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ORIGINAL ARTICLE

Dense cancellous bone as evidenced by a high HU value is predictive of late implant failure: a preliminary study

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Abstract

Objectives The mechanism of late implant failure is unclear. This study examined the association between sclerosing cancellous bone images and the risk of late implant failures using multi-detector row computed tomography (CT) imaging data.

Methods We performed a case–control study. The study group consisted of consecutive patients with implant failures treated at Kyushu Dental University between 2001 and 2016. CT data for late failure of 36 implants in 16 patients were available. The study cohort consisted of 16 patients with 36 late failed implants and 28 patients with 113 successful implants.

Results The mean survival rate was 6.9 months for early implant failure, 76.6 months for late failure with marginal bone resorption, inflammation symptoms, and so-called peri-implantitis, and 95.0 months for late failure caused by implant fracture. The mean HU value for cases in the control group was 507 compared with 1231 for cases with late failure implants. Logistic regression was used for analysis. There were signs of high radiodensity of peri-implant cancellous bone when comparing adjusted radiodensity per 100 HU using CT data (OR 2.35; 95% CI 1.73–3.20; $p < 0.001$).

Conclusions Within the limits of our study, the presence of high radiodensity and cancellous bone consolidation on imaging may be related to risk factors for late implant failure. Therefore, CT images of the host cancellous bone status for observation of visible sclerosis could be a useful diagnostic indicator for late implant failure.

Keywords Late implant failure · Cancellous bone · Bone sclerosing image

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Introduction

Endosseous dental implants have a high level of success, but occasionally fail, and elucidation of the mechanism for their failure is critical to achieve better clinical results [1–4]. Although numerous studies on failing and failed implants have been conducted, the mechanisms of implant loss are not fully understood [5, 6]. It is important to understand why and how these complications occur to avoid implant failure [7]. The types of implant loss can be divided into early loss and late loss [8]. Early loss is

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defined as failure to achieve osseointegration, while late loss is defined as failure to maintain established osseointegration. Signs and symptoms of implant failure associated with inadequate osseointegration include implant disintegration, pain, and discomfort [9]. In this failure pattern, the patient does not achieve proper osseointegration between the bone and the implant. The causes of early failure include excessive surgical trauma to the bone, including that caused by poor surgical technique, infection with impaired healing, including that associated with bone grafts, and loading of the implant arising from premature osseointegration [8–11].

Late implant failure typically begins with symptoms of marginal bone resorption and is thought to result from chronic bacterial infection, so-called "peri-implantitis", or overload arising from the load-bearing capacity of the surrounding bone [12]. Implant fracture is a late and infrequent biomechanical complication [13].

In a published systematic review, peri-implant mucositis was found in 63% of patients and approximately 31% of implant sites compared with 19 and 10% for peri-implantitis, respectively [14]. In addition, smokers were at a higher risk for both conditions. These observations agree with the results of a network meta-analysis and other systematic reviews [15–18]. Peri-implantitis is sometimes difficult to treat, and currently has no specific treatment modalities, despite the high number of treated cases published [19–21]. The peri-implant bone is essential for prevention of implant loss. However, few studies have assessed the comprehensive characteristics of the bone around implant sites using computed tomography (CT) in cases of failing or failed implants. Clinically, CT is currently the only diagnostic imaging technique that can allow determination of bone structure and density [22, 23].

The aims of the present study were to assess the types of failing or failed implants and to identify the risk factors associated with late implant failure using a retrospective case–controlled study design and CT data.

Materials and methods

All procedures followed were accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. All patients provided informed consent to be enrolled in the study and agreed to follow the study design. The Ethical Committee of Kyushu Dental University approved the study protocol (approval number: 2013 12-38). The STROBE guideline was followed in this investigation.

Inclusion and exclusion criteria

The study participants consisted of all consecutive patients with implant failures treated at the Division of Oral and Maxillofacial Reconstructive Surgery and Division of Oral Medicine at Kyushu Dental University between 2001 and 2016. The patients ranged in age from 21 to 82 years (mean 61.4 ± 12 years). A total of 63 endosseous root form design implants were retrieved from 39 patients, comprising 33 implants placed in our department and 30 placed in other clinics. The overall implant survival rate for our department was 95.9% (493/514 implants). Demographic information, including medical problems and smoking habits, was recorded for all patients. Dental information was also recorded, including implant position, type of implant suprastructure, bone augmentation procedure, reason for implant failure, and interval from implant insertion to removal. CT data were available for 44 implants, comprising eight implants in cases with early failure and 36 implants in cases with late failure. The 36 cases of late failure were included in the case–control study. Historical implant designs, such as blade type and subperiosteal implants, were excluded. Cases with implants retrieved for specific medical reasons, such as trauma or oral cancer invasion, were also excluded.

