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Healing without Grafts: Insights from a 3D Study of Bone Regeneration after Cyst Enucleation

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Abstract

Background: Bone defects following cyst enucleation raise the question of whether bone grafting is necessary. This study aimed to evaluate spontaneous bone regeneration using a 3D segmentation-based method. **Materials and Methods:** Seven patients who underwent cyst enucleation at the Department of Surgical Dentistry in Casablanca were included. Cone-beam CT scans were performed at baseline (T0) and 12 months postoperatively (T1). A 3D imaging software was used to measure the initial cyst volume and residual defect volume. Changes in volume and density were analyzed with respect to patient demographics, lesion location, histological type, and defect configuration. **Results:** All patients showed a reduction in defect volume at 12 months. The largest initial volume was 10.62 cm^3, and the smallest was 3.12 cm^3. The three youngest patients—all female—showed the highest regeneration rates. The average bone regeneration rate across the sample was 84.2%. **Conclusion:** Spontaneous bone healing occurred even in large defects, suggesting that, under appropriate surgical conditions and with periosteal preservation, graft-free healing is a viable and cost-effective alternative. This approach may be particularly effective in younger patients.

Subject Areas

Dentistry

Keywords

Odontogenic Cyst, Bone Regeneration, CBCT, Enucleation, Spontaneous Healing

1. Introduction

Cysts are bone lesions characterized by one or more cavities lined with an epithelial membrane. They may originate from odontogenic or non-odontogenic tissues [1]. The primary treatment goal is complete removal to prevent recurrence. Two main surgical techniques have been described: decompression and enucleation—the latter involving total excision of the cyst [1] [2]. The postoperative cavity may be left unfilled, relying on spontaneous bone regeneration, either from the blood clot replaced by osteogenic granulation tissue, or from surrounding osseous margins covered by mucosa [1] [3].

Although this approach is generally accepted for small lesions, its application to larger defects remains debated [4]. Some authors advocate filling the cavity with autologous bone or substitutes to enhance regeneration [1] [4]. However, few studies have investigated graft-free spontaneous bone healing after cyst enucleation.

Most evaluations in the literature rely on either bone density comparisons with adjacent or contralateral sites [3]-[9], or linear measurements of residual cavity dimensions over time [2] [10]. These often use panoramic radiography, which, despite lower radiation, offers limited volumetric precision. In contrast, computed tomography—particularly CBCT—provides more accurate and reproducible data for assessing lesion volume and healing.

Accordingly, the objectives of this study were to:

- Develop a standardized 3D method to assess bone defect evolution post-enucleation.
- Objectively evaluate the quantity and quality of spontaneous bone regeneration without grafting.

2. Materials and Methods

This prospective pilot study was conducted over a 27-month period and included patients over the age of 18 who presented to the Department of Surgical Dentistry at the Casablanca Dental Consultation and Treatment Center with jaw lesions of cystic appearance measuring more than 3 cm in diameter. Eligible patients had both preoperative and postoperative CBCT imaging and were treated by cyst enucleation without the use of bone graft materials.

Exclusion criteria comprised systemic conditions that could affect bone metabolism, such as diabetes, thyroid disorders, and metabolic bone diseases. Patients receiving medications known to interfere with bone healing—including bisphosphonates, corticosteroids, calcium supplements, or similar agents—were also excluded. In addition, patients with a history of radiotherapy to the oro-facial region were not included.

All surgical procedures were performed by a single operator under local or locoregional anesthesia, using a tissue-conserving approach aimed at conserving as much bone as possible to favor subsequent bone regeneration and to provide structural support for the soft tissues during healing. All patients followed a standardized postoperative protocol: amoxicillin 2 g/day for seven days, corticosteroids at 1 mg/kg/day for four days, paracetamol 1 g immediately after surgery and every six hours for four days, and chlorhexidine mouthwash initiated the day after surgery, three times daily for seven days.

