Bone quality assessment in patients with healing mandibular fracture sites: a computed tomography investigation

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The objective of this retrospective study was to assess the bone quality of healing mandibular fracture sites by measuring the Hounsfield units (HU) on computed tomographic (CT) images obtained presurgery and postsurgery in patients treated with rigid internal fixation (RIF). The HU values of healing fracture sites were compared to those of corresponding nonfractured (control) sites on the opposing side and cervical vertebrae sites in the same patients. In total, 31 patients with 45 mandibular fractures treated with RIF underwent presurgical and postsurgical CT examinations. The scans performed after surgery (1, 3, 6, 12, or 18 months) were taken only when there was a need for radiographic evaluation due to a complaint of discomfort from the patient or when the surgeon needed to verify the postsurgical outcome, and each patient underwent only a single postsurgical CT. At the presurgical CT examination, the HU values were lower in the fracture sites than in the control sites. At 3 months postsurgery, the HU values in the fracture sites had increased as the mandibular bone healed. At 6 months postsurgery, the HU values in the fracture sites were higher than those of the control sites. At 12 and 18 months postsurgery, the HU values of both sites were similar. The HU values of the cervical vertebrae remained constant with time. These results suggest that, in patients who have been treated with RIF for mandibular bone fracture, HU values measured by CT vary across time, expressing the physiologic bone healing process.

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Craniomaxillofacial injuries are the most prevalent type of trauma and are a major concern in public health systems worldwide due to their high morbidity and mortality outcomes.[1] Maxillofacial trauma can comprise injuries of differing severity, such as fractures in the mandible or maxilla.[2] Maxillofacial fractures represent 80% of maxillofacial traumas and account for 3.2% to 3.8% of all body fractures.[3]

The main objectives for the treatment of maxillomandibular fracture are functional and esthetic recovery.[4] Rigid forms of bone fixation, such as rigid internal fixation (RIF), are frequently applied when a surgical approach to fracture treatment is required.[5] The goal of rigid fixation is to absorb part or all of the functional load and to prevent motion along the fracture, as the mechanical stability of a fracture site determines the type of fracture healing.[5] Primary bone healing develops when there is minimal strain and acceptable anatomical fracture reduction.[5]

The effective stabilization of bone segments allows for adequate tissue repair on the fracture line, initially with a primary cartilaginous callus, which later undergoes revascularization and calcification and is then replaced by bone tissue.[6] Unlike other tissues, bone tissue regenerates and repairs without the formation of scar tissue, although optimum reduction must be ensured.[7] However, fracture healing is a complicated physiologic process with well-orchestrated biologic events and distinct restorative stages.[8]

Physiologic bone repair depends on essential factors such as the activation of mesenchymal stem cells and the production and release of growth factors.[9] Adequate blood supply is also important for bone healing, providing the optimal signaling molecules and delivering oxygen and other cell metabolism nutrients.[9] Any alteration characterized by poor bone quality, such as age-related changes in bone metabolism or osteoporotic conditions, can delay the healing process, thus leading to fewer mesenchymal stem cells and the replacement of red marrow by adipose tissue; a decreased response to humoral stimuli, resulting in reduced osteogenic differentiation; and an impaired osteoblastic response to mechanical stimuli, resulting in reduced osteoblast proliferation.[9,10]

Inadequate bone healing during repair of facial trauma fractures may be associated with the patient's bone quality. Poor bone mineral density related to osteoporosis could delay bone healing, especially alveolar bone healing.[11] Hence, assessment of bone quality is valuable for predicting the time of bone repair and consolidation.