Case and control definitions

The study group consisted of 36 cases of retrieved late failure implants. Patients for whom adequate CT imaging data were not available were excluded. The control group contained 113 clinically asymptomatic implants. If the study group patients had multiple implants, the successful implants were counted as controls. Forty-two asymptomatic implants within 12 study group patients were included as control implants. The remaining control cases were consecutive patients who wished to be treated with additional implants at different positions after a previous implant treatment, and underwent CT imaging prior to the secondary implant placement. In the additional cases, the CT data for 71 implants from 16 patients were included as control implants. The control group did not present with any problematic clinical symptoms in the treated implants that maintained osseointegration. A total of 149 implants were analyzed in this study.

CT image analysis

CT was performed for evaluation of the jaw bone using a Toshiba X Vision RE™ machine with a single row of detectors (Toshiba Co. Ltd., Tokyo, Japan). CT images were obtained before implant retrieval surgery in cases with a failing implant where the implant still existed in the

jaw bone. In cases with a failed implant where the implant had already fallen out of the jaw bone, CT images were collected at the time of patient admission. The CT images for all patients were obtained in the occlusal plane perpendicular to the ground in a helical manner with contiguous 2-mm-thick sections. The images were captured with bone tissue windows using a 400-Hounsfield unit (HU) window level and 2000-HU window width. The entire maxilla or mandible was initially confirmed on axial images, followed by cross-sectional images. In cases with failing implants, the HU value around the implant at a distance of 2 mm from the bottom of the implant on an axial image in one slice was investigated on the monitor using the software program associated with the CT scanning system. In cases with failed implants, the HU value was measured around the region from the bottom of the implant at a distance of 2 mm from where the implant had been placed on an axial image in one slice (Fig. 1). The region of interest (ROI) was adjusted to avoid strong artifacts around the implants.

All CT measurements in this study were recorded separately in a random order by two trained independent observers (a radiologist and a specialist in oral and maxillofacial surgery) to avoid any observer bias. One observer (I.M. or T.T.) served as the primary observer, and intraobserver reliability was assessed among three measurements obtained separately to eliminate memory bias. The Cohen's kappa value was determined for panoramic radiograph evaluation as the degree of congruence, with a value of >0.80 considered to indicate very good congruence. All images were examined twice with a 21-day interval. For reliability testing, the intraclass correlation coefficient (I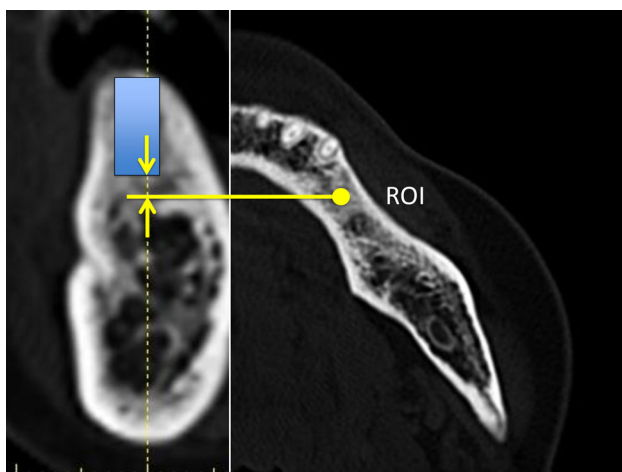CC) was used for continuous variables. To determine the reliability of the HU value (continuous variable), the ICCs and their 95% confidence intervals (CIs) were used to summarize intraobserver and interobserver reliability.

Statistical analysis

As this was an observational retrospective study, no formal sample-size calculation was performed. Continuous variables were recorded as mean $\pm$ standard deviation. The unpaired Student's t test was used to compare the mean HU values between cases and controls. One-way analysis of variance (ANOVA) was used to compare the clinical patterns of implant failure and HU values. For post hoc multiple-comparison procedures, we used the Tukey-HSD test with the level of significance set at 0.05 per number of comparisons.

