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**Axial four-dimensional computed tomographic images to analyze crosswise differences in
protrusive condylar movement in patients who underwent mandibulectomy and free flap
reconstruction**

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Summary

Objective: Few studies evaluate condylar movement following mandibular reconstruction. The main objective of this study was to show that axial four-dimensional computed tomography (4DCT) could visualize bilateral protrusive condylar movement directly. We used axial 4DCT images to assess condylar protrusion in patients who underwent mandibular reconstruction.

Methods: We enrolled seven healthy volunteers (median age 30 years, range 27–38 years) and seven patients (median age 65 years, range 52–80 years) who underwent mandibulectomy (segmental in five, hemi in one, marginal in one) and free flap reconstruction (using the fibula in six and the radial forearm in one). Six study subjects were instructed to masticate a cookie during the 4DCT scan (the seventh made chewing motions). The distance between the most anterior and posterior positions of the bilateral condyles on 4DCT (axial view) images were then measured and compared between controls and patients using the Mann–Whitney U-test.

Results: The crosswise difference in the distances of condylar protrusion was significantly greater in patients than that in the controls.

Conclusion: Axial 4DCT images can visualize a bilateral condylar protrusive path. Axial 4DCT images for patients who underwent mandibulectomy and reconstruction may be useful for evaluation of functional movement of condyles.

Keywords: four-dimensional computed tomography (4DCT), axial view, protrusive condylar movement, mandibulectomy, free flap reconstruction.

1 **Introduction**

2 Functional movements of the human mandible during chewing and speaking have both
3 translatory and rotatory components (*Naeije.*, 2003). For functional evaluation of the
4 mandibular musculoskeletal system, three movements are investigated: (1) opening–closing; (2)
5 protrusion; (3) laterotrusion (*Pinheiro et al.*, 2008). These complex movements of the mandible
6 rely on temporomandibular joint (TMJ) function. The terminal hinge axis is often used to
7 describe the movements of the temporomandibular joint (*Naeije.*, 2003). A previous observation
8 from a sagittal view indicated that a kinematic reference point of the condyle moves during
9 symmetric mandibular movements (protrusive–retrusive, border, opening–closing) within a
10 belt-shaped field (*Naeije.*, 2003).

11 Refining imaging techniques to assess jaw movements is of great importance. A previous
12 study showed that motion-adapted, semi-dynamic magnetic resonance imaging (MRI) could be
13 used to visualize the complexity of TMJ movements in patients with TMJ-related symptoms
14 (*Eberhard et al.*, 2000). Another study evaluated tongue and jaw movements during mastication
15 in healthy humans using anteroposterior fluorographic images (*Taniguchi et al.*, 2013). It is
16 noteworthy that those previous imaging evaluations of condylar movements used sagittal or
17 coronal views.

1 We previously reported good visualization of jaw movements using four-dimensional
2 computed tomography (4DCT) to evaluate postoperative outcomes in patients who underwent
3 segmental mandibulectomy and free fibula flap reconstruction (*Akashi et al., 2016*). Through the
4 experience of that study, we found that 4DCT could visualize detailed condylar movement. The
5 primary purpose of the current study was to show that axial 4DCT was adequate for evaluating
6 the symmetry of condylar movements. We assessed the condylar protrusion in patients who
7 underwent mandibular reconstruction by using axial 4DCT images. Because there are few
8 studies that evaluate detailed condylar movement after mandibulectomy and free flap
9 reconstruction.

11 **Materials and Methods**

12 This study includes seven patients (five men, two women) who underwent mandibular resection
13 and reconstruction with free flaps at our department between April 2011 and July 2014, and
14 seven healthy subjects (six men, one woman) as controls. All subjects gave written informed
15 consent to participate in the study after receiving full explanation of the purposes and structure
16 of the current study that had already been approved by Medical Ethics Committee of Kobe
17 University (No. 1445, 2014). 4DCT examinations were additionally undertaken for patients as
18 routine follow-up imaging after surgery to monitor for tumors or osteoradionecrosis recurrence

1 and to confirm plate fixation. Healthy control subjects who had no history of TMJ disorders
2 (TMDs) participated voluntarily in this study. All of them were authors and colleagues.

