Title: Long-term changes in bone height after mandibular reconstruction using a free fibula graft in an elderly population

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Abstract

Purpose. This study evaluated short-term and long-term changes in bone height after mandibular reconstruction using an osteotomized fibula graft, with the aim of identifying factors associated with atrophy of the graft in an elderly population.

Methods. This retrospective study involved patients who underwent mandibular reconstruction using a free vascularized fibula graft between 2005 and 2015 and had at least 12 months of follow-up. Postoperative panoramic radiographs were used to measure bone height at standardized locations on each segment of the graft at 1 postoperative year and at late follow-up.

Results. The sample was composed of 30 patients (15 men, 15 women; mean age, 62.6 years; age range, 50-80 years). According to the HCL classification, mandibular defect types were L (n = 19), LC (n = 7), LCL (n = 3), and H (n = 1). There were 0-3 segmental osteotomies with the fibula graft. None of the patients received an osseointegrated dental implant during a mean follow-up of 4.0 years (range, 1.5-9.7 years). All patients underwent reconstruction of the mandibular body, 10 of whom also underwent reconstruction of the mandibular ramus. Atrophy of the fibula graft was observed in 9.9% and 15.0% of the body segment and 5.9% and 6.6% of the ramal segment at 1 postoperative year and at late follow-up, respectively. Graft hypertrophy occurred in the ramal segment in 2 patients. Multivariate analysis revealed a significantly higher rate of graft atrophy in women than in men at late follow-up (P = .033).

Conclusions. Fibula grafts showed long-term stability, and in 2 cases even a gain in bone

height, in this elderly population. Female sex was identified as a risk factor for atrophy of the fibula bone graft in the body segment of the reconstructed mandible.

Introduction

The vascularized free fibula graft has become the preferred technique in surgical oncology for mandibular reconstruction after tumor ablation.[1,2] The segmental blood supply to the fibula periosteum allows for multiple osteotomies to match the shape of the mandible in patients with large bony defects.[2] However, there is variability in the atrophy rate of the graft, and scant information is available on the factors associated with this atrophy.[2-5] To date, one small retrospective study has suggested that segmental osteotomies and female sex may be associated with fibula bone atrophy,[5] and only two long-term follow-up studies have evaluated the bone height of fibula grafts over time at standardized locations, such as the central, body, and ramal segments of the mandible.[2,3] However, there are no detailed reports of the bone height of each segment when using multiple osteotomized fibula grafts. In addition, the populations studied previously were middle-aged,[2,3] but with aging of the population, a growing number of elderly patients are being considered for mandibular reconstruction. As yet, the long-term stability of fibula bone height after mandibular reconstruction has not been appropriately evaluated in the elderly patient population.

This study evaluated the short-term and long-term changes in bone height of the osteotomized fibula graft in elderly patients, with the aim of identifying factors that potentially influence atrophy of the bone graft.

Patients and Methods

Subjects

This retrospective study involved patients who underwent mandibular reconstruction using a free vascularized fibula graft at Hokkaido University Hospital between 2005 and 2015 and had at least 12 months of follow-up. When required, additional soft tissue surgery, such as vestibuloplasty, was performed with or without removal of fixation hardware. The study was approved by the institutional review board at Hokkaido University Hospital (No. 015-0341) and adhered to the tenets of the Declaration of Helsinki.

Measurements

Changes in fibula bone height over time were determined using postoperative digital panoramic radiographs. Bone height was measured at the midpoint of each segment of the fibula graft and compared at the same sites on subsequent radiographs taken at the initial evaluation after the operation, at 1 postoperative year, and at late follow-up. Each segment was divided into the body or ramus and the mean height at each anatomic site of reconstruction was calculated. Fixation hardware was used for reference points to avoid magnification errors.

Data on patient characteristics and operative variables were collected and included age, sex, indication for surgery, radiation therapy, opposing dentition on the reconstructed side, use of a conventional denture for the reconstructed side, type of mandibular defect, and number of osteotomies. Mandibular defects were classified according to the HCL method

described by Jewer et al[6] as follows: H, hemimandibular segment including the condyle; C, central segment including both mandibular canine teeth; and L, lateral segment without the condyle.