The physiologic process of bone healing, from the earliest organized callus to complete bone healing, corresponds to radiologic findings, particularly those of computed tomography (CT).[12] CT is useful for determining the affected areas and

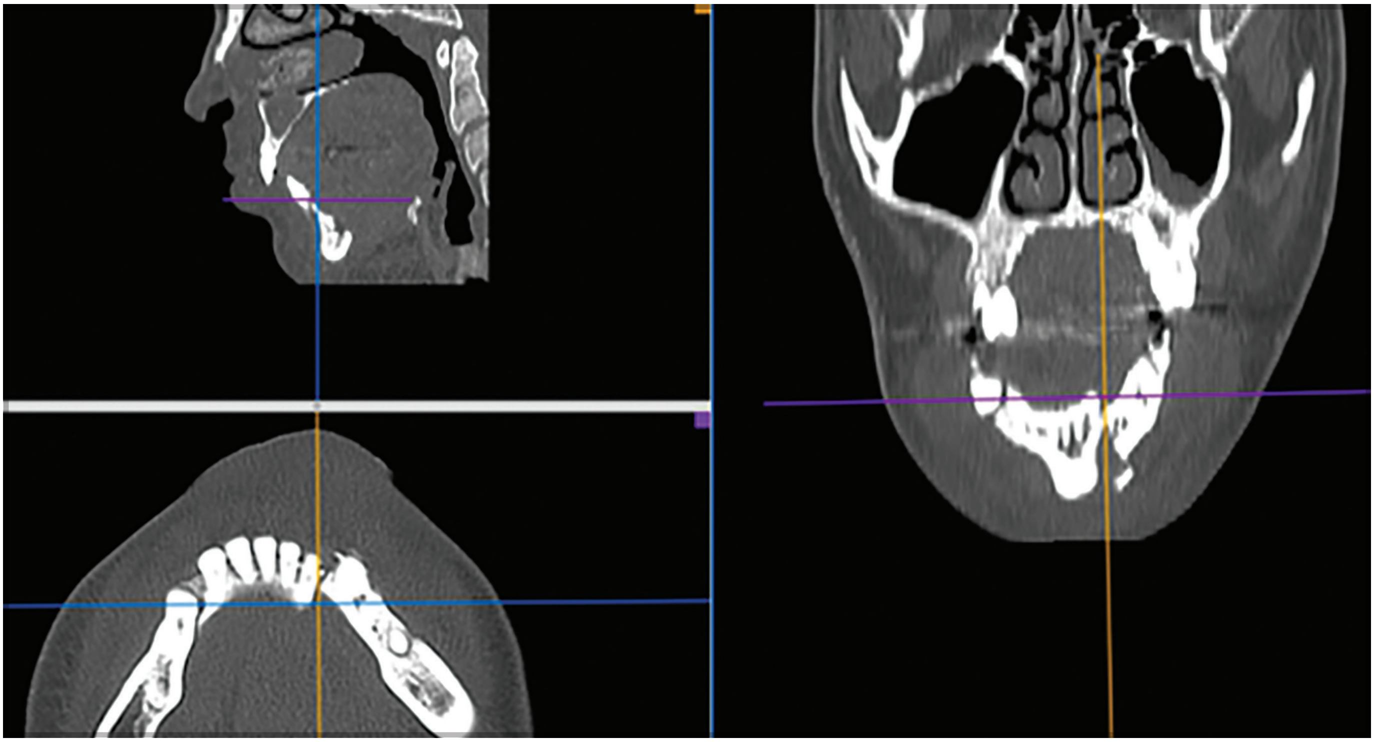


Fig 1. Assessment of axial, sagittal, and coronal CT slices to locate the fracture sites and corresponding control sites.

extent of an injury, as well as for defining the progression of fracture healing. Hounsfield units (HU), a measure of tissue radiation attenuation on a linear scale, can be applied for assessment of regional bone mineral density and bone quality, particularly in multislice CT.[13-15] On the HU scale, 0 is defined as water and −1000 is defined as air.[15] The HU values for bone range from 300 (cancellous bone) to 3000 (cortical bone).[14]

The aim of this study was to assess the bone quality in healing mandibular fracture sites using HU values obtained by multislice CT at different postsurgical timepoints in patients treated with RIF. Moreover, HU values from healing fracture sites (fracture sites) were compared to those of nonfractured (control) sites and cervical vertebrae sites in the same patients.