3 Mandibulectomy defects were classified according to the CAT classification, as described
4 in our previous study (*Akashi et al.*, 2016; *Akashi et al.*, 2015). In brief, the defects were
5 classified according to the anatomical landmarks of the mandible: Condyle; mandibular Angle;
6 mental Tubercle. During surgical procedures, fibular flaps were transferred in alignment with
7 the lower border of the residual mandible as a mono-barrel graft. Fibular osteotomies were
8 performed only at the T and A positions.

9 The imaging protocols in our previous study were applied in seven subjects (*Akashi et al.*,
10 2016). In those seven subjects, CT examinations were performed with an Aquilion ONE
11 (Toshiba Medical Systems Corporation, Otawara, Japan) at Kobe University Hospital (tube
12 current: 30–50 mA; tube voltage: 120 kV; scanning time: 10–15 s; rotation time: 0.35 s/rotation;
13 slice thickness: 0.5 mm; field of view: 220 mm). The modified imaging protocol to reduce
14 radiation exposure (tube current 20 mA; tube voltage 120 kV; scanning time 5 s) was applied in
15 the newly added seven subjects. All images were acquired axially with a 320-detector row CT to
16 allow for multiple phases of unenhanced 3D volume acquisition with 10 cm coverage.

17 The study subjects' foreheads were fixed with tape to prevent bodily movement. All study
18 subjects chewed a cookie containing contrast agent during the scan, except for only one patient

1 who could not chew. This edentulous patient underwent hemiglossectomy with free radial
2 forearm flap reconstruction, neck dissection, and radiotherapy for tongue cancer, and
3 subsequently segmental mandibulectomy with fibula flap reconstruction for osteoradionecrosis.
4 He was instructed to move the jaw so it imitated eating. The gantry was angled to limit radiation
5 to the eyes and the inferior aspect of the field of view was tailored to minimize radiation to the
6 thyroid. Exposure doses in all study subjects were within the notification values recommended
7 by the AAPM Working Group on Standardization of CT Nomenclature and Protocols about
8 4DCT (<https://www.aapm.org/pubs/CTProtocols/documents/Notification>).

9 For image post-processing, a volume rendering (VR) image was generated using
10 commercial software (Ziostation2, AMIN Inc., Tokyo, Japan). In our previous study, we
11 measured the amount of mouth opening, mastication time, and change in the mandibular angle
12 from sagittal multiplanar reconstruction or maximum intensity projection images (*Akashi et al.*,
13 2016). The current study aimed to measure the protrusive distance of the condyle. First, the
14 most anterior and posterior positions of the posterior portion of the condyle during mastication
15 were marked manually by each observer. Next, the values of the distances between the most
16 anterior and posterior positions of the posterior portion of the condyle during mastication were
17 measured automatically with imaging software on axial VR 4DCT images for all study subjects
18 (Fig. 1). In the patient who underwent hemi-mandibulectomy and free fibula flap reconstruction,

the most posterior portion of the fibula flap was assessed. All measurements were performed by two independent radiologists in a blind manner. It was additionally evaluated whether the condyle protruded forward to the articular tubercle on sagittal VR 4DCT images.

Statistical analyses were performed using R software (R Development Core Team, 2011). The Mann–Whitney U-test was performed. Interobserver reliability was analysed using interclass correlation coefficient. Data are presented as the mean deviation. A value of $P < 0.05$ was considered to indicate statistical significance.