Statistical analysis

All continuous variables were divided into categorical variables. Type of mandibular defect and number of osteotomies were dichotomized into “L or other” and “zero or more than zero”, respectively. The univariate relationship between each independent variable and fibula bone height was evaluated using Student's *t* test or analysis of variance. Variables with a *P*-value of less than .2 in univariate analysis were entered into the multiple regression model. A *P*-value of less than .05 was considered to be statistically significant. The strength of the predictive ability of factors identified in the multivariate model was determined using regression coefficients with 95% confidence intervals. Performance of the multiple regression model was evaluated using the value of R^2. All statistical analysis was performed using JMP software (version 12.2.0; SAS Institute Inc., Cary, NC).

Results

Data are presented as the mean ± standard deviation (Tables 1 and 2). A retrospective chart review identified 36 patients who underwent mandibular reconstruction using a free fibula graft at our hospital during the study period. Of these patients, 30 patients (15 men, 15

women; mean age, 62.6 years; age range, 50-80 years) were included in the analysis. Six patients were excluded because of non-attendance for follow-up radiography (tumor recurrence, n = 2; death due to disease, n = 1; missed visit, n = 1) or graft loss secondary to vascular complications (n = 2). The indications for surgery were malignant tumor (n = 23), benign tumor (n = 4), and osteoradionecrosis (n = 3). Seventeen patients underwent preoperative radiation therapy and 2 patients underwent pre- and postoperative radiation therapy. Sixteen patients had opposing dentition and 14 patients had a denture for the reconstructed site. None of the patients received an osseointegrated dental implant during follow-up. According to the HCL classification, mandibular defect types were L (n = 19), LC (n = 7), LCL (n = 3), and H (n = 1). There were 0-3 segmental osteotomies of the fibular graft (0, n = 10; 1, n = 13; 2, n = 6; and 3, n = 1).

Initial radiographs were taken between 6 and 99 postoperative days (20 ± 23 days), 1-year follow-up radiographs were taken between 231 and 602 days (375 ± 82 days), and the late follow-up radiographs were taken between 1.5 and 9.7 years (4.0 ± 2.3 years). No fractures or non-unions of the reconstructed mandible were observed during follow-up.

Mandibular body reconstruction was performed in all patients. Radiographic analysis revealed that fibula bone height ranged initially from 13.0 mm to 24.4 mm (17.9 ± 3.0 mm). Mean atrophy rate of the graft was 9.9% ± 5.9% (range, 1.7%–26.0%) at 1 postoperative year and 15.0% ± 10.0% (range, 3.1%–49.1%) at late follow-up.

Mandibular ramal reconstruction was performed in 10 patients. Fibula bone height

ranged initially from 13.7 mm to 17.9 mm (16.0 ± 1.7 mm). Mean atrophy rate of the grafts was 5.9% ± 8.4% (range, -10.7% to 18.3%) at 1 postoperative year and 6.6% ± 11.1% (range, -9.7% to 22.5%) at late follow-up (Table 1). Two patients (20%) showed bone hypertrophy in the ramal segment of the graft at late follow-up (Figure 1).

Statistical analysis was not applied to the results for the ramal segment because of the small number of cases. For the body segment, univariate analysis revealed no significant effect on the atrophy rate of patient age, indication for surgery, radiation therapy, load-bearing status of the mandible (i.e., presence of opposing teeth or use of a denture), type of mandibular defect, or number of osteotomies (Table 2). Multivariate analysis revealed a significantly higher atrophy rate of the graft in women than in men at late follow-up (regression coefficient, 7.4; 95% confidence interval, 0.6–14.2; P = .033; Table 3). The model explained 24% of the total variance (R^2 = .24). There was no significant difference in mean age between men and women (60.3 versus 64.8 years; P = .15).