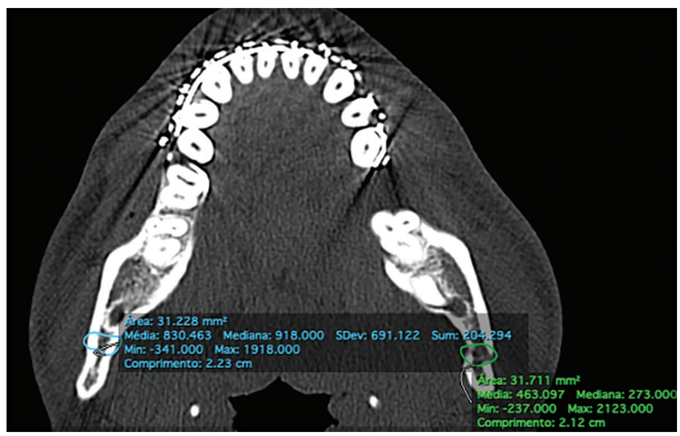


Fig 2. Measurement of Hounsfield units on an axial CT slice.

Methods

Ethical approval was obtained from the University of São Paulo, São Paulo, Brazil (No. 2.441.529). The guidelines established by the Declaration of Helsinki were followed in this investigation.

Study participants

This retrospective study included 31 participants (27 men and 4 women) aged 18 to 61 years with mandibular fractures and available CT examinations who were referred to the university hospital for surgical treatment between 2016 and 2018. All patients with mandibular fractures were treated surgically with RIF.

Exclusion criteria included the presence of metabolic bone diseases, a history of medication intake affecting bone metabolism (eg, bisphosphonates or glucocorticoids), and chronic use of tobacco or alcohol. Moreover, CT images with technical failures or artifacts in the region of interest (ROI) were considered an exclusion criterion.

Data on the demographics of the patients, trauma etiology, trauma features (side, mandibular anatomical structure involved, etc), and type of RIF were collected.

CT examinations

CT scans were performed before the surgical procedures (T0) and 1 (T1), 3 (T3), 6 (T6), 12 (T12), or 18 months (T18) after the surgical fixation procedures. The scans performed after surgery were taken only when there was a need for radiographic evaluation due to a complaint of discomfort from the patient or when the surgeon needed to verify the postsurgical outcome, and each patient underwent only a single postsurgical CT.

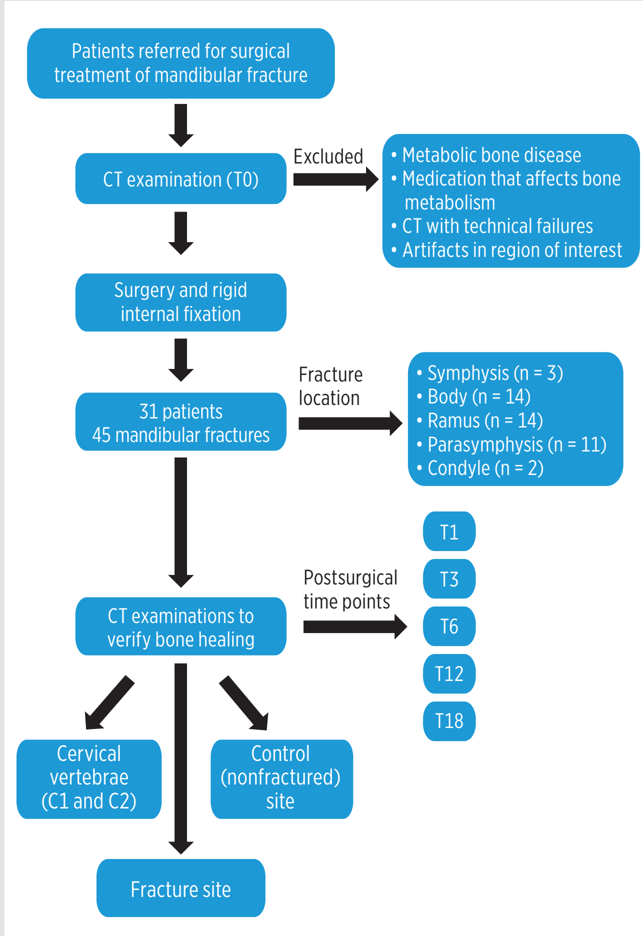
All CT examinations were performed using the same device (Brilliance CT 16 slice, Philips) with the following settings:

Table 1. Characteristics of the mandibular fractures and treatment.

Variable	n (%)
Trauma etiology (N = 31)	
Motorcycle with helmet	8 (25.8)
Motorcycle without helmet	3 (9.7)
Aggression in the face	10 (32.3)
Fall	8 (25.8)
Blunt injury	1 (3.2)
Gunshot injury	1 (3.2)
Trauma areas (N = 31)	
Mandible only	27 (87.1)
Mandible and middle face	2 (6.5)
Mandible, middle face, and other bones	2 (6.5)
Mandibular fracture type (N = 31)	
Unilateral	14 (45.2)
Bilateral	16 (51.6)
Midline	1 (3.2)
Mandibular fracture side (N = 45)	
Right	23 (51.1)
Left	22 (48.9)
Anatomical region of the fracture (N = 45)	
Symphysis	3 (6.7)
Parasymphysis	11 (24.4)
Body	14 (31.1)
Angle	14 (31.1)
Ramus	1 (2.2)
Condyle	2 (4.4)
RIF system (N = 45)	
2.0 mm (1 plate)	10 (22.2)
2.0 mm (2 plate)	33 (73.3)
2.4 mm (1 plate)	2 (4.4)
Time of CT examination (N = 31)	
T0	31 (100.0)
T1	5 (16.1)
T3	4 (12.9)
T6	5 (16.1)
T12	11 (35.5)
T18	6 (19.4)

Abbreviations: CT, computed tomography; RIF, rigid internal fixation; T0, presurgery; T1, 1 month postsurgery; T3, 3 months postsurgery; T6, 6 months postsurgery; T12, 12 months postsurgery; T18, 18 months postsurgery.

Chart 1. Study methodology.



Abbreviations: CT, computed tomography; T0, presurgery (N = 31); T1, 1 month postsurgery (n = 5); T3, 3 months postsurgery (n = 4); T6, 6 months postsurgery (n = 5); T12, 12 months postsurgery (n = 11); T18, 18 months postsurgery (n = 6).

1- to 2-mm thickness, 250-mm field of view, 120-kVp tube voltage, and 250-mA tube current. DICOM (digital imaging and communications in medicine) files of the CT examinations were assessed using OsiriX MD DICOM Viewer (Pixmeo).

All fractured areas were assessed and measured using axial, coronal, and sagittal slices (Fig 1). The HU values were collected in 3 distinct areas: the fracture sites, the nonfractured control sites, and the cervical vertebrae. The ROIs for collecting HU values were positioned using only axial slices due to the complexity of the fractures (Fig 2). The diameter of each ROI varied according to the fracture features and extension. One ROI was applied to the fracture line (fracture sites), and a second ROI with the same features as the first was positioned on the side of the mandible opposite to the fracture side to collect HU values from the corresponding nonaffected area (control sites). When the fracture was in the midline (symphysis) or bilateral fractures were present, the nearest healthy bone was selected as control. The HU values of cervical vertebrae C1 and C2 were also measured.

