Spine (Phila Pa 1976)* 25 (20), 2588–2594.
- Tsai, P., Torabinejad, M., Rice, D., Azevedo, B., 2012. Accuracy of cone-beam computed tomography and periapical radiography in detecting small periapical lesions. *J. Endod.* 38 (7), 965–970.
- World Health Organization, 2015. WHO report on the global tobacco epidemic, Raising taxes on tobacco.
- Willershausen, B., Kasaj, A., Willershausen, I., et al, 2009. Association between chronic dental infection and acute myocardial infarction. *J. Endod.* 35 (5), 626–630.
- Zhang, M.M., Liang, Y.H., Gao, X.J., Jiang, L., Van der Sluis, L., Wu, M.K., 2015. Management of apical periodontitis: healing of post-treatment periapical lesions present 1 year after endodontic treatment. *J. Endod.* 41 (7), 1020–1025.