Discussion

Vascularized free bone grafts from the iliac crest, radius, scapula, or fibula are frequently used for mandibular reconstruction and are reported to have a lower atrophy rate than non-vascularized bone grafts.[7,8] The free fibula graft has become the preferred technique for reconstruction of segmental mandibular defects.[1,9,10] There has been some discrepancy in the reported atrophy rate of the fibula graft following mandibular reconstruction, ranging from

2% to 17%, but this was in populations that were younger (mean age, 45-57 years)[2-5,8] than the patients in the present study. Our results of an atrophy rate of 15% in the body segment and 6.6% in the ramal segment indicate that the fibular graft can afford long-term stability even in elderly patients.

We believe that severe atrophy of the fibula graft makes prosthodontic rehabilitation difficult. Therefore, it is important to investigate the degree and time course of atrophy of the fibula graft for subsequent vestibuloplasty and prosthodontic rehabilitation. Moreover, investigation of factors associated with fibula bone atrophy may influence prosthodontic procedures as well as the timing of prosthodontic rehabilitation.

Bone atrophy was mainly found in the body segment in the first postoperative year, which is consistent with previous reports.[2,3,8] An atrophy rate > 20% was seen in 7 of our patients and the highest rate was 49%, which was seen at late follow-up (Figure 2). This distribution of results is similar to that reported previously.[2,3,5] We paid special attention to preserve the peroneal pedicle during secondary procedures such as vestibuloplasty with tissue debulking. However, the possibility of the vascularized fibula graft becoming non-vascularized during follow-up because of obstruction of the anastomosed vessels cannot be excluded. One study reported that up to 50% of fibula bone height can be lost by 7 postoperative years because atrophy of a non-vascularized fibular bone graft continues at a regular rate.[8]

One retrospective study reported segmental osteotomies with a fibular graft to be a

significant risk factor for bone atrophy and demonstrated the importance of preserving the arterial blood supply to the graft.[5] In contrast, both we and Disa et al[2] found no effect of multiple osteotomies on atrophy of the fibula graft. This suggests that multiple osteotomies—specifically ≤3—with a fibular graft can be performed to better match the shape of the mandible.

In our study, atrophy of the fibula graft was higher in women than in men. The women in our study were aged ≥50 years, and most were probably menopausal given that the estimated mean age of menopause is 50 years in Japan. Our finding in this regard is consistent with that of a previous report in which 8 of 11 female patients were aged >50 years.[5] Postmenopausal osteoporosis or its precursor state may contribute to atrophy of the fibula graft. Accordingly, it is worth investigating the long-term stability of fibula bone height after mandibular reconstruction in elderly patients.

Bone hypertrophy of the fibula graft has been reported only rarely after mandibular reconstruction,[5] whereas it was reported in 38% of patients undergoing reconstruction of skeletal defects of the limbs.[11] Makiguchi et al[5] found that delayed placement of an osseointegrated dental implant correlated with inhibition of fibula bone atrophy. They hypothesized that pressure from the tongue, lips, maxillary teeth, and food is transmitted to the bone graft via a dental implant and that this intermittent kinetic load might contribute to bone formation. Hypertrophy of the bone graft is considered to be secondary to subperiosteal deposition of new bone.[2] Fibula hypertrophy was observed only in the ramal segment in our

study and may have resulted from residual periosteum of the ramus. Because the distal resection margin of the ramal segment was usually far from the primary lesion, the periosteum tended to be preserved more than the proximal resection margin of the body segment.

Some limitations are associated with the retrospective nature of this study. Although computed tomography scans would have been ideal for accurate evaluation of fibula bone mass, they were seldom performed immediately after the operation in terms of radiation exposure and cost. Therefore, a comparative evaluation was difficult because of a lack of reference values from the early postoperative period. However, use of panoramic radiographs as an indirect measure of bone mass made it possible to compare our results with those reported previously.[2-5]

In summary, atrophy of the fibula graft mainly occurred within the first postoperative year. At late follow-up, 85% and 93% of fibula bone height was preserved in the body and ramal segments, respectively. Female sex was identified as a risk factor for fibula bone atrophy in the body segment of the mandible.