Table 2. Hounsfield unit values according to sites and CT timepoint.[a]

CT	Fracture sites			Control sites			Cervical vertebrae sites		
	Min	Med (IQR)	Max	Min	Med (IQR)	Max	Min	Med (IQR)	Max
T0 (N = 31)	166.2	454.0 (356.0)	944.5	1.0	681.9 (564.1)	967.8	175.9	394.4 (342.2)	571.5
T1 (n = 5)	154.4	538.1 (496.2)	800.5	605.1	769.6 (622.3)	922.1	243.4	367.2 (343.1)	504.9
T3 (n = 4)	140.4	582.9 (299.0)	776.5	701.0	740.3 (705.4)	820.2	281.6	419.2 (376.2)	698.5
T6 (n = 5)	458.9	812.5 (551.4)	1050.0	490.0	717.4 (616.2)	999.6	261.4	347.0 (322.8)	579.7
T12 (n = 11)	102.4	714.8 (610.5)	921.0	102.5	689.8 (484.2)	937.7	198.6	377.4 (334.0)	557.9
T18 (n = 6)	572.8	846.0 (669.4)	1002.0	681.1	781.1 (717.5)	981.7	257.6	350.3 (275.8)	497.3

Abbreviations: CT, computed tomography; IQR, interquartile range; Max, maximum; Med, median; Min, minimum.

[a]Hounsfield unit values of the total sample studied without considering median age. All 3 sites consisted of CT images of the same patient sample (N = 31): fracture sites, mandibular sites with traumatic fracture; control sites, corresponding bone site opposite the side of the fracture or, if the fracture was in the midline (symphysis) or bilateral, the nearest healthy bone; cervical vertebrae sites, vertebrae C1 and C2.

Statistical analysis

The Shapiro-Wilk test showed that the sample data were nonparametric ($P < 0.05$), so the nonparametric Kruskal-Wallis test with Dunn post hoc test was used for analysis. The HU values were grouped by area assessed and timepoint and calculated as maximum, minimum, and median. Comparisons of HU values were performed considering the 3 different sites (fracture, control [nonfracture], and cervical vertebrae) and the 6 distinct timepoints (T0, T1, T3, T6, T12, and T18). Statistical analyses were performed using SPSS software (version 25, IBM).

Results

The study sample included 31 patients (median age 25 years) with a total of 45 mandibular fractures. Eighteen participants (58.1%) were White, and 13 (41.9%) were Afro-descendant. The majority of the patients were male (27; 87.1%) and had fractures in the mandible only (27; 87.1%). The most frequently affected areas of the mandible were the body and the angle (Table 1).

Chart 1 summarizes the study methodology as well as the number of CT examinations according to the mandibular region evaluated. Most patients underwent CT at 12 months postsurgery, and only a few underwent CT at 3 months postsurgery. Furthermore, most patients presented no symptoms, and the postsurgical CT examinations were performed routinely to verify bone healing.

Table 2 presents the HU values of the various sites as medians and interquartile ranges. Variations in median HU values according to time of CT examination are presented in Chart 2. At T0, the median HU value of the fracture sites was, as expected, lower than that of the control sites. At T1 and T3, the HU values of the fracture sites had increased as the mandibular bone healed. At T6, the HU value of the fracture site was slightly higher than that of the control sites. At T12, the HU values of both sites were similar. The median HU values of the cervical vertebrae remained constant with time.

Comparisons of the HU values among sites at different timepoints indicated statistically significant differences ($P < 0.0001$; Kruskal-Wallis test). Specifically, significant differences were observed in the fracture sites between T0 and the postsurgical timepoints T6, T12, and T18. Moreover, comparison of the HU values in the fracture and control sites revealed significant differences between the fracture sites at T0 and the control sites at all postsurgical timepoints. No differences in the HU values were detected between the fracture and cervical vertebrae sites ($P = 0.1418$) or between the control and cervical vertebrae sites ($P = 0.987$).