To investigate the association between bone sclerosing images (radiodensity per 100 HU on CT) and the risk of late implant failures, a logistic regression analysis was performed to estimate the odds ratios (ORs) for cases with late implant failure and their 95% CIs. The ORs were adjusted for the potential confounders of age, sex, treated jaw (maxilla/mandible), type of suprastructure (implant-supported fixed prosthesis/implant-retained overdenture), bone augmentation procedure (yes/no), and smoking habit (yes/no). A forced entry method was used for selection of variables. In addition, we used multilevel logistic regression (mixed effect logistic regression) models to account for cluster effects of multiple implants when placed and evaluated in a single patient. The reason for this was that the outcomes for different implants in a single patient must be more closely correlated to one another than the outcomes for implants in separate patients, and ignoring these correlations could result in a bias. To investigate the variation between clusters by comparing two patients from two randomly chosen different clusters, the median odds ratio (MOR) was estimated. The measure of MOR is always equal to or greater than 1. If the MOR is 1, there is no variation between clusters (no second-level variation) [24].

The results were considered statistically significant if the corresponding p value was less than 0.05. SPSS software (SPSS for Windows 19.0; IBM Corporation, Armonk, NY, USA) and Stata 11.2 software (Stata Corporation, College Station, TX, USA) programs were used for analysis.

Fig. 1 The HU value was measured around the region from the bottom of the implant at a distance of 2 mm from where the implant had been placed on an axial image. The region of interest (ROI) was adjusted to avoid strong artifacts around the implants

Results

The recorded demographic and dental parameters for all patients were as follows. A total of 63 removed implants were included in the study. The position of the retrieved

implants was the anterior maxilla in 19% of cases (12 implants, 11 patients), the posterior maxilla in 38% (24 implants, 12 patients), the anterior mandible in 8% (five implants, four patients), and the posterior mandible in 35% (22 implants, 17 patients). The specific clinical history prior to implant removal included bone augmentation procedures (27 implants, 20 patients), bone grafting of cleft palate (four implants, three patients), chronic sclerosing osteomyelitis (15 implants, nine patients), radiation therapy for oral cancer (two implants, one patient), overheating at time of implant insertion (one implant, one patient), bruxism (six implants, three patients), and chemotherapy for leukemia (one implant, one patient). The detailed bone augmentation methods included sinus floor elevation with the lateral window approach (10 implants, five patients), onlay bone grafting (nine implants, nine patients), titanium mesh with autologous bone grafting (three implants, two patients), alveolar distraction osteogenesis (two implants, one patients), split crest (two implants, one patient), and guided bone regeneration (one implant, one patient). The implant manufacturers were Astra (34 implants), Nobel Biocare (10 implants), Straumann (five implants), POI (two implants), and unclear (12 implants). All implants were of the root form design.

The reasons for implant removal in all patients with or without CT data were early failure (disintegration, pain, and discomfort of implant; 13 implants, 12 patients; Fig. 1a, b), late failure with marginal bone resorption, inflammation symptoms, and so-called peri-implantitis (35 implants, 20 patients; Fig. 2a, b), and late failure caused by implant fracture (15 implants, 11 patients; Fig. 3a, b). The mean survival rate in the groups was 6.9 ± 4.43 months for implant disintegration, 76.6 ± 76.07 for late failure caused

by so-called peri-implantitis, and 95.0 ± 51.41 months for implant fracture (Fig. 4). There were significant differences in clinical symptoms between the groups (ANOVA and Tukey-HSD: $p < 0.001$). There was no correlation between onset and development of so-called peri-implantitis, while the onset of implant fracture was a late complication and usually developed after 5 years of implant placement. The clinical outcomes after implant removal were additional implant insertion (18 implants, 11 patients), prosthetic treatment without additional implant insertion (19 implants, 12 patients), observation (19 implants, 15 patients), and drop-out (seven implants, five patients).

Among the patients, a total of 36 cases and 113 controls with CT data were evaluated in this study (Fig. 5). The baseline information for the study is shown in Table 1. The study group had a mean age of 65.8 years and comprised 36 implants in 16 patients (nine males, seven females), while the control group had a mean age of 67.8 years and comprised 113 implants in 28 patients (12 males, 16 females). The HU values showed favorable reliability in terms of the Cohen's Kappa index (0.89; $p = 0.001$) and the ICCs, which supported the reliability of the radiographic assessment and HU measurement (Table 2).