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Tables

Table 1. Bone height and atrophy rate of fibula bone grafts after mandibular reconstruction

Site of mandibular reconstruction	*n*	Initial fibula bone height (mm)	Atrophy rate of fibula bone graft (%)	
			First postoperative year	Late follow-up
Body	30	17.9 ± 3.0	9.9 ± 5.9	15.0 ± 10.0
Ramus	10	16.0 ± 1.7	5.9 ± 8.4	6.6 ± 11.1

Table 2. Factors associated with fibula bone atrophy of the body segment after mandibular reconstruction

		Atrophy rate of fibula bone graft (%)			
Factor	*n*	First postoperative year	*P*-value	Late follow-up	*P*-value
Age (years)			.44		.32
65 ≥ years	8	8.5 ± 4.5		11.6 ± 4.8	
65 < years	22	10.4 ± 6.3		16.1 ± 11.2	
Sex			.22		.041
Male	15	8.6 ± 4.7		11.3 ± 7.2	
Female	15	11.3 ± 6.8		18.7 ± 11.3	
Indication for surgery			.25		.70
Malignant tumor	23	10.9 ± 6.0		15.4 ± 7.8	
Benign tumor	4	7.7 ± 6.8		15.9 ± 22.2	
Osteoradionecrosis	3	5.6 ± 0.5		10.2 ± 3.6	
Preoperative radiation therapy			.28		.75
Yes	17	11.0 ± 6.3		15.5 ± 8.1	
No	13	8.6 ± 5.3		14.3 ± 12.4	
Postoperative radiation therapy			.81		.95
Yes	2	10.9 ± 2.7		14.5 ± 1.6	
No	28	9.9 ± 6.1		15.0 ± 10.4	
Opposing dentition			.27		.090
Present	16	8.8 ± 5.5		12.1 ± 7.2	
Absent	14	11.2 ± 6.2		18.3 ± 11.9	
Denture			.96		.26
Present	14	9.9 ± 6.3		17.2 ± 13.3	
Absent	16	10.0 ± 5.8		13.0 ± 5.6	
Mandibular defect			.42		.98
L	19	9.3 ± 5.3		15.0 ± 7.8	
LC, LCL, or H	11	11.1 ± 6.9		14.9 ± 13.5	
Number of osteotomies			.32		.28
0	10	8.4 ± 5.0		12.1 ± 7.8	
>0	20	10.7 ± 6.3		16.4 ± 10.9	

Abbreviations: H, hemimandibular segment including the condyle; C, central segment including both mandibular canine teeth; L, lateral segment without the condyle.

Table 3. Multivariate analysis of factors associated with fibula bone atrophy of the body segment after mandibular reconstruction

