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Computed tomography assessment of alveolar filling with an injectable bone substitute

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Introduction

Alveolar bone is particularly resorbable and tends to disappear when teeth are lost. General as well as local factors cause or intensify alveolar resorption [32], which continues throughout an individual's lifetime, in a manner defined by Atwood and Willard [4] as ''irreversible, cumulative and chronic'' (see also [3, 5, 29]). The consequences for the individual who has lost teeth are both aesthetic and functional and can complicate prosthetic rehabilitation considerably [2, 3].

Various techniques have been used with more or less success to conserve or increase bone [29]. Grafts of synthetic materials are now preferred to those of human or animal origin.

Despite the increasing development of techniques for conserving bone ridges [6, 10, 23, 24], the clinical results of alveolar filling in man have not been assessed precisely [17]. The available techniques, including probe measurements, retroalveolar [17] or panoramic [10] radiography, and lateral teleradiography [4, 7, 22, 24], are not sufficiently reliable and precise [11, 13, 15, 16, 19, 21, 27].

This study tested the reliability of computed tomography (CT) for assessment of alveolar filling. CT images were compared with those of retroalveolar radiography (the most precise radiographic technique, providing standardized images), direct measurements, and images obtained in scanning electron microscopy.

After a preliminary study *ex vivo*, a study was performed *in vivo* on three beagles. The three mandibular premolars of the dogs were extracted, and the resulting extraction site were filled with an injectable bone substitute (IBS) composed of calcium phosphate associated with hydroxypropyl methylcellulose (HPMC) [8, 9, 14].

Materials and methods

Materials

The filling material used was an IBS composed of biphasic calcium phosphate for 50% (60% hydroxyapatite + 40% β tricalcium phosphate [8, 9, 14]) associated with a polymer for 50% (hydroxypropyl methylcellulose E4M® in a 3% aqueous solution). The biomaterial was prepared in ready-to-use throw-away syringes packaged in hermetically closed bags. Luer-Lock® tips facilitated injection (Fig. 1).

Extractions and alveolar fillings were performed on three beagles obtained from a breeder approved for animal experimentation by local veterinary services. The animals were housed in accordance with the recommendations of European directive 86/609/CEE of 24 November 1986. Three mandibular premolars were extracted bilaterally. One side was filled and the other left unfilled to serve as a control. A calibrated lacuna was made in the vestibular wall of the second and third premolars.

CT images

CT images were obtained with a spiral mode scanner and studied on a SUN system equipped with Easy Vision CT/MR Version 2® analytic software (Philips Medical System, The Netherlands BV 1996). The examination was performed during brief general anaesthesia induced by intravenous injection of ketamine (Imalgèn®, Mérial SAS, Lyon, France) associated with xylazine (Rompun®, Bayer Pharma, Puteau, France). Sections were observed directly after reorientation [wide density window: 2000 Hounsfield units (HU) centered on 400 HU] and then processed to obtain the best definition of bone contours and to perform distance and density measurements (wide window: 2200 HU centered on 1100 HU). As the CT slices were oriented as a function of the dog's position at the time of acquisition, it was necessary to reorient them so that measurements could always be performed at the same spot. Reorientation was accomplished by aligning anatomic points in the three spatial planes. A repositioning system was developed, using titanium wires as reference points, to guide the reorientation.

Ten measurements of height, width and density were performed for each structure: one set of five by direct detection with a cursor and another set of five by density changes on five successive reorientations of CT sections (Figs. 8 and 9). Examinations were conducted before, one week after, and two months after extractions, and the