The mean HU value in the control group was 507 ± 265 compared with 1231 ± 292 in the late failure implant group. There were significant differences in the radiodensity of the peri-implant cancellous bone (Student's t test: $p < 0.0001$; Fig. 6). The mean HU value in the cases with early failure ($n = 8$) was 627 ± 260 compared with 1154 ± 276 in the cases with late failure caused by the so-called peri-implantitis ($n = 25$) and 1405 ± 245 in the cases with late failure caused by implant fracture ($n = 11$) (Fig. 7). The mean HU values of the peri-implant cancellous bone at the time of implant removal differed significantly between the groups (ANOVA and Tukey-HSD: $p < 0.001$).

The statistical results showed that it was possible to detect cancellous bone consolidation using radiodensity per 100 HU on CT (OR 2.35; 95% CI 1.73–3.20; $p < 0.001$). No other factors were found to be significantly associated with implant failure ($p > 0.05$; Table 3). A multilevel analysis (mixed effect logistic regression) was performed to consider cluster effects. Although the variance between individuals was large and the MOR was 132.3, the analysis revealed that detection of bone consolidation using radiodensity per 100 HU on CT was correlated with a significant risk for late implant failures (OR 10.4; 95% CI 1.08–99.51; $p = 0.042$).
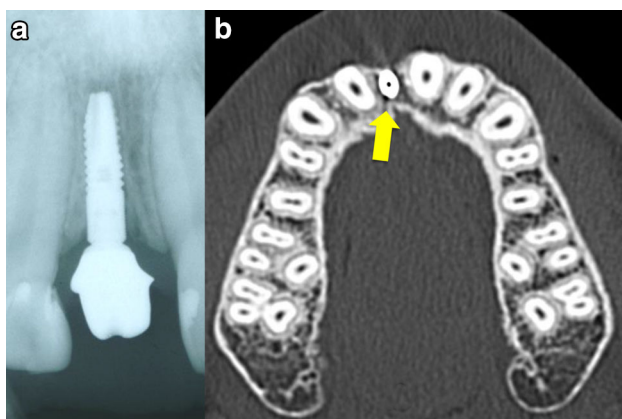

Fig. 2 Typical disintegration seen in early failure of an implant. Provisional restoration was applied immediately after the implant–abutment connection. One week later, implant mobility was clinically observed and the implant failed. There was no clear sign of sclerotic cancellous bone around the implant on a radiograph (**a**) or CT (**b**; *arrow*) image

Discussion

Based on the present results, there are several patterns of failing/failed implants with clinical symptoms that occur in a time-dependent manner. According to our results, early

Fig. 3 **a** Panoramic radiograph depicting progressive peri-implant bone resorption that was visible in the left mandible. The *yellow arrow* shows bone resorption and cancellous bone consolidation around the failed implant. The implant was retrieved prior to CT scanning. **b** There were signs of cancellous bone consolidation around the left mandible (*yellow arrow*); conversely, there was no cancellous consolidation visible around the right side implants (*red arrow*)
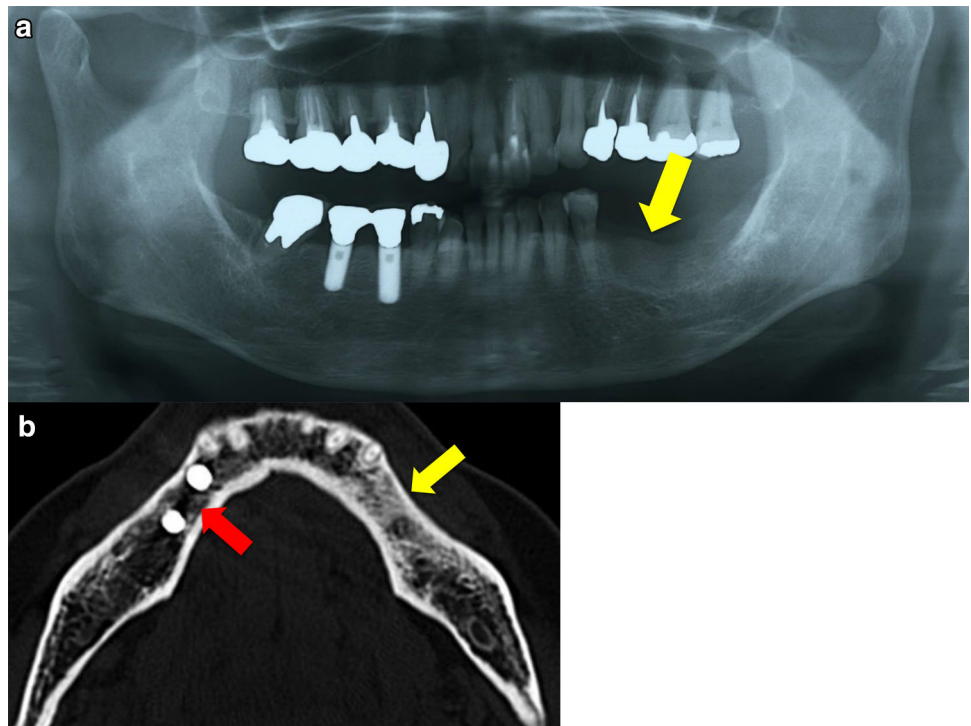