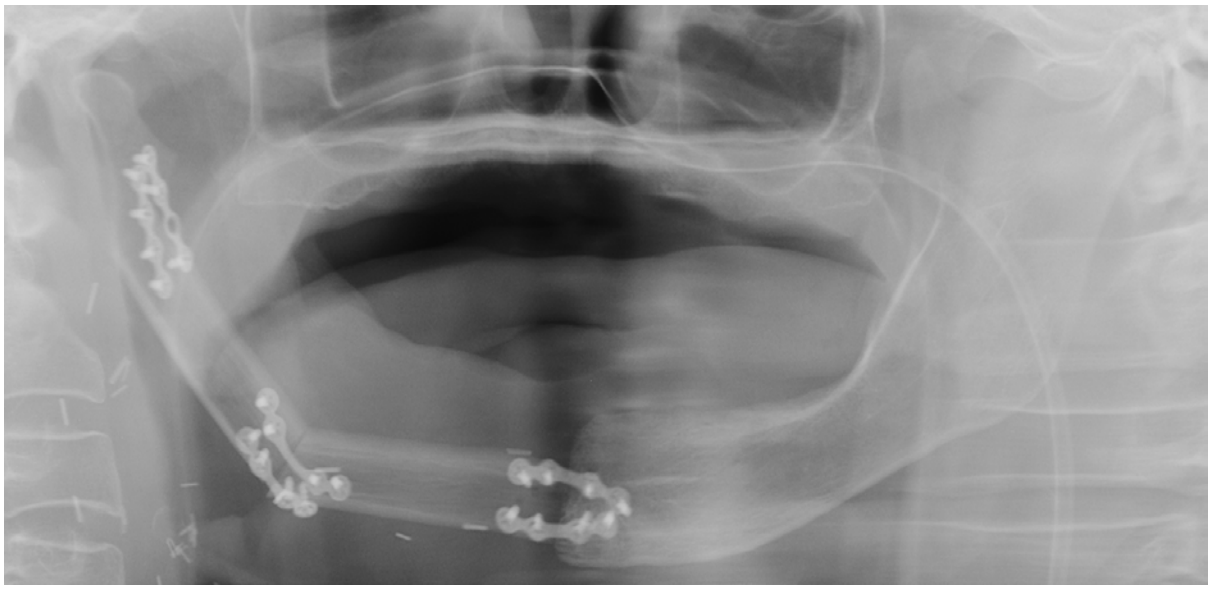
Factor	Regression coefficient (95% CI)	*P*-value
Female sex	7.4 (0.6-14.2)	.033
Absence of opposing dentition	6.2 (-0.6-13.0)	.071

Abbreviation: CI, confidence interval.

Figure legends

Figure 1. Panoramic radiographs of a 64-year-old woman with mandibular gingival carcinoma who had received preoperative radiation therapy. Fixation hardware was removed and vestibuloplasty performed for denture placement at 3 postoperative years. *A*, Initial radiograph at 7 postoperative days with fibula bone height of 15.4 mm in the body segment and 13.8 mm in the ramal segment. *B*, Follow-up radiograph at 1 postoperative year showing fibula bone atrophy of 9.1% and 2.7% in the body and ramal segments, respectively. *C*, Late follow-up radiograph at 9.7 postoperative years showing fibula bone atrophy of 19% in the body segment and fibula bone hypertrophy of 9.7% in the ramal segment.

A



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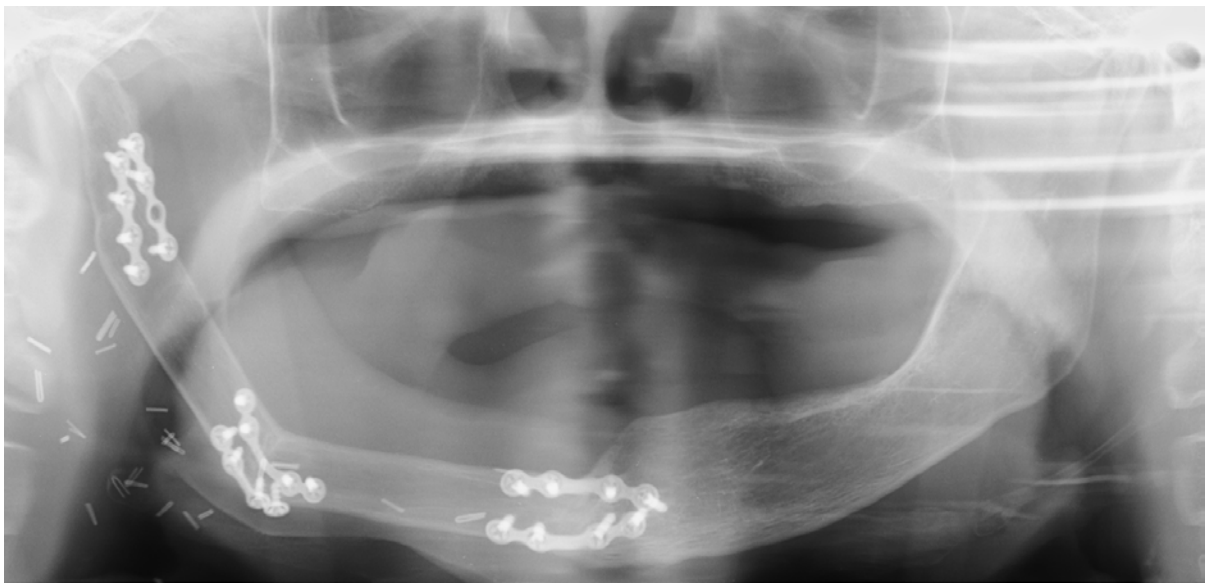