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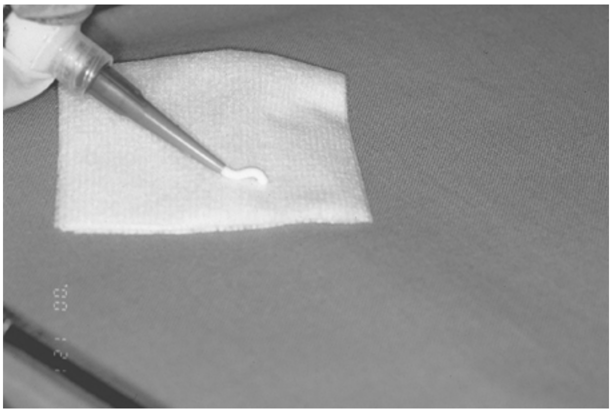

Figure 1 Injectable form in which the biomaterial is used.

measurements obtained in the different examinations were compared. The data were grouped in recapitulative tables and processed statistically and by Student tests. Image acquisition and the examination were carried out in consistently identical pre-determined conditions: thickness 1.0, MA 175 mA, KV 100, scan time 1.0, FOV 195, filter 2, matrix 512, delay time 4, BAC on, Auto zoom on, *60 rotations*, Table Index 0.5, recon index 0.3, seq index 00.

Radiological images

Retroalveolar radiography (Agfa Dentatus M2® films) was performed with a Matig® generator (Trophy) at the beginning and end of general anaesthesia for extractions and then two months later. The images were standardized by a repositioning system and strictly identical processing, as customarily described in the literature [11, 15, 16, 19, 21, 33]. The repositioning system consisted of a PMMA resin plate placed against canine cuspids and central cuspids of the first molars (Fig. 4). The support for radiography was a modified RINN® system in which the angulation arm was interdependent with the X-ray generator. This set-up allowed the same distance and angulation to be maintained between the X-ray beams, the film and the object, as well as between the object and the film itself. The film was processed manually in developing and fixing baths (Periomat® Durr Dental), which were renewed and thermostated each time according to the manufacturer's instructions. The X-rays were observed directly on a viewer and then with a magnifying glass before being digitized (Epson film scan®) for study on a PC Quantinet 500 MC® image analysis unit (Leica, Cambridge, UK). Tools were used to measure length and density.

Images obtained in scanning electron microscopy (SEM)

The dogs were euthanized by intravenous injection of an overdose of pentobarbitol sodium two months after the extractions and fillings. Mandibles were immediately removed and placed in a paraformaldehyde-based fixative. The axis of the alveoli was determined by microradiography, and the preparation was studied in SEM with backscattered electrons as in Fig. 10 (JSM 6300 scanning electron microscope, Jeol, Japan). The images obtained were analyzed after digitization on the PC Quantimet 500 MC image analysis unit (Leica, Cambridge, UK).

Results

Ex vivo Syringes containing the biomaterial were scanned and radiographed during a preliminary study.

In vivo Healing after the operation was quite satisfactory. The dogs ate normally after 24 h, the sutures were still in place a week later, and no gingival erythema was apparent (Fig.5). After two months, there was no longer any trace of the operation, and the mucosa appeared normal (Fig. 6). On palpation, a slight depression could be felt opposite the vestibular lacunae, which was more marked on the unfilled side.

Four of the 36 alveoli treated were withdrawn from the study because of apical fractures in the corresponding teeth or bone decay.

CT images were studied directly without preparation (window width: 2000 HU, level: 400 HU).

- One week after the extractions and fillings, material leaked through the vestibular lacunae and density was not perfectly homogeneous (existence of ''bubbles'') in filled alveoli. This lack of homogeneity, with a density very similar to that of adjacent bone, prevented the study of volumes by selection of grey levels. Observations on the side with unfilled alveoli showed a density close to that of adjacent soft tissues.
- Two months after the extractions and fillings, the two sides could not be compared in direct observation. Density in the alveoli as a function of section site was equivalent or slightly lower than that of adjacent bone. The two sides could be identified as well as the non-X-ray-dense zones, which were apparently not occupied by biomaterial or mineralized tissue.