Fig. 4 Implant fracture. Before implant placement, there were few signs of bone consolidation (**a**; *yellow arrow*); however, there were signs of cancellous bone consolidation around the anterior implant at 38 months after implant insertion (**b**; *yellow arrow*). **c** Severe local bone resorption around the fracture region (*yellow arrow*) and cancellous bone consolidation around the fractured implant were observed on a panoramic radiograph
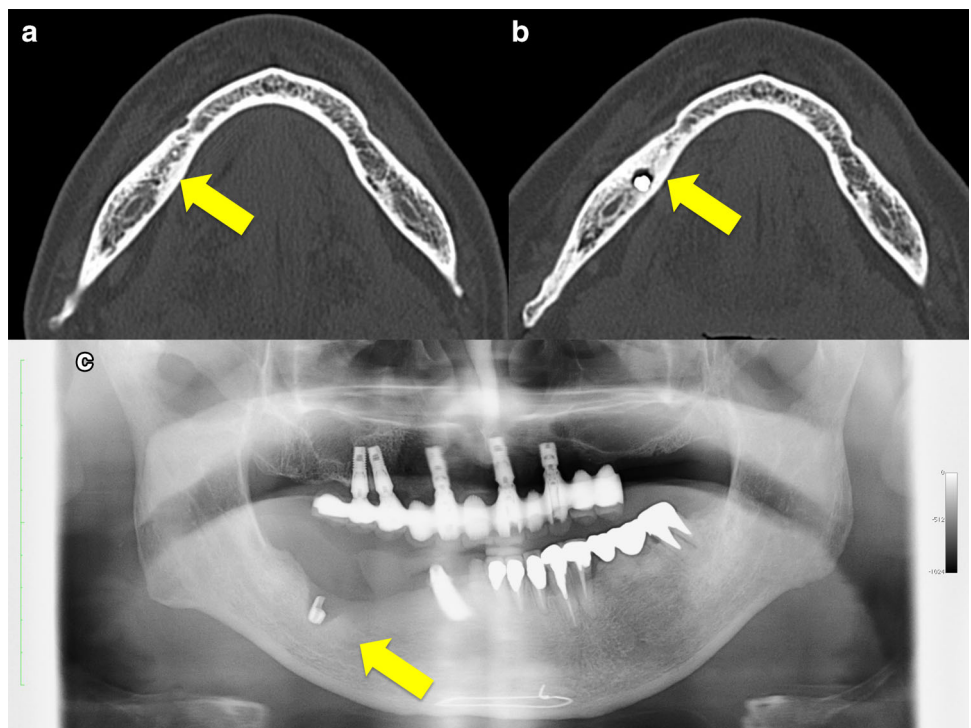
failure (implant disintegration, pain, and discomfort) does not present with a clear sclerosing CT image. Meanwhile, the so-called peri-implantitis and implant fracture are classified as causes of late failure [8, 9, 12]. In this study, there were no trends in the timing of onset of so-called peri-implantitis, while implant fractures occurred as late