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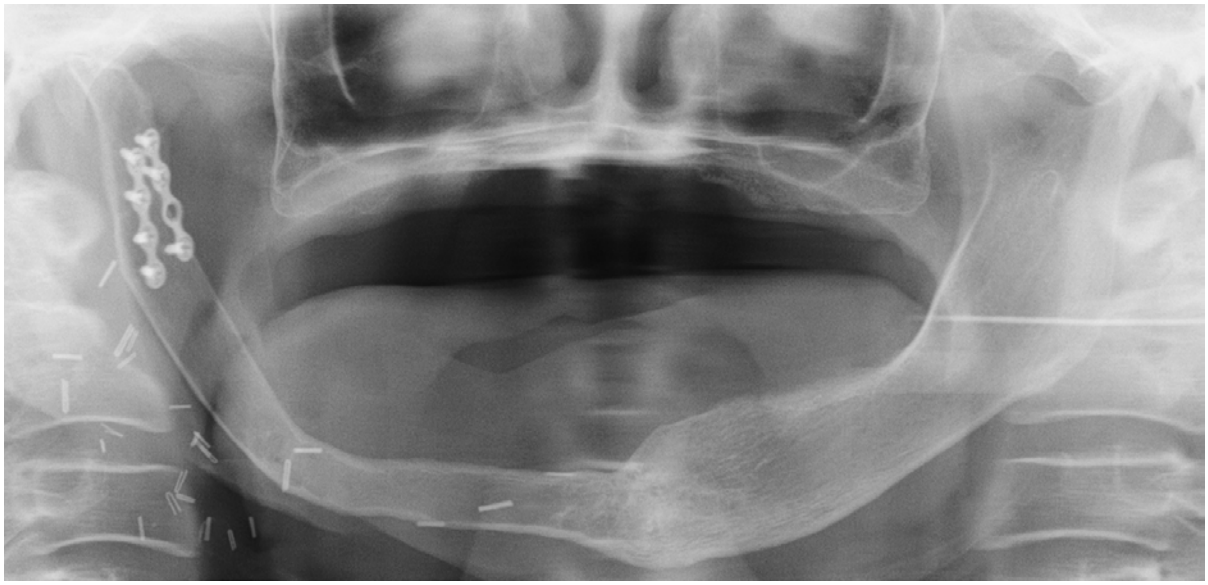
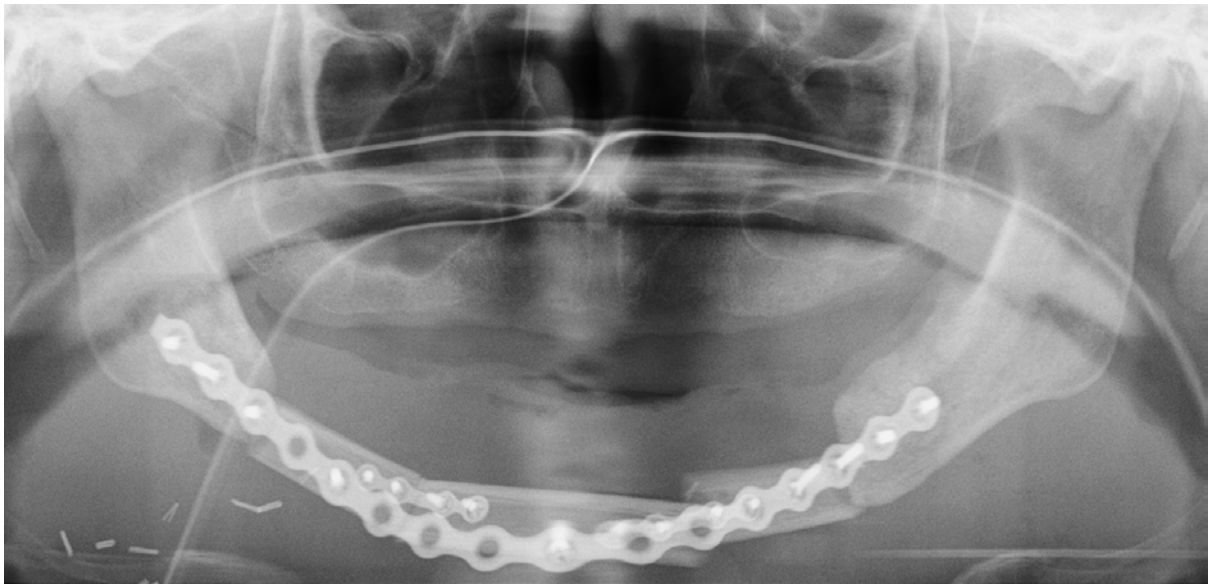