Discussion

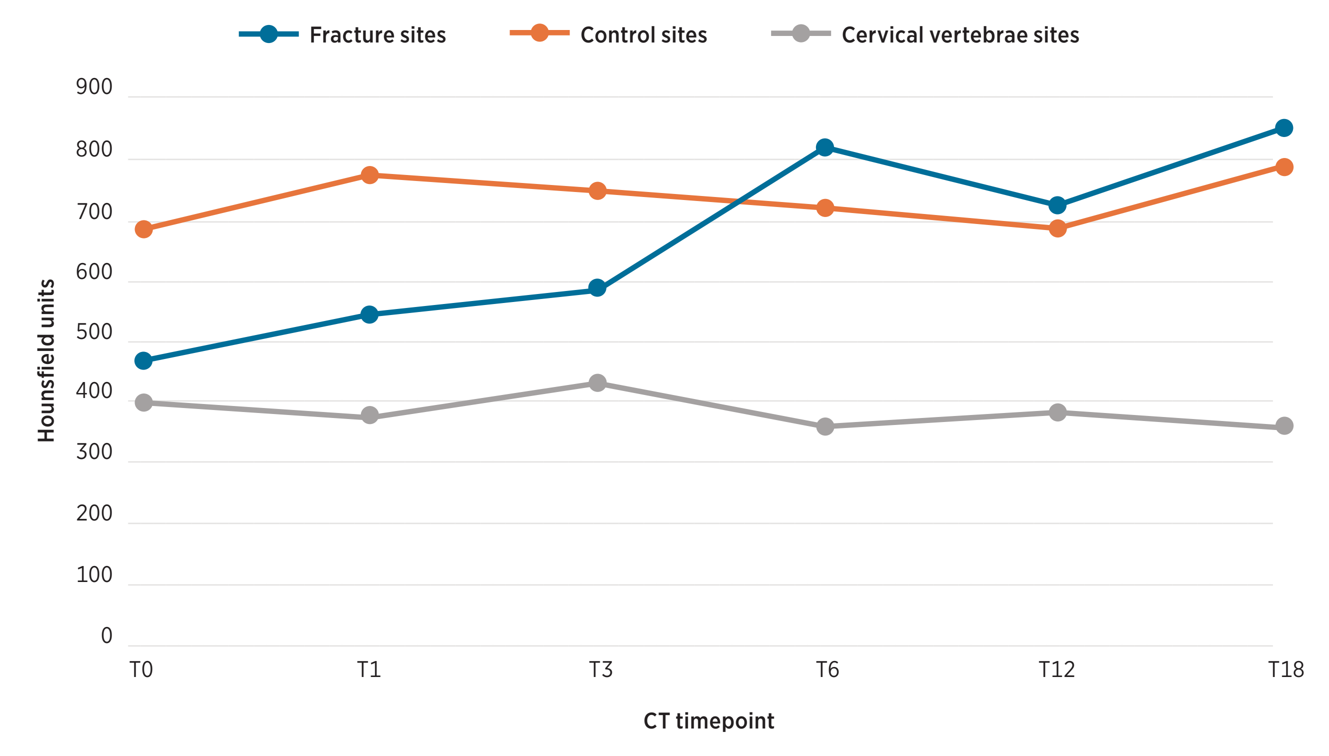
This study examined variations in HU values of healing mandibular fracture sites in comparison to control sites according to postsurgical timepoint. The present findings demonstrate that HU values are consistent with the physiology of bone fracture healing.

The patients included in this study were all treated with RIF. As primary healing is desirable in bone healing, RIF is important for providing adequate bone healing by reducing the bone callus formation and optimizing the bridging between bone fragments.

Fracture healing involves a complex series of events to restore bone tissue to its preinjury anatomical and histologic forms.[5] The HU values obtained from CT examinations at distinct timepoints over the course of bone repair are representative of this entire process. Specifically, the fracture healing process occurs in 4 distinct stages. The first stage, immediately following the fracture, involves blood clotting (hematoma formation) and inflammation within the fracture line area (granulation tissue).[8] This first stage was represented by the HU values at T0; the lower HU values in the fracture sites compared to the control sites at this timepoint were expected, considering that bone loss, presence of inflammation, and blood clots decrease the radiation attenuation in the fractured area.