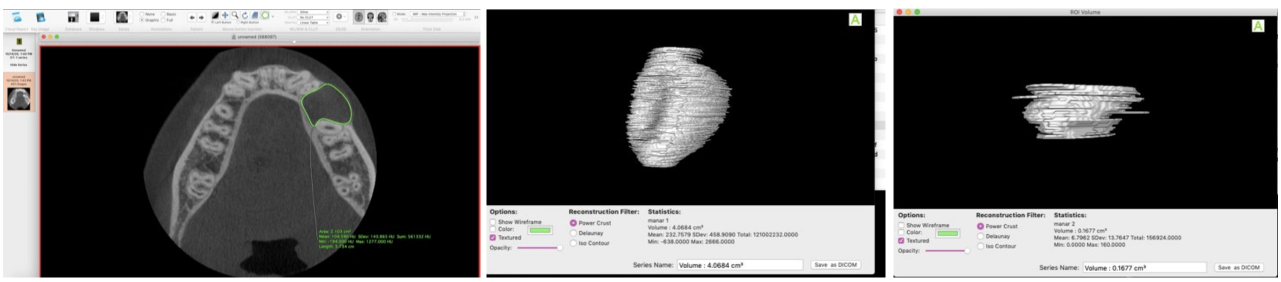
Postoperative follow-up included of a clinical examination at day 7 (with suture removal if needed), a clinical visit at 3 months, and both clinical and radiographic evaluations at 6 months (panoramic radiograph) and at 12 months (cone beam computed tomography, CBCT).

Volumetric 3D Analysis Method:

For the imaging analysis, preoperative DICOM-format CT scans were imported into Horos™ software (© The Horos Project & OsiriX Team 2020, Annapolis, MD, USA), and the cyst surface areas were manually delineated on each axial slice using the Region of Interest (ROI) tool. The actual cyst volume at baseline (T0) was then automatically computed by the software. The same procedure was applied to the postoperative DICOM data acquired 12 months after surgery to calculate the volume of the residual bone defects (T1). Additionally, Horos enabled the calculation of bone density within each manually defined ROI across all axial slices of both pre- and postoperative scans, allowing for the determination of mean density values expressed in Hounsfield Units (HU). The healing rate, which reflected the degree of spontaneous bone regeneration, was calculated using the following formula:

$$\text{Healing Rate}(\%) = \left[\ (\text{Volume T0} - \text{Volume T1}) / \text{Volume T0}\right] \times 100$$

The segmentation and volumetric analysis workflow is illustrated in Figure 1.



(a) (b) (c)

Figure 1. Volumetric evaluation workflow at baseline (T0) and 12 months (T1). (a) Manual segmentation of the cystic cavity on axial slices using the ROI tool; (b) 3D rendering of the initial cyst volume (T0); (c) Volumetric measurement of the residual bone defect at 12 months (T1).

3. Results

A summary of clinical, volumetric, and densitometric data for all patients is presented in Table 1.

Out of an initial sample of 12 patients, 7 were ultimately included in the study. The sample consisted of 3 women and 4 men, with a mean age of 46.14 years and a standard deviation of 19.06 years. The female patients were the youngest, aged 18, 33, and 40 years. Six of the patients had mandibular cysts, while only one had a maxillary cyst. Among the mandibular cases, the cystic defects were located in the posterior region (cases 1, 2, and 3), in the ramus (cases 4 and 5), and in the mandibular body (case 6). The number of remaining cortical boundaries for each initial defect was also recorded.

Table 1. Summary of clinical data, 3D volumetric analysis (cm^3), and densitometric values (in HU) at T0 and T1, assessed using Horos™ software.

Case	Age (yrs)	Sex	Location	Histological Diagnosis	Cortical Boundaries	V. T0 (cm^3)	V. T1 (cm^3)	V. Reduction (%)	D. T0 Min (HU)	D. T0 Max (HU)	D. T0 Mean (HU)	D. T1 Min (HU)	D. T1 Max (HU)	D. T1 Mean (HU)
1	48	M	Right mandible	Keratocyst	1	8.47	0.73	91.33	−454	1295	−5.63	−497	1788	237.95
2	18	F	Left mandible	Keratocyst	2	4.07	0.16	95.87	−638	2666	232.76	0.00	160.00	6.80
3	33	F	Right mandible	Keratocyst	3	3.12	0.00	100	−520	1849	166.06	45	1300	533.96
4	66	M	Left mandible + ramus	Keratocyst	2	4.07	1.25	69.21	−407	3241	507.41	−440	1768	91.64
5	40	F	Ramus	Keratocyst	2	5.59	0.07	98.7	−358	1244	−98.14	0.00	1170	38.43
6	74	M	Mandibular body	Keratocyst	1	10.62	4.22	60.22	−565	1822	−26.57	−782	1463	4.32
7	44	M	Maxilla	Radicular cyst	1	8.79	2.28	74.09	−755	2245	227.60	−825	1885	178.33

F: Female; M: Male; V: volume (cm^3); D: density (HU).