Figure 2. Panoramic radiographs of a 57-year-old woman with mandibular ameloblastoma. Fixation hardware was removed and vestibuloplasty performed for denture placement at 1.1 postoperative years. *A*, Initial radiograph at 9 postoperative days showing fibula bone height of 13.3 mm in the body segment. *B*, Follow-up radiograph at 1 postoperative year showing fibula bone atrophy of 17% in the body segment. *C*, Late follow-up radiograph at 3.7 postoperative years showing fibula bone atrophy of 49% in the body segment.

A



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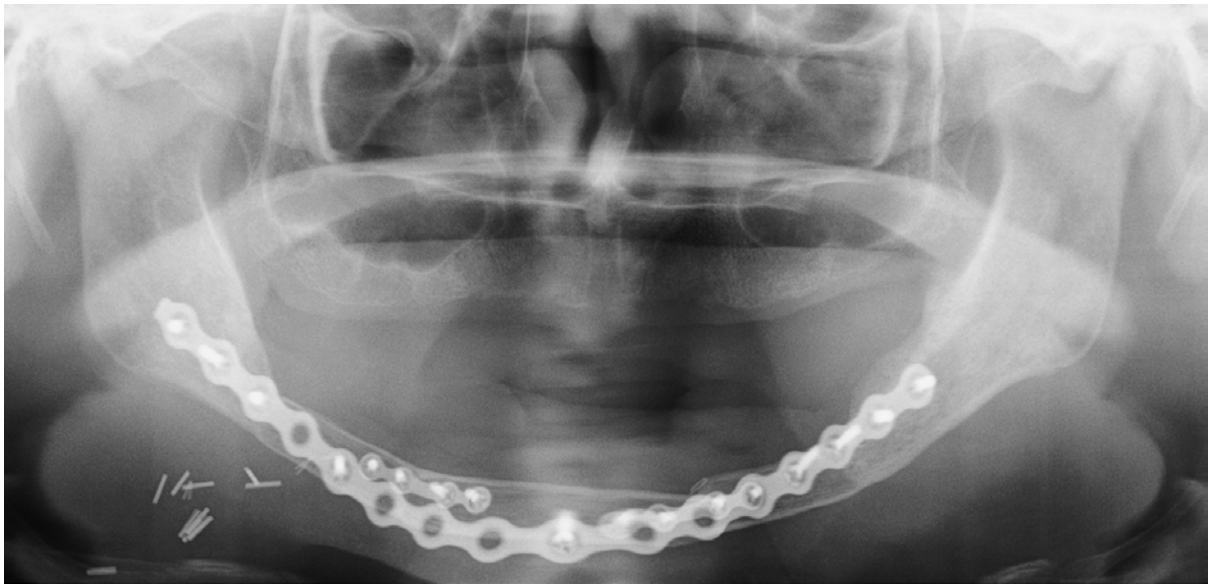

C