

# Differential Diagnosis of Large Periapical Lesions Using Cone-Beam Computed Tomography Measurements and Biopsy

James H.S. Simon, DDS,\* Reyes Enciso, PhD,<sup>†</sup> Jose-Maria Malfaz, DDS, MD, PhD,\*  
Ramon Roges, DDS,\* Michelle Bailey-Perry, RDA,<sup>†</sup> and Anish Patel, DMD\*

## Abstract

This study compared the differential diagnosis of large periapical lesions (granuloma versus cyst) to traditional biopsy using Cone Beam Computed Tomography (CBCT), the NewTom 3G. Large lesions were scanned and a preoperative diagnosis based on gray value measurements of the imaged lesion area was made. After surgery a biopsy report was obtained and compared to the CBCT diagnosis. In 13 out of 17 cases, the diagnosis coincided. In 4 out of 17 cases, the CBCT read cyst with the oral pathologist's diagnosis being granuloma. Thus, the CBCT may provide a more accurate diagnosis than biopsy and histology providing a diagnosis without invasive surgery and/or waiting a year to see if non-surgical therapy is effective. (*J Endod* 2006;32: 833–837)

## Key Words

Biopsy, cone beam computed tomography, diagnosis, NewTom, periapical lesions

From the \*Division of Surgical Therapeutic & Bioengineering Sciences, and <sup>†</sup>Division of Craniofacial Sciences and Therapeutics, School of Dentistry, University of Southern California, Los Angeles, California.

Address requests for reprints to Dr. James HS Simon, School of Dentistry, University of Southern California, 925 West 34<sup>th</sup> St, room 124C, Los Angeles, CA 90089-0641. E-mail address: simon@usc.edu.

0099-2399/\$0 - see front matter

Copyright © 2006 by the American Association of Endodontists.

doi:10.1016/j.joen.2006.03.008

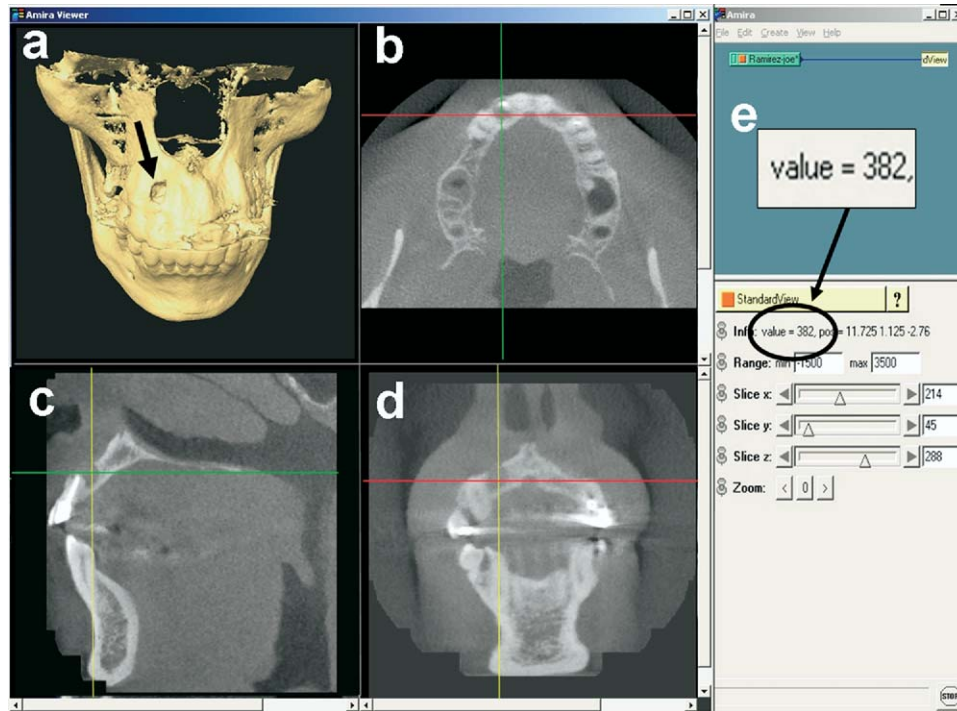
One of the controversial questions in Endodontics is “do cysts heal with nonsurgical treatment?” (1, 2). The difficulty in answering this question is that until a biopsy is taken, the clinician does not know the histologic diagnosis. Once a biopsy is taken the treatment is no longer only nonsurgical. Attempts to diagnose, the lesion before surgery with periapical radiographs (3), contrast media (4), Papanicolou smears (5), and albumin tests (6) have proven to be inaccurate. Recently with the advent of other imaging modalities such as computed tomography (CT), magnetic resonance imaging (MRI), and cone-beam CT, differences in density may permit more accurate preoperative diagnosis. Trope et al. (7) stated that a cyst could be differentiated from a granuloma by a CT scan. Using cadavers an oral radiologist selected four granulomas and four cysts, and CT was performed on the root tips and lesions. In the CT, seven lesions had a cloudy appearance with a density similar to surrounding tissue. The eighth lesion had a different density and histologically was a cyst. This study did not measure the density, was done on cadavers and had only one specimen, but they concluded that a cyst could be differentiated from a granuloma by density. Shrouf et al. (8) digitized radiographic images using a 256 grayscale and computed a cumulative percent histogram. Granulomas had a narrower range and lower grayscale value than did cysts. Camps et al. (9) also used a gray level correction method to assess treatment results. Other uses for CT scans in endodontics have been reported by Cotti et al. (10) and Rhodes et al. (11).