The reproducibility of measurements was tested by determining the length and width of the mesial root of the first mandibular molar (Fig. 2). For five successive reorientations (on the structure to be analyzed), the

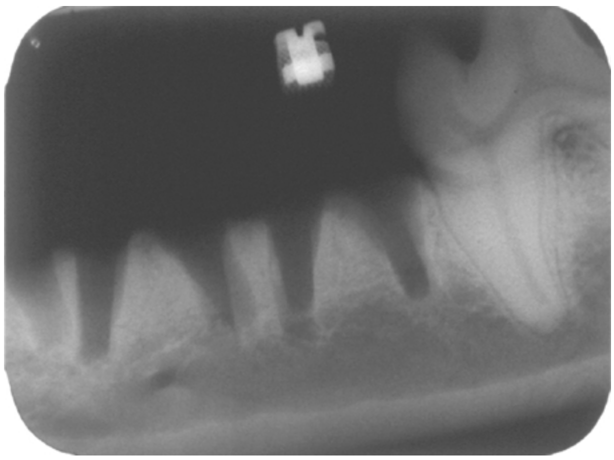

Figure 2 Mesial root of the first premolar invisible.

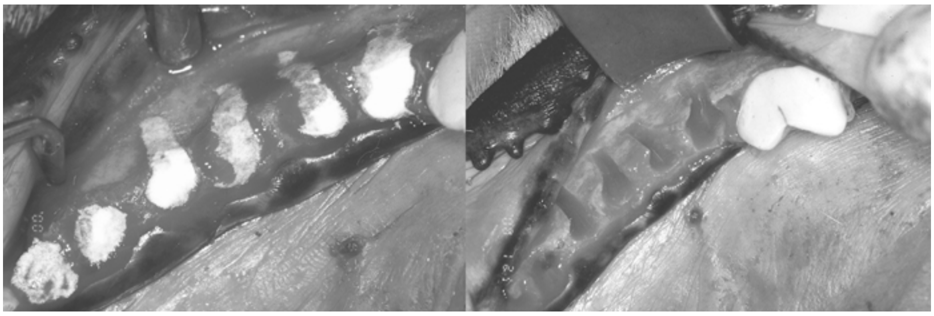

Figure 3 Filled and unfilled alveoli, showing a calibrated vestibular lacuna.

Figure 4 Repositioning device for scanner studies.

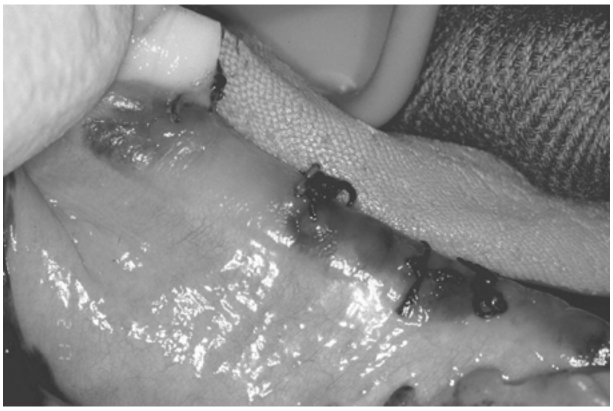

Figure 5 Healing at three weeks.

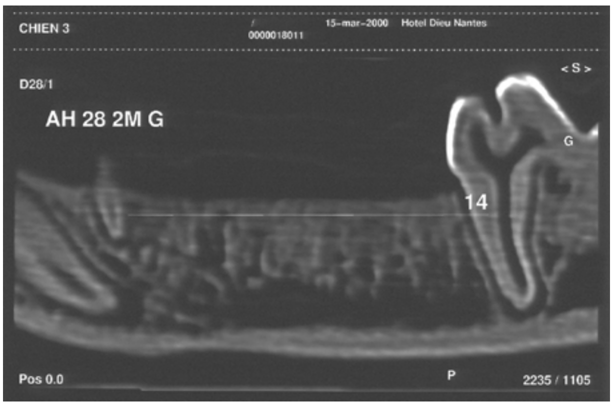

Figure 6 CT image after two months of healing.

measurements obtained by direct observation were on average greater than those obtained by density determinations (mean standard deviation: 0.07).