Three-dimensional analysis revealed that the largest initial intraoperative cyst volume was 10.6198 cm^3 (case 6). The largest postoperative residual cavity volumes were found in case 6 (4.22 cm^3) and case 7 (2.28 cm^3). All patients demonstrated a reduction in the volume of the residual cavity over the 12-month period. The highest regeneration rates were observed in case 3, with a complete (100%) regeneration, and in case 5, with a regeneration rate of 98.7%. The overall mean regeneration rate among all patients was 84.20%, with a standard deviation of 14.8%.

In addition, we assessed the density of the cystic lesions at T0 and of the bone defects at T1. An increase in density was observed in all cases, except for cases 2, 4, and 7, which involved cysts surrounding impacted teeth.

4. Discussion

Despite the limited sample size, the observed distribution of age and sex aligned with existing trends reported in the literature. Four of the seven patients were male, consistent with the male predominance described by Davidson *et al.* [11]. The mean age in our study was 46.14 years (±19.06), compared to 33.2 years in Davidson's cohort. Previous studies have shown that younger patients tend to exhibit more favorable bone healing [5] [12]. In our series, the highest regeneration rates (95.87%, 100%, and 98.7%) were found in the three youngest patients—female subjects aged 18, 33, and 40 years. These findings support prior evidence that bone healing is age-dependent, with diminished regeneration in older individuals due to reduced inflammatory response, fibroblast activity, collagen synthesis, angiogenesis, and stem cell responsiveness to key growth factors such as PDGF, IGF, FGF, TGF-β, and BMP [13]. Some authors suggest that cultured osteoprogenitor cells may improve healing outcomes in older patients [5].

Regarding the influence of lesion location, data in the literature remain inconclusive. While some authors report no significant difference between maxillary and mandibular healing [1] [2], others have observed less favorable outcomes for maxillary bone defects [5] [12]. This discrepancy may be attributed to differences in anatomical architecture. Mandibular defects are often enclosed by intact cortical bone, providing a stable scaffold for blood clot retention and facilitating predictable healing. Moreover, within the mandible, defects located in the body tend to have reduced regenerative capacity compared to those in the symphysis or angle, likely due to limited blood supply [5]. During the initial four weeks post-surgery, angiogenic and osteogenic cells from adjacent bone and periosteum progressively replace the blood clot with granulation tissue and newly formed bone [5]. In our study, bone defects located in the mandibular angle (cases 3, 4, and 5) exhibited an average regeneration rate of 89.30%, compared to 82.47% for defects located in the mandibular body (cases 1, 2, and 6).

Histologically, odontogenic keratocysts were the most frequent lesion type in our series (6 out of 7 cases), in line with previous epidemiological data indicating that radicular, follicular, and keratocysts are the most common odontogenic cysts [14] [15]. Zhao *et al.* evaluated spontaneous regeneration of 58 keratocysts using panoramic densitometry and reported a 71.77% increase in bone density after 12 months [9]. Rubio and Mombru reported a spontaneous regeneration rate of 88.5% in a randomized trial, with no significant differences between cyst types [7]. Similarly, Buchbender *et al.* concluded that histological type was not a determining factor for healing, provided that the cortical bone and periosteum were preserved [16].

Several studies have demonstrated that the configuration and size of the bone defect influence healing outcomes [1] [9] [16]. Healing is enhanced when multiple cortical walls remain intact, allowing for effective clot stabilization and cell migration. Panoramic studies have shown that the loss of buccal or lingual cortical bone can lead to incomplete healing or fibrous scar formation [3]-[5] [7]. However, CBCT-based evaluations by Buchbender *et al.* did not show significant differences between defects with one to two versus three cortical walls [1]. Some authors suggest that monocortical defects may heal more rapidly than bicortical ones [5] [17]. In our study, case 3 presented with a three-wall defect and achieved complete regeneration. However, bone loss from surgical access was not quantified. Conservative surgical approaches, particularly when access is limited to less than 10 mm, have been shown to preserve surrounding bone and promote osteogenesis, even when the remaining walls are thin [4] [5] [13] [17]. Moreover, periosteum preservation is essential, as it contains osteogenic cells that contribute to new bone formation [6].