Periapical lesions are usually composed of solid soft tissue (granulomas) or they have a semisolid, liquefied cystic area (bay cyst or true cyst). Therefore, to diagnose these lesions the least dense area of the radiographic lesion should be measured. The gray value measurements allow differentiation of soft tissue and fluid or empty areas. The purpose of this study is to compare the diagnosis of periapical lesions by gray value measurements with the three-dimensional CBCT (NewTom 3G) and then compare the findings to a surgical biopsy report.

## Materials and Methods

Seventeen large periapical radiolucencies equal to or greater than 1 cm × 1 cm radiographically were imaged by a dentomaxillofacial volumetric imaging system, CBCT, the NewTom 3G (QA sri, Via Silvestrini 20, 37135 Verona, Italy) at the Redmond Imaging Center, University of Southern California. This study was approved by the Institutional Review Board of our University with number 03C031.

The NewTom 3G results in a fraction of the effective absorbed dose of radiation (E) compared to traditional CT scan. Imaging of a maxillomandibular volume with the NewTom 3G results in an E of 57  $\mu$ Sv (12) whereas traditional medical CTs result in an E of 1400  $\mu$ Sv for a maxillary CT scan and 2100  $\mu$ Sv for a maxillo-mandibular exam (13). For purposes of comparison a panoramic radiograph results in an E of 6  $\mu$ Sv (14) and a full mouth series results in an E from 33 to 84  $\mu$ Sv (15) and 14 to 100  $\mu$ Sv (16) depending upon variables such as film speed, technique, kVp, and collimation. The NewTom 3G acquires 360 images at 1-degree intervals in 36 seconds, with reconstructed image resolution of 512 × 512 pixels and 12 bits per pixel (4096 grayscale). The pixel size varies between 0.25 and 0.42 mm depending on the user's choices (large or small field and the sensor, 9" or 12"). The axial slice thickness can be set up between 0.1 mm to 5 mm. In the study, the axial slices were 0.2 mm. The reconstructed axial



**Figure 1.** (a) 3-Dimensional visualization of the jaws showing bone lost over the apex of the upper right lateral incisor. (b–d) Axial, sagittal and coronal views of the lesion in the Amira software, all cut at the same point as shown by the lines crossing. (e) Positive gray value reading.