In the second stage, bone tissue repair begins when the granulation tissue is replaced by cartilaginous tissue, which stabilizes and temporarily connects the fractured bone.[8,12] Late in this stage, a hard callus of woven bone forms at the fracture line.[8] Callus arrangement and maturation are interconnected chronologically and involve the formation and degradation of distinct tissue types. The formation of a hard bone callus requires the apposition of minerals from the blood serum,

Chart 2. Median Hounsfield unit values according to time of CT examination.



Abbreviations: CT, computed tomography; T0, presurgery (N = 31); T1, 1 month postsurgery (n = 5); T3, 3 months postsurgery (n = 4); T6, 6 months postsurgery (n = 5); T12, 12 months postsurgery (n = 11); T18, 18 months postsurgery (n = 6).

particularly ionized calcium and phosphorus, which is guided by osteoinductive factors.[16] When compared to secondary bone healing, primary bone tissue healing is predicated on the restoration of the lamellar bone via a minimal bone callus.[5,17] The earliest organizing callus is visible in radiographs and CT scans 2 or 3 weeks postsurgery; by around 12 weeks, abundant callus is present, which means that the HU values should also intensify.[12] Thus, the observed increase in the HU values of the fracture sites at T3 is representative of this stage, due to the higher radiation attenuation of the callus tissue compared with the granulation tissue present at T0.

In the third stage, osteoblasts form woven bone on the calcified matrix.[8] The resorption of the hard callus and the formation of woven bone are activated by specific inflammatory cytokines that transform the rigid callus into lamellar bone tissue with a central medullar cavity.[18] Woven bone is a fast-forming osteoid tissue with a mineral apposition rate 2 to 4 times higher than that of lamellar bone.[8] Moreover, woven bone contains plentiful osteocytes and is characterized by a disorganized microstructure.[19] When woven bone is fully mineralized, the presence of abundant organic content results in lower stiffness than lamellar long-term bone tissue.[19]

Last, in the fourth stage, the remodeling process proceeds with conversion of the woven bone into lamellar bone.[8] Medullar bone repairs earlier than cortical bone, and medullar bone tissue formation allows for capillary blood supply and osteogenic elements to reach beyond the fracture line, in turn allowing for longitudinal bone healing.[5] This healing phase lasts about 3 to 4 weeks.[5] The repair of cortical bone occurs via the growth of capillaries across the fracture line through cortical tunnels.[20] Cortical bone tissue is the last to repair, healing completely at about 16 weeks after fracture stabilization.[20] In the present study, although the difference was not statistically significant, the HU values in the fracture sites obtained at T6 were higher than the control sites at the same timepoint, indicating the intense repair activity of osteoblasts and the apposition of minerals in the collagenous matrix. The similar HU values in the fracture and control sites at T12 and T18 demonstrate complete bone tissue healing as assessed by radiographic imaging. However, the microstructural remodeling process that was initiated may take years to complete and achieve a fully regenerated bone structure.[21]

Measurement of HU values on CT scans is valuable for assessing craniomaxillofacial injuries, surgical outcome, postsurgical complaints, and bone healing quality in the fracture area. It can also be applied as an alternative tool for assessing bone mineral density.[14] The HU values of the cervical vertebrae have been shown to correlate with bone mineral density obtained by dual-energy X-ray absorptiometry.[14,22] Thus, cervical HU values were used in the present study to ensure that no important bone mineral density alterations existed in the study sample. The HU values of the patients' cervical vertebrae were constant over time, a finding that is valuable for monitoring systemic bone mineral density during bone repair.

Direct comparisons with similar studies could not be performed because, to the authors' knowledge, no previous studies have considered HU values when assessing bone quality in healing mandibular fracture sites at distinct timepoints after fixation surgery.

Conclusion

The present results suggest that, in patients treated with RIF for mandibular bone fracture reduction, HU values measured by CT vary with time, representing the physiologic bone healing process.

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Conflicts of interest

None reported.

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