complications over 5 years after implant placement. In addition, late implant failure was associated with high cancellous bone radiodensity around the implant on CT scans (Fig. 8). An important result is that the host bone condition causes implant failure. The presence of cancellous bone consolidation around the implant is not a healthy
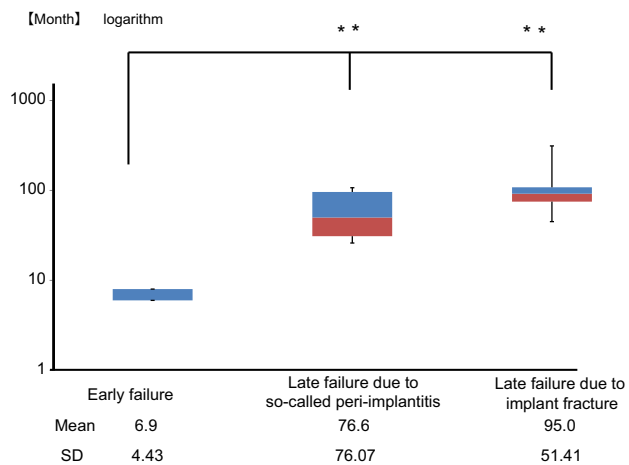
Fig. 5 Box and whisker plot showing the median (central line), 25th (red) and 75th (blue) percentiles (boxes), and entire range (whiskers). The graph shows the duration from implant placement to failure with respect to onset of clinical symptoms. There were significant differences in clinical symptoms between the groups (ANOVA and Tukey-HSD test: **p < 0.001)

Table 1 Baseline information

	Study group	Control group
Sex		
Male	20 (56%)	53 (47%)
Female	16 (44%)	60 (53%)
Age		
Mean (±SD)	65.8 (±10.00)	67.8 (±11.38)
Maxilla/mandible		
Maxilla	22 (61%)	55 (49%)
Mandible	14 (39%)	58 (51%)
Radiodensity per 100 HU on CT		
Mean (±SD)	12.3 (±2.92)	5.07 (±2.65)
Bone augmentation		
Yes	13 (36%)	25 (22%)
No	23 (64%)	88 (78%)
Implant suprastructure		
Fixed prosthesis	32 (89%)	95 (84%)
Implant-retained overdenture	4 (11%)	18 (16%)
Smoking habit		
Yes	11 (31%)	29 (26%)
No	25 (69%)	84 (74%)

The study group contained 36 implants in 16 patients, and the control group contained 113 implants in 28 patients. Data are shown as number of implants (%), unless otherwise indicated

environment with respect to bone cell viability or bone quality.

Regarding pathogenic mechanisms, there are two possible patterns of cancellous bone consolidation around the implant. One pattern reflects the patient's history before implant placement. For example, refractory periodontal or odontogenic bone infections may be present with cancellous bone consolidation [25]. The other pattern involves cancellous bone consolidation acquired after implant insertion. Surgical bone damage, including damage caused by overheating of the bone, chronic infection, or excessive mechanical overloading, may be a major cause, as indicated in several reports [8, 9, 13, 26, 27].

The possible mechanisms for cancellous bone sclerosis include direct or indirect damage to bone-related cells in the peri-implant bone. Chvartszaid et al. [26] assumed that severe trauma to the site of the implant would lead to implant failure. Although physiological stimuli do not preclude the ability to obtain or maintain osseointegration, excessive stimulation may destroy the balance between the capacity for bone healing and bone damage. Osseointegration is a foreign body response, and long-term clinical function is dependent on the tissue equilibrium [28, 29].

Similarly, asymptomatic osteomyelitis around the third molar was reported to affect bone quality [30]. Bone quality is closely related to the function of osteocytes, and specifically to the cell viability. The previous report described the bone response to chronic bone stimulation, such as bacterial infection around the third molar, which has several similarities to that observed in peri-implant tissue. Chronic stimulation to peri-implant tissue induces damage, particularly to the bone containing an osteocyte network, resulting in a reduction in the number of osteocytes in both cortical and cancellous bone [31]. Furthermore, osteocyte reduction induces "micropetrosis" of the bone tissue, leading to sclerotic changes in cortical and cancellous bone [32, 33]. These processes are irreversible, and chronic sclerosing osteomyelitis occurs with or without clinical symptoms. There are limited reports of dental implant failure related to osteomyelitis, although onset of osteomyelitis following removal of an infected implant is commonly reported in the orthopedic literature [34–36]. Diagnostic imaging is, therefore, an excellent technique for understanding the mechanisms of implant failure, and the condition of the peri-implant bone reflects the patient's long-term clinical results. However, this discussion is highly speculative, and further studies are needed to clarify the mechanism of bone damage around an implant.