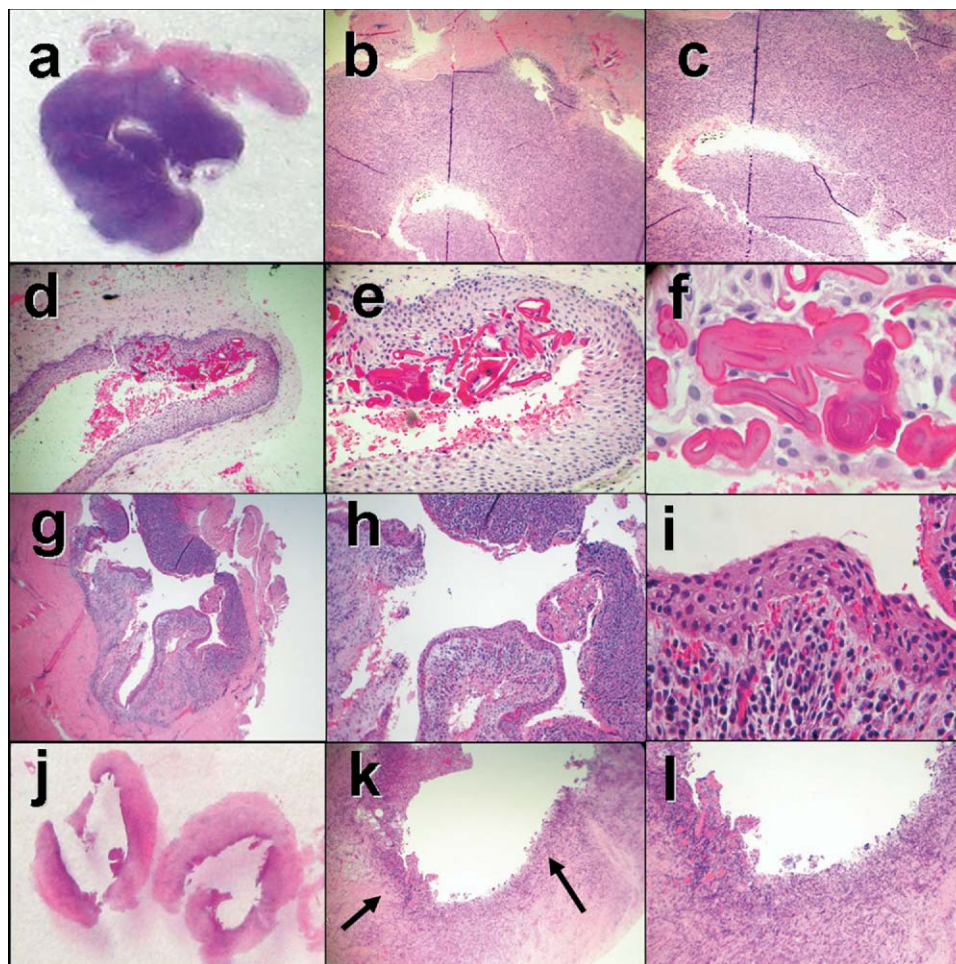
tomographic images were imported into Amira software (Mercury Computer Systems/3D Viz group, San Diego, CA). The 12-bit image grayscale (4096 grayscale) was mapped to –1500 to 3500 (values below –1500 are mapped to black and values above 3500 are mapped to white). Values between –1500 and 3500 are mapped linearly. The lowest sinus readings were used to calibrate the gray values between scans. Negative grayscale values correspond to air (sinus area) and fluid tissue (cyst). Positive readings correspond to solid soft-tissue, bone, metal and fillings. After this mapping, the lesion was scanned for the

lowest gray value measurement at the center of the lesion above the root (Fig. 1) and the minimum and maximum gray values in the lesion area. Standard measurements were recorded for cortical buccal and lingual bone, lips and sinuses. Soft tissue solid lesions and fluid filled cavities were differentiated by gray value measurements. Positive measurements represented solid soft tissue as opposed to negative numbers representing fluid filled cavities or cavity (air filled) space. The lesions were then surgically removed and sent for routine biopsy to an oral pathology laboratory (Scripps Oral Pathology Service, San Diego, CA) for hema-

**TABLE 1.** Results of seventeen large periapical lesions scanned by the CBCT-scan and by biopsy report

Case #	Tooth #	Dx NewTom/ biopsy	(a) Center	(b) Min	(c) Max	(d) Lips	(e) Buccal cortical bone	(f) Lingual cortical bone
<b>Caps</b>								
1	9,10	CAP/CAP	301	–49	521	–996	2200	1413
2	10	CAP/CAP	203	–169	246	–842	1507	1254
3	7	CAP/CAP	125	8	438	–537	1436	990
4	10	CAP/CAP	226	233	451	–605	1439	964
5	8	CAP/CAP	564	496	642	–429	1592	1384
6	8–9	CAP/CAP	692	451	717	–426	1974	2120
<b>Cysts</b>								
7	9,11	CYST/CYST	–348	–634	–147	–865	1536	1078
8	12	CYST/CYST	–358	–657	–316	–716	1195	1267
9	8,9	CYST/CYST	–468	–563	–113	–670	993	1605
10	7,8	CYST/CYST	–160	–384	–169	–703	1211	1501
11	7	CYST/CYST	–43	–88	197	–462	1562	928
12	10	CYST/CYST	–127	–316	–43	–449	1829	1231
13	6,7,8,9	CYST/CYST	–462	–546	–166	–813	1549	1029
<b>Differential diagnostic</b>								
14	9,10	CYST/CAP	–358	–563	–17	–436	1423	1114
15	8	CYST/CAP	–139	–675	66	–735	1844	797
16	9	CYST/CAP	–143	–387	54	–660	1536	1455
17	7	CYST/CAP	–306	–514	–98	–472	1442	1387

The following grayscale value readings were provided by the CBCT-scan and Amira software: (a) reading at the center of the lesion, (b) the minimum and (c) maximum grayscale value inside the lesion, (d) the lip, and the (e) buccal and (f) lingual cortical bone readings.



**Figure 2.** (a) A  $\times 40$  photomicrograph of CAP (H&E stain); (b)  $\times 100$  photomicrograph; (c)  $\times 400$  showing mostly chronic inflammation; (d)  $\times 40$  photomicrograph showing the lumen surrounded by squamous epithelial lining; (e)  $\times 100$  photomicrograph of the epithelium containing Rushton bodies; (f)  $\times 400$  photomicrograph of pleomorphic Rushton bodies; (g)  $\times 40$  low power photomicrograph showing lumen, epithelium, and connective tissue capsule (H&E stain); (h)  $\times 100$  view of lumen and thin epithelium lining; (i) high power views of the thin epithelial lining; (j) 1-1 view of the histology section; (k)  $\times 40$  micrograph of the lumen surrounded by inflammatory cells and connective tissue (H&E stain); (l)  $\times 100$  photomicrograph of luminal lining by acute and chronic inflammatory cells.

toxylin and eosin (H&E) staining and analysis. The samples obtained were part of an apicoectomy procedure that included the lesion and apex portion as a whole specimen. Our null hypothesis is that there is no significant difference in the diagnosis by biopsy with the CBCT scan.

## Results

The results are presented in Table 1. Thirteen of the 17 lesions had the same diagnosis by the CBCT-scan data and the biopsy report. Figure 2a–c shows a chronic apical periodontitis (CAP) or granuloma, and Fig. 2d–f show a cyst with coincident diagnostic by CBCT-scan data and by biopsy. Four of the 17 lesions had a split diagnosis. In all four the CBCT-scan data read compatible with a cyst and the biopsy report said apical periodontitis (granuloma). Figure 2g–i show a cyst with a discontinuous epithelial lining. The epithelium is thin and only several layers thick where it is present. Figure 2j–l and 3 show a CAP with a cavity lined by inflammatory cells that physiologically may be acting as a cyst.

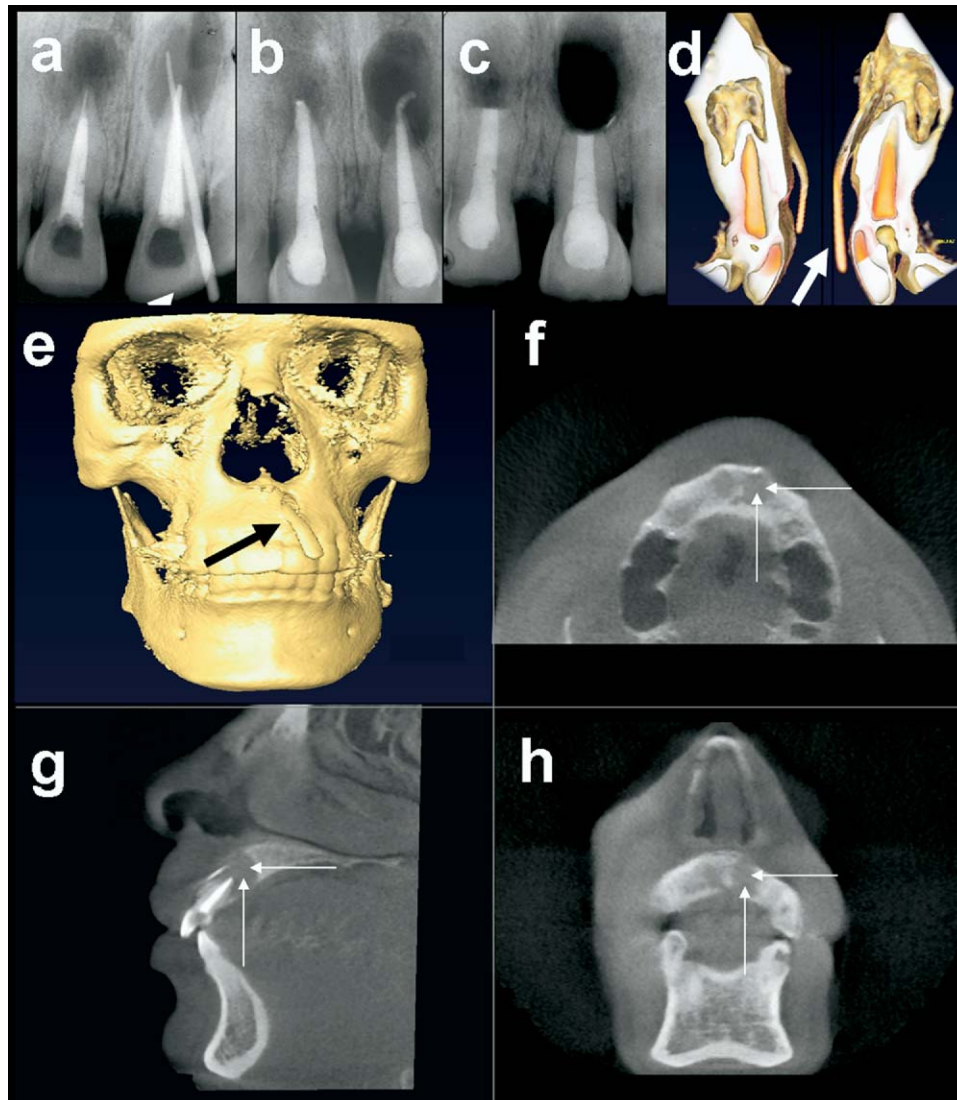
## Discussion

The question now arises who is right: the histology or the CBCT-scan? The negative CBCT-scan readings put the diagnosis in the cyst category. The readings should be made in the central area or at the tip

of the root and should be accurate. The CBCT-scan shows the lower gray values indicative of a fluid filled cavity. It does not show whether or not it is lined by epithelium.

Looking at the histological slides of the four split biopsies with a diagnosis of CAP, two of the lesions were small, fragmented pieces. Because very few sections were made, it may not represent the full lesion and may have missed the epithelial area. In addition the diagnosis of one read “no epithelium or other evidence of cystic organization” but under surgical findings was the statement “fluid filled cavity.” The third lesion had the comment “although this lesion has the architecture of a cyst, it presently lacks evidence of lining epithelium. The fibrotic connective tissue wall is lined by inflamed granulation tissue.” The fourth lesion had “consistent with cavitated chronic apical periodontitis” and the comment: “the histomorphology is also consistent with an apical radicular cyst that has undergone inflammatory epithelial destruction.” Thus it is possible that the lesions have lost the epithelium in these sections but are physiologically acting like a cyst. The CBCT-scan may be a more accurate diagnostic than biopsy and histology.

By use of the CBCT-scan grayscale readings we were able to differentiate solid from cystic or cavity type lesions. Correlation of these findings with histology is not complete because of shortcomings in



**Figure 3.** (a) Preoperative radiograph with gutta-percha cone in the sinus tract. (b) Post retreatment radiograph. (c) Post-surgical X-ray. (d) Volumetric reconstruction of teeth 8 and 9 with the gutta-percha cone (arrow) into the lesion. (e) Three-dimensional view showing the gutta-percha cone inserting in the sinus track of the upper left central incisor. (f) Axial view of the lesion. (g) Sagittal view of the lesion. (h) Coronal view of the lesion. All three views have a common point at the crossing of the arrows.

histological technique. First of all, the lesion is curetted and therefore distorted and sometimes only small multiple pieces are obtained. To be accurate the biopsy should have the apex with the lesion attached and be sectioned through the apical foramen to provide an accurate diagnosis. Secondly, the diagnosis may be distorted because the pathologist looks for an epithelial lining that appears to be lining a lumen. An epitheliated granuloma, bay cyst or true cyst could account for this histologic picture. In addition the area of sectioning of the lesion can also distort the diagnosis. For example a bay cyst can be sectioned in such a way that it can look exactly like a true cyst. Thirdly to be accurate serial sections through a tooth with the lesion attached are necessary. This is expensive, time consuming and is rarely done. Thus, the four-biopsy reports with a CAP diagnosis (not coincident with the CBCT-scan) could have been lesions with a cavity that were functioning as cysts.

In conclusion, the CBCT-scan may provide a better, more accurate, faster method to differentially diagnosis a solid from a fluid filled lesion or cavity. However, to get an accurate reading the whole lucency should be scanned for the most lucent or least dense area. If the least dense area has

a negative grayscale value on the CBCT-scan then this may be a semi-solid or fluid filled area. It is either the lumen of a bay or true cyst. Whether or not epithelium is present, these are cavitated lesions. If it is a positive grayscale value, then the lesion is an epitheliated granuloma or a granuloma. This allows the clinician to decide whether or not surgery is necessary without waiting the recall period to see if healing has occurred. The CBCT-scan does not differentiate cyst or granuloma but only a solid soft tissue lesion from one that has soft tissue plus an area that is less dense i.e. a cavity with fluid semi solid substance in the lumen. According to Dorland's Medical Dictionary a cyst is "any closed cavity or sac, normal or abnormal, lined by epithelium, and especially one that contains a liquid or semi solid material." However, Shear (17) has added, "it is frequently, **but not always lined by epithelium.**"

**Summary**

Seventeen large periapical radiolucencies were scanned using the CBCT-scan machine to determine densities. The lesions were then re-

moved surgically after cleaning, shaping, and filling the canals and sent to an oral pathology laboratory for histologic description and diagnosis. Thirteen out of 17 had the same diagnosis with both the CBCT-scan and biopsy; four out of 17 had a split diagnosis. All four were labeled "cyst" by the CBCT-scan and chronic apical periodontitis by the Oral Pathologist. In evaluating the last four lesions, it was found that the CBCT-scan may be clinically more accurate and more useful than the biopsy.

### Acknowledgments

*The authors wish to thank the following residents who contributed the cases and biopsies: Andrew Lulloff, Adrian Silberman, Jose Maria Malfaz, Christopher Redd, Aesbna Mathur, Esbter Cho, Darin Lee, Afsbin Mazdey, Ali Vaziri, William Chen, Janice Chou, and Robert Salebrabi.*

*Sources of support: This project was supported by a grant from the AAE Foundation and the USC Endodontic Fund.*

### References

1. Simon JHS. Incidence of periapical cysts in relation to the root canal. *J Endod* 1980;6:845–8.
2. Nair PNR. New perspectives on radicular cysts: do they heal? *Int Endod J* 1998;31:155–160.
3. McCall JO, Wald SS. *Clinical dental radiology*, 4th ed. Philadelphia: Saunders, 1954:234–51.
4. Cunningham CJ, Penick EC. Use of a roentgenographic contrast medium in the differential diagnosis of periapical lesions. *Oral Surg Oral Med Oral Pathol* 1968;26:96–102.
5. Howell FV, De la Rosa VM. Cytologic evaluation of cystic lesions of the jaws: a new diagnostic technique. *J Calif Dent Assoc* 1968;36:161–6.
6. Morse DR, Patnik JW, Schacterle GR. Electrophoretic differentiation of radicular cysts and granulomas. *Oral Surg Oral Med Oral Pathol* 1973;35:249–64.
7. Trope M, Pettigrew J, Petras J, Barnett F, Tronstad L. Differentiation of radicular cyst and granulomas using computerized tomography. *Endod Dent Traumatol* 1989;5:69–72.
8. ShROUT MK, Hall JM, Hildebolt CE. Differentiation of periapical granulomas and radicular cysts by digital radiometric analysis. *Oral Surg Oral Med Oral Pathol* 1993;76:356–61.
9. Camps J, Pommel L, Bukiet F. Evaluation of periapical lesion healing by correction of gray values. *J Endod* 2004;30:762–6.
10. Cotti E, Vargiu P, Dettori C, Mallarini G. Computerized tomography in the management and follow-up of extensive periapical lesion. *Endod Dent Traumatol* 1999;15:186–9.
11. Rhodes JS, Pitt Ford TR, Lynch JA, Liepins PJ, Curtis RV. Micro-computed tomography: a new tool for experimental endodontology. *Int Endod J* 1999;2:165–70.
12. Ludlow JB, Brooks SL, Davies-Ludlow LE, Howerton B. Dosimetry of 3 CBCT units for oral and maxillofacial radiology. *International Association of Dentomaxillofacial Radiology*, 15th Congress: Cape Town, South Africa, 2005.
13. Ngan DC, Kharbanda OP, Geenty JP, Darendeliller MA. Comparison of radiation levels from computed tomography and conventional dental radiographs. *Aust Orthod J* 2003;19:67–75.
14. Ludlow JB, Davies-Ludlow LE, Brooks SL. Dosimetry of two extraoral direct digital imaging devices: NewTom cone beam CT and Orthopos Plus DS panoramic unit. *Dentomaxillofac Rad* 2003;32:229–34.
15. Danforth RA, Clark DE. Effective dose from radiation absorbed during a panoramic examination with a new generation machine. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2000;89:236–43.
16. Gibbs SJ. Effective dose equivalent and effective dose: comparison for common projections in oral and maxillofacial radiology. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2000;90:538–45.
17. Shear M. *Cysts of the oral regions*, 3rd ed. Oxford: Wright, 1992.