The size of the bone defect is another major factor influencing spontaneous healing. In animal models, defects measuring 10 × 10 mm often fail to regenerate completely within 12 months [13]. In humans, however, spontaneous healing has been reported in defects up to 5 mm. Chiapasco *et al.* found a 43.46% reduction at 12 months and 81.30% at 24 months in patients with cysts larger than 40 mm, without bone grafting [4]. Chacko *et al*. also reported near-complete healing within 12 months [10]. In our study, volumetric analysis revealed an average volume reduction of 84.20% after one year, consistent with findings by Jeong *et al*. (~75% regeneration for 6 cm^3 cysts) [12] and Vitale *et al*. (99.72% for 11 cm^3 defects) [18]. While some protocols used automated segmentation, our method involved manual delineation of regions of interest (ROI) on 1 mm axial slices, providing detailed control over measurements.

Although complete healing was not achieved at 12 months in all cases, a systematic review suggests that bone regeneration may take up to 12 months for defects smaller than 3 cm^3, and up to 24 months for larger ones [16]. Thus, the healing timeline must be taken into account when evaluating the effectiveness of spontaneous regeneration.

In terms of bone density, our study found increased values at 12 months in all cases except for Patients 2 and 4, both of which involved impacted teeth within the lesion. In the present series, cases involving impacted teeth (Cases 2, 4, and 7) did not show a significant increase in mean bone density over the follow-up period, despite marked volumetric reduction of the defects. This finding can be primarily explained by the fact that the impacted teeth were completely encompassed by the cystic lesions and therefore included within the region of interest at baseline (T0). As a result, the presence of dental structures within the ROI at T0 led to artificially elevated initial density values, which consequently limited the apparent increase in mean density over time, even after tooth removal and progressive bone regeneration. Therefore, while volumetric healing was clearly observed, changes in radiographic density should be interpreted with caution in cases where impacted teeth are initially included in the analyzed volume.

These findings should be interpreted in light of previously published studies reporting high percentages of radiographic density recovery after cyst enucleation. Ihan and Milijavec reported 97% final density in small defects (20 - 30 mm) and 84% in larger defects [5], while Yim and Lee observed more than 97% radiopacity recovery in defects measuring 3 - 4 cm within 12 months [5]. Zhao *et al*. reported a 71.77% increase in density, whereas Chiapasco *et al*. and Pradel *et al*. reported gains of approximately 48% following grafted enucleations [4] [9] [19]. However, most of these studies relied on two-dimensional imaging techniques, in which radiographic normalization and superimposition may overestimate true mineralized tissue regeneration. In contrast, the use of CBCT-based 3D volumetric and density assessment in the present study may provide a more conservative but anatomically accurate evaluation of bone healing.

<u>Study Strengths and Limitations:</u>

Study limitations include the small sample size, heterogeneous data, and lack of histological analysis to confirm the quality of the regenerated bone. In contrast, the strengths of this study lie in its standardized 3D volumetric methodology and its prospective design.

5. Conclusion

This prospective pilot study suggests that spontaneous bone regeneration may occur even in large bone defects following cyst enucleation without bone grafting. When a conservative surgical technique is applied and periosteal integrity is preserved, this biologically and economically favorable approach may represent a potential alternative to bone grafting in selected cases. However, given the limited sample size and the radiographic nature of bone assessment, conclusions regarding the quality of the regenerated bone should be interpreted with caution. Larger-scale prospective studies combining standardized three-dimensional imaging and, when feasible, histological evaluation are required to further validate these findings.

Authors' Contributions

Wafaa Mahfoud: study conception, data acquisition, 3D analysis, drafting and final revision of the manuscript. Sidi Mohamed Bouzoubaa: imaging validation and methodological support. Mokrane Khazana: clinical supervision, critical revision of the manuscript. Ihsane Ben Yahya: project supervision and final approval of the manuscript. All authors read and approve the final manuscript.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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