Measurement reliability was assessed by comparison between determinations of the diameter of the drill used to perform vestibular lacunae and the mean width of the lacuna on CT sections. Mean width was 2.47 mm for a drill diameter of 2.50 mm in the upper part of the lacuna, and 2.13 mm for a drill diameter of 2.00 mm in the lower part.

All measurements were performed using a reorientation for all alveoli on the same side. This reduced the reliability of reorientation as compared to a structure-by-structure procedure, but saved image-processing time. The mean standard deviation for all measurements was 0.14, and there were large standard deviations for some of the measurements performed at two months and for one dog at the level of the right half of the mandible. If these large deviations are eliminated, the mean standard deviation becomes 0.12. In 74% of cases, the standard deviation was greater for direct measurement than for density measurement, and the mean difference between the two measurement systems was 0.06 mm. The measurements showed a loss of alveolar ridge height that was always greater than for the unfilled side (Fig. 7). Density profiles provided additional information, indicating that mean density in alveoli (550 HU) was close to that of adjacent bone (600 HU) after two months of healing. A collapse of density curves occurred in non-X-ray-dense zones for both filled and unfilled sides, with a slightly higher mean for the filled side.

Retroalveolar radiography did not cover all the teeth concerned. Two months after extractions and fillings, radiography indicated that density in alveoli was always closer to that of natural bone on the filled than unfilled

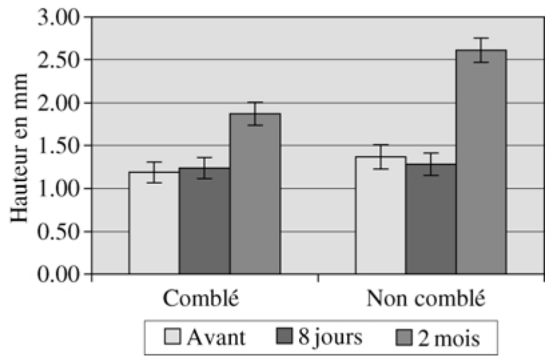

Figure 7 Height of alveolar ridges as compared to a stable anatomic reference point.

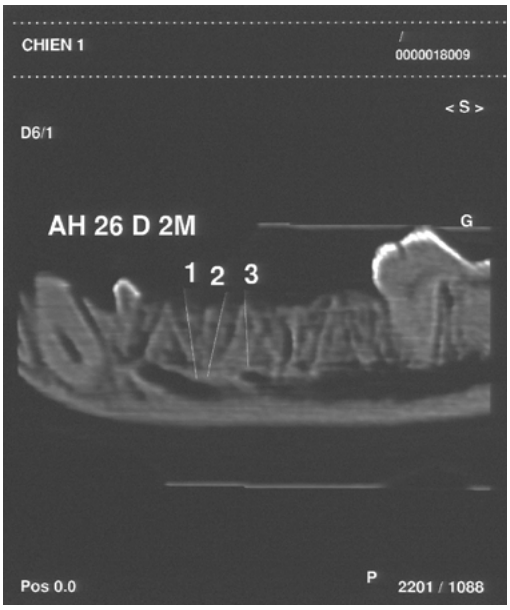

Figure 8 CT section.

side (Fig. 3). The measurement study showed large standard deviations. Density in the alveoli appeared to be uniform from the apex to the alveolar ridges.

The first studies of SEM images seemed to show a greater bone volume on the filled side in transverse sections through the middle of the lacuna. These images revealed non-electron-dense zones in alveoli on both filled and unfilled sides. After two months, there was only a small amount of ceramic granules in the calcified tissue formed within filled alveoli. These granules were in close contact with the tissue formed.