Results

The median age of the seven patients was 65 years (range 52–80 years), and that of the seven healthy volunteers was 30 years (range 27–38 years). Five of the patients underwent segmental mandibulectomy, with the mandibular defects located in the “AT” region in three patients and in the mandibular body in two. One patient underwent hemi-mandibulectomy (i.e., mandibular defect was in the CAT region). One patient underwent marginal mandibulectomy and radial forearm free flap reconstruction (i.e., reconstruction of only the soft-tissue defect). The primary lesions were oral squamous cell carcinoma in two patients, osteoradionecrosis of the mandible in two, and osteomyelitis of the mandible, ameloblastoma, and ameloblastic carcinoma in one. The median postoperative duration was 2 years (range 1–5 years).

Representative coronal, bilateral oblique (i.e., parallel to contralateral canine), and bilateral sagittal VR images from a healthy control are shown in Figure 2 and Video 1. Representative axial 4DCT image on which to measure the distance of bilateral condylar protrusions in a healthy control is shown in Figure 1 and Video 2.

Table 1 shows the measured condylar protrusive movements for the controls and patients. The crosswise difference in the protrusive distance of the condyles in patients was significantly greater than that in the controls both in observer 1 ($P = 0.006$) and 2 ($P = 0.013$). The values of interclass correlation coefficient were 0.836 in the controls, 0.974 in the diseased side, 0.991 in the nondiseased side, and 0.980 in the crosswise difference in the patients.

The condyle protruded forward to the articular tubercle in all healthy controls, as shown in Videos 1A and 1E. In contrast, bilateral condyle protruded forward to the articular tubercle only in 2 of 7 patients. Figure 3 and Video 3 shows the condylar protrusion forward to the articular tubercle on both the diseased and non-diseased sides in the patient who underwent segmental mandibulectomy and free fibula flap reconstruction. The condyle did not protrude forward to the articular tubercle on the non-diseased side in 2 of 7 patients. The condyle on the diseased side did not protrude forward to the articular tubercle in 3 of 7 patients. In one patient, bilateral condyles did not protrude forward to the articular tubercle (Fig. 4 and Video 4). In one patient

who underwent hemi-mandibulectomy and free fibula flap reconstruction, the most cranial portion of the fibula flap did not protrude forward to the articular tubercle.

For image acquisition, the overall mean dose was 2.5 ± 1.7 mSv for all of the subjects in this study. For the seven subjects in whom the previous imaging protocol was applied, the mean dose was 4.0 ± 0.7 mSv. In the newly added seven subjects in whom the current imaging protocol was applied, the mean dose was 0.9 ± 0.4 mSv.

Discussion

The current pilot study introduces the novel imaging technique to directly visualize bilateral protrusive condylar movement, and revealed significantly greater crosswise differences in the distances of the condylar protrusion in patients who underwent mandibulectomy and free flap reconstruction than in controls. Our previous study (Akashi et al., 2016) and the current study showed that coronal and sagittal 4DCT images could visualize jaw movements. However, frontal and lateral images can be acquired fluoroscopically, for which radiation exposure is lower than that of CT. In contrast, bilateral protrusive condylar movements can be visualized only on axial views.

Condylar movements are often evaluated in patients with TMDs. In a previous study, an optoelectric jaw-tracking system that could show condylar motion on both the

1 disc-displacement and non-disc-displacement sides during mastication was inhibited in subjects
2 with unilateral TMD (*Miyawaki et al., 2011*). In another study that used cinematographic MRI,
3 sagittal images provided additional information about disc and condyle mobility (*Eberhard et*
4 *al., 2000*). Also reported were a 4D analytical system of stomatognathic function combined with
5 three-dimensional (3D) CT of the cranium and mandible, dental surface imaging with a
6 noncontact 3D laser scanner, and mandibular movement data from an optoelectronic analysis
7 system (*Terajima et al., 2008*). A system employing a low-cost video camera and a computer
8 program was also previously introduced to analyze mandibular movement (*Pinheiro et al.,*
9 *2008*). Recently, a new software application was introduced that directly combines and merges
10 3D cone beam CT and electronic jaw motion tracking data (*Hanssen et al., 2014; Kordatz et al.,*
11 *2015*). Using those modalities is time-consuming, however, whereas 4DCT requires only a few
12 minutes to complete a scan. To the best of our knowledge, this is the first report about the utility
13 of axial images to evaluate bilateral condylar movement.