A clinical study on bone grafts reported that onlay bone grafting results in a relatively lower success rate [37]. Our results agreed with that study, in that failure occurred in patients treated with onlay bone grafts, particularly in clinically severe cases such as those involving cleft palate, treatment with high-dose irradiation, or severe trauma. The bone in these patients may display less vascularity because of the presence of scar tissue or fibrosis. In cases with bone grafting among these patients, insufficient bone cell

Table 2 Cohen's Kappa index of the radiograph evaluation and interobserver and intraobserver reliability of the HU measurement

Cohen's Kappa index	0.89		$p = 0.000$
	Intraclass correlation coefficient		95% Confidence interval
Interobserver reliability	0.88		0.86–0.90
Intraobserver reliability	0.91		0.90–0.92

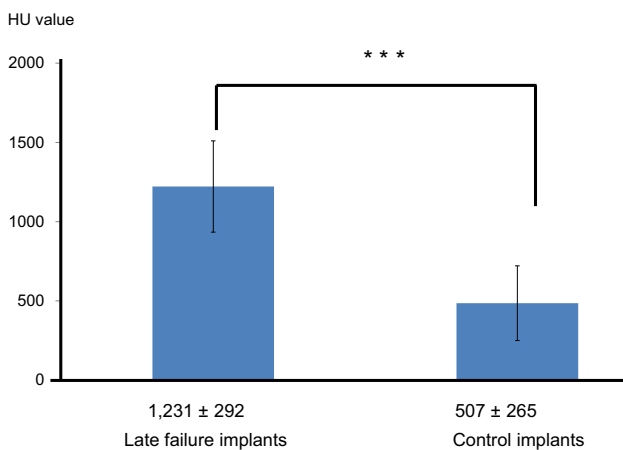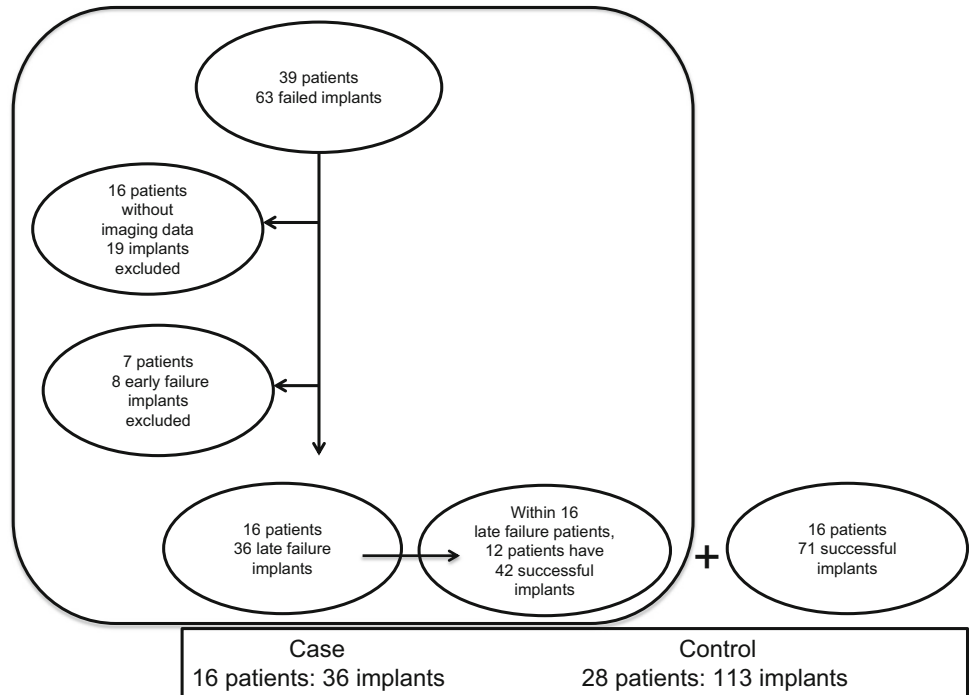**Fig. 6** Flowchart of the case–control study

HU value

Fig. 7 The mean HU value in the late failure group was 1231 ± 292, compared with 507 ± 265 in the control group. Significant differences were observed in the radiodensity of the peri-implant cancellous bone (Student's *t* test: ***$p < 0.0001$)

viability provoking incomplete bone healing may be a risk factor for poor osseointegration [38, 39]. Therefore, vascularized bone grafts should be considered in cases involving a severe condition of the host bone [40]. The quantity of bone itself is important for stabilization of the implant, although bone quantity is not the only parameter of the patient's bone condition, and bone quality is not directly related to bone quantity [30, 41].