Discussion

Maximal conservation of bone tissue after extraction is a priority for the practitioner. However, extractions, even when non-traumatic, are followed by resorption [2, 4, 5, 12, 18, 22]. The filling of extraction sites with biomaterial suitable for reducing bone loss is a common practice today. Scientific literature has demonstrated the value of calcium phosphate ceramics [6, 10, 23, 24], and their use in injectable form improves handling [14].

Histological studies provide reliable evaluation and are usually used for animal experimentation [6, 26, 28]. However, this approach is impracticable in man because of the impossibility of obtaining systematic samples. The various choices classically described for the evaluation of clinical results have many disadvantages:

- Clinical observation allows only relative evaluation, depending on the experience of the practitioner. Probe measurements down to the bone [17] can only be of value relative to an

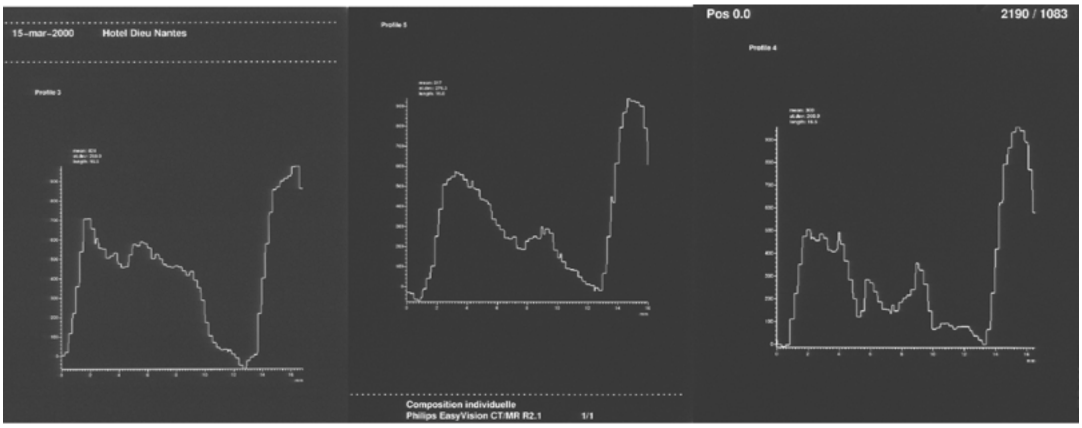

Figure 9 Density patterns corresponding to the section shown in Fig. 8.

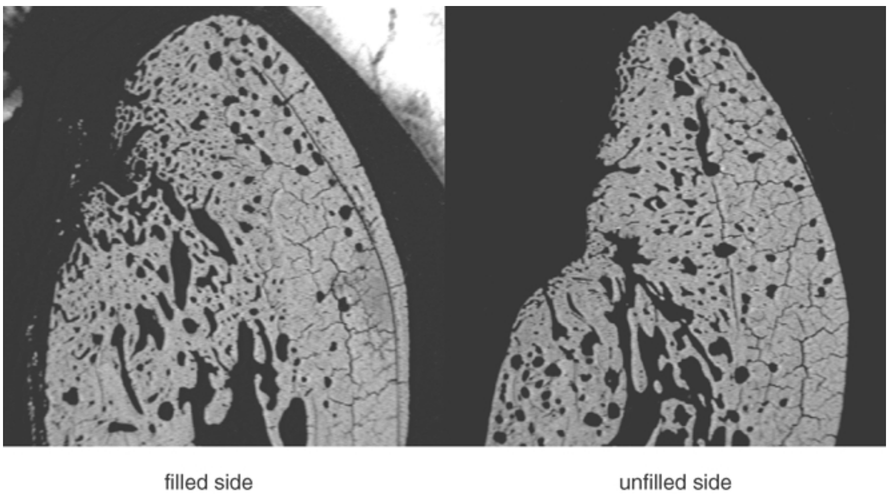

Figure 10 Scanning electron microscopy with backscattering two months after extraction and filling.

efficient reference point not modified with time and for a reliability of the order of a millimeter.