14 There have been few studies on jaw movement following mandibular reconstruction
15 (*Bolzoni et al., 2015*). Our previous pilot study showed that the maximum mouth opening and
16 protrusive distance while chewing a cookie tended to decrease on the diseased side in patients
17 who underwent mandibular reconstruction with a free fibular flap, compared with controls,
18 whereas we found no difference in the mastication time between controls and patients (*Akashi et*

al., 2016). In the current study, we found that the crosswise difference in the amount of condylar protrusion was significantly greater in patients than in controls. This result was surely due to the decreased amount of condylar protrusion on the diseased side in patients. We think, however, that the larger crosswise difference in condylar protrusion does not necessarily reflect the postoperative disturbance of condylar movement in patients. A previous study on TMD notes that the limited condylar movement on the disc-displacement side influences the movements of contralateral condyle without TMD during jaw movement (*Miyawaki et al., 2011*). In the current study, the median value of the crosswise difference in condylar protrusion in patients was 3.1 mm (observer 1) and 2.1 mm (observer 2). In two patients in whom the crosswise difference of condylar protrusion was <3.1 mm and <2.1 mm, there was a decreased amount of bilateral condylar protrusion (diseased side/non-diseased side: 4.9–3.5 mm/2.6–3 mm [observer 1] and 3.2–1.6 mm/4.1–2.1 mm [observer 2]). One patient (4.9–3.5 mm [observer 1] and 3.2–1.6 mm [observer 2] on diseased side/non-diseased side) received marginal mandibulectomy and only soft-tissue reconstruction. Another (2.6–3 mm [observer 1] and 4.2–2.1 mm [observer 2] on diseased side/non-diseased side) was the patient in whom bilateral condyles did not protrude forward to the articular tubercle (Fig. 4 and Video 4). The only one patient in whom the crosswise difference in condylar protrusion was <3.1 mm and <2.1 mm, without decrease in the amount of bilateral condylar protrusion (diseased side/non-diseased side

7.6–8.6 mm [observer 1] and 8.2–7.8 mm [observer 2]), was the patient who could not chew the cookie. Hence, the result in that patient might not reflect condylar movement during functional mastication. In our previous pilot study, 4DCT showed no obvious crosswise differences in excursion of the mandibular angle in the sagittal plane in controls. The excursion of the mandibular angle on the diseased side, however, was lower than that on the non-diseased side in patients with mandibular reconstruction, indicating asymmetric jaw movement in those patients (Akashi et al., 2016). We had one patient who achieved symmetric movement of the mandibular angle (i.e., there was little crosswise difference between the diseased and non-diseased sides), indicating the possibility that postoperative symmetric movement of the mandibular angle may be an indicator of good functional outcome following mandibular reconstruction (Akashi et al., 2016). In the current study, the smaller crosswise difference may reflect the decreased amount of bilateral condylar protrusion, and the larger crosswise difference may reflect condylar protrusion without disturbance on the non-diseased side. Another causative factor of the decreased amount of bilateral condylar protrusion is remaining teeth. Occasionally, patients can not wear dental prostheses after mandibular reconstruction. In fact, the patient shown in Video 4 had only anterior teeth, and could not to wear dental prostheses in the molar regions after surgery. In this patient, bilateral condyles did not protrude forward to the articular tubercle. A recent important study showed that trismus is associated with a significant impact on quality of

1 life in patients with head and neck cancer (*Johnson et al., 2015*). However, amount of maximum
2 mouth opening does not reflect functional jaw movement. On the other hand, 4DCT has the
3 potential to assess actual functional jaw movements affected by the presence or absence of
4 denture wearing and the number of remaining teeth. In this study, two patients with mandibular
5 osteoradionecrosis received head and neck irradiation. In one irradiated patient, bilateral
6 condyle protruded forward to the articular tubercle (Fig. 3 and Video 3). Another irradiated
7 patient could not chew as mentioned above. Impact of irradiation on condylar movement still
8 remains elusive.

9 Finally, we must note limitations in the current study. First, radiation exposure is the most
10 problematic concern with 4DCT. Although we achieved reduced radiation exposure compared
11 with that in our previous pilot study, the radiation dose of our modified imaging protocol was
12 about 1.7 times higher than the dose applied for general facial CT in our hospital. The increased
13 noise and degraded image quality related to using a lower radiation dose were within an
14 allowance, particularly for the purpose of evaluation of condylar movement. We consider that
15 the difference of two protocols have little effect on the results of the current study. The second
16 limitation is the heterogeneity of study subjects. Healthy volunteers included in this study were
17 younger than patients. Furthermore, the heterogeneity in primary disease, mandibular defect and
18 reconstruction method, and time interval between 4DCT and surgery within the patient group is

also a problem. Third, further refinement of 4DCT assessment is necessary. Our previous and current studies evaluated only maximum mouth opening, mastication time, and movements of the mandibular angle and condyles. Nevertheless, we think that the images acquired with 4DCT provided more detailed information about the kinematics and dynamics of the human mandible. Fourth, although the interobserver reliability was high, the measurement errors existed as shown in Table 1. To improve in accuracy, the automation of measurement will be required. Overcoming these limitations is our future task.

Conclusions

Axial 4DCT images are adequate for evaluating bilateral protrusive condylar movement. The crosswise difference in condylar protrusion was greater in patients who underwent mandibulectomy and reconstructive procedures than that in the controls.

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Conflict of interest statement

1 The authors have no conflicts of interest to disclose.

2

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Figure captions

Fig. 1. Axial volume rendering image of bilateral condyles of a healthy control. (A) Axial view can visualize bilateral condyles directly. (B) Path of condylar protrusive movement. (C) Enlarged view.

Fig. 2. Representative lateral (A and E), oblique (B and D), and coronal (C) volume rendering images of a healthy control. Arrows indicate the cookie containing contrast agent.

Fig. 3. Representative lateral (A and B), and coronal (C) volume rendering images of a patient. In this patient, bilateral condyles protruded forward to the articular tubercle. The crosswise difference was 5.3 mm (observer 1) and 4.7 mm (observer 2). See Video 3.

Fig. 4. Representative lateral (A and B), and coronal (C) volume rendering images of a patient. In this patient, bilateral condyles did not protrude forward to the articular tubercle. The crosswise difference was 0.4 mm (observer 1) and 2 mm (observer 2). See Video 4.

Video 1. Representative lateral (A and E), oblique (B and D), and coronal (C) 4DCT motion images of a healthy control.

Video 2. Representative axial four-dimensional computed tomography images of the motion of bilateral condyles of a healthy control.

- 1 **Video 3.** Lateral (A and B) and axial (C) motion images of a patient in whom bilateral condyles
- 2 protruded forward to the articular tubercle. The crosswise difference was 5.3 mm (observer 1)
- 3 and 4.7 mm (observer 2).
- 4 **Video 4.** Lateral (A and B) and axial (C) motion images of a patient in whom bilateral condyles
- 5 did not protrude forward to the articular tubercle. The crosswise difference was 0.4 mm
- 6 (observer 1) and 2 mm (observer 2).

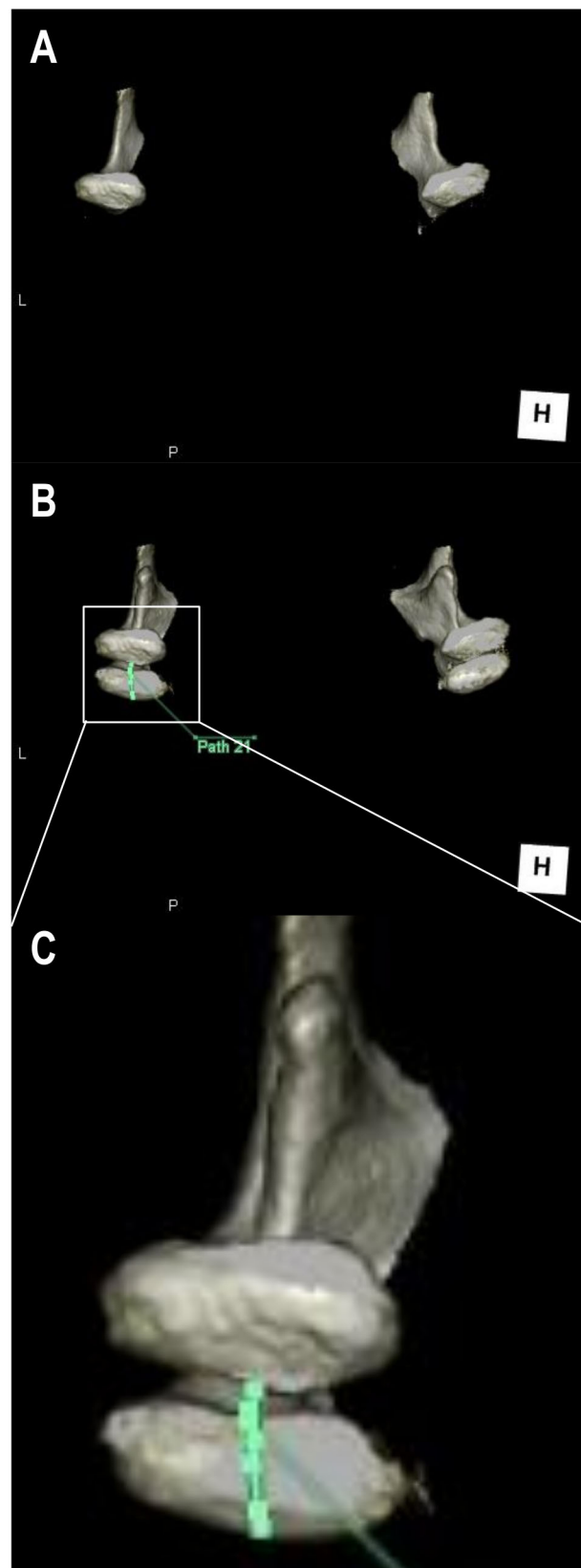


Figure 1

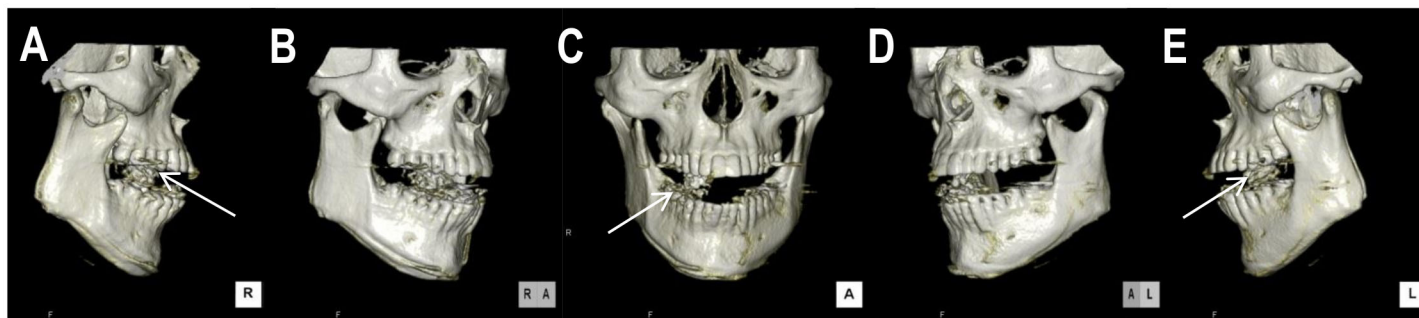


Figure 2