To avoid bias, we performed a comprehensive statistical analysis adjusted for multiple confounders and used multilevel models to solve data clusters. However, several limitations remained that could not be addressed in this study. The most concerning issue was the timing of the CT. Specifically, the HU value measurement only occurred at the time of implant failure or measurement of control implants, and there were no baseline data for comparison. Unfortunately, it is impossible to quantitatively confirm cancellous bone consolidation in all cases of implant failure. However, the sclerosing reaction of cancellous bone is irreversible. Therefore, knowledge of the presence of sclerotic tissue is important to understand the bone condition. Further studies using baseline CT data should be conducted to confirm the time-dependent changes in the HU value around the implant. An additional limitation was that, owing to the lack of oral hygiene information available for our study participants, we were not able to account for the degree of so-called peri-implantitis, which may be a predictor for implant success [42]. As the present study

Table 3 Risk factor analysis for late implant failures

| Variables	Crude analysis			Fully adjusted model			Multilevel analysis		
	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value
Sex	0.71	0.33–1.50	0.367	1.78	0.22–14.7	0.593	4.96	0.0005–48550	0.733
Age	0.98	0.952–1.02	0.335	1.03	0.96–1.10	0.478	1.04	0.80–1.34	0.786
Maxilla/mandible	1.66	0.77–3.56	0.196	1.19	0.23–6.07	0.837	7.22	0.019–2730.9	0.514
Radiodensity per 100 HU on CT	2.15	1.66–2.78	<0.001	2.35	1.73–3.20	<0.001	10.39	1.08–99.51	0.042
Bone augmentation	1.99	0.88–4.48	0.097	4.33	0.76–24.5	0.098	0.025	1.09×10^{-5}–59.35	0.353
Implant suprastructure	0.66	0.21–2.10	0.480	0.39	0.03–4.76	0.458	8.94	0.00069–116492.4	0.651
Smoking habit	1.27	0.56–2.91	0.565	0.54	0.05–5.67	0.606	1.83	0.00021–16226.4	0.897

CI confidence interval, *OR* odds ratio
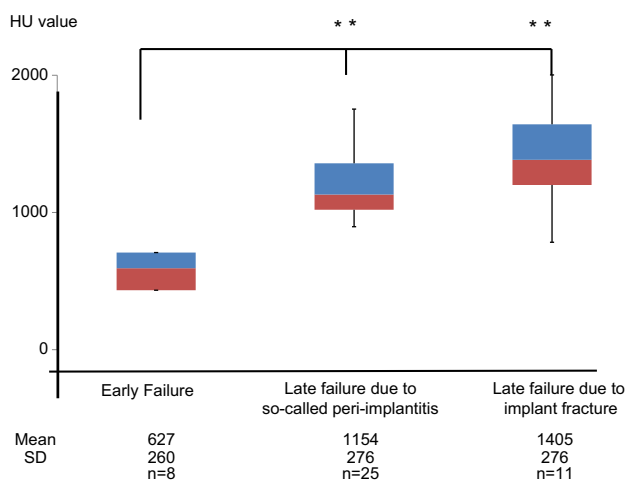
Fig. 8 *Box* and *whisker* plot showing the median (*central line*), 25th (*red*) and 75th (*blue*) percentiles (*boxes*), and entire range (*whiskers*). The mean HU values of the peri-implant cancellous bone at the time of implant removal showed significant differences between the groups (ANOVA and Tukey-HSD test: $**p < 0.001$)

contains several biases, randomized clinical trials should be conducted to confirm our results.

In conclusion, within the limits of our study, the presence of high radiodensity and cancellous bone consolidation on imaging may be related to risk factors for late implant failure. Therefore, CT images of the host cancellous bone status to observe visible sclerosis could be a useful diagnostic indicator for late implant failure.

Compliance with ethical standards

Conflict of interest Ikuya Miyamoto, Tetsu Takahashi, Tatsurou Tanaka, Bunichi Hirayama, Kenko Tanaka, Toru Yamazaki, Yasuhiro Morimoto, and Izumi Yoshioka declare that they have no conflict of interest.

Human rights statement All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions.

Informed consent Informed consent was obtained from all patients for being included in the study.

Ethical statement The Ethical Committee of Kyushu Dental University approved the study protocol (Approval Number: 2013 12-38). The STROBE guideline was followed in this investigation.

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