- Pantomography has many limitations, including the impossibility of spatial localization or the measurement of height, width or density [13, 27].
- Lateral teleradiography at a distance of four meters has often been used to study bone resorption in the mandible [2, 3, 5, 7, 12, 18, 22]. It appears to provide greater measurement reliability, but the superposition of mandibular structures on one side, in association with right–left superposition, complicates considerably the detection of the elements to be measured and prevents reliable density measurements.
- Retroalveolar radiography, which provides greater precision and reproducibility, is often used for monitoring periodontal disease (measurement reliability of 0.4 mm in the best cases) [15, 16] and the detection of density modifications [11, 15, 16]. Digitization of the image and processing by subtraction are essential to detect small changes in density.

As these different techniques all show imprecision in the evaluation of the clinical results of alveolar filling, our study compared CT images with standardized retroalveolar radiographs to assess the advantages and limitations of the former.

The dog model has already been used in various studies in odontology [6, 20]. The slope of the horizontal branches of the mandible made it impossible to obtain reliable images of all alveoli concerned. The completely flat palate in the dog did not allow standardized radiography of the maxilla.

All the acquisition and reconstruction parameters for CT images were chosen to improve the reliability of measurements in millimeters. The thinness of sections made it difficult to evaluate grey levels, and image processing increased low-density zones. Repositioning of the images was only reliable when the reference points chosen were quite close to the measurement zone, and the titanium wires used as reference points only allowed the general orientation to be verified. Thus, to ensure good correspondence of measurements with reality, it was essential to choose reference points in stable structures as close as possible to the element to be measured. This repositioning method for measurements has already been used by Howel *et al.* [17] and Kohavi *et al.* [20] in similar circumstances. Errors can be avoided in long-term study of mandibular resorption in man by using a repositioning device covering a larger area than the teeth next to the missing ones. Measurement reliability is altered by general reorientation for one-half of the mandible (mean standard deviation of 0.14 compared to 0.07 for direct reorientation on the structure to be measured). Direct observation of images gives a good general impression of the zone to be studied, but height and density measurements are necessary for precise evaluation. The results for direct observation may seem contradictory, i.e. the better conservation of alveolar ridges on the filled side two months after extractions could give the mistaken impression that filling is better on the unfilled side. However, measurements indicated that the quantity of restored bone was always greater on the filled side. This was confirmed by analysis of SEM images, whereas retroalveolar radiography could not make this distinction. Isolated analysis of CT images, depending on the processing they received and without reference to density or correction curves by alignment on a density phantom [17, 33], is not indicative of reality. The study of density patterns does not allow identification of the tissues, but locates non-X-ray-dense zones that are also apparent on SEM images. However, it will be necessary to perform precise mapping of the zones detected with the two imaging techniques to be sure that they correspond. Retroalveolar radiography did not show non-X-ray-dense zones within alveoli at two months. Moreover, the leakage of material from alveoli was apparent on CT sections, but not in retroalveolar radiography. As the superposition of structures in radiography masks some details, the density differences and volumes modified must be adequate to be visualized. However, this superposition provides an overall notion of volume that is not apparent on thin CT sections.

Conclusion

This study provides a first approach to using the scanner for quantitative evaluation of alveolar filling. The measurements were more precise (within 0.36 mm) than those obtained by retroalveolar radiography (0.4 mm in the best cases). The study of density patterns, in the present state of our research, did not allow identification of tissues, but localized non-mineralized zones invisible in radiography. On the whole, the scanner provided more precise and complete results than retroalveolar radiography on argentic film. The constant improvement of intrabuccal sensors for retroalveolar radiography and of associated image-analysis software should provide better results in the near future. The major problems involved in the use of the scanner are the cost and the irradiation during the examination. Otherwise, CT sections are currently the best means of evaluating the clinical results of alveolar filling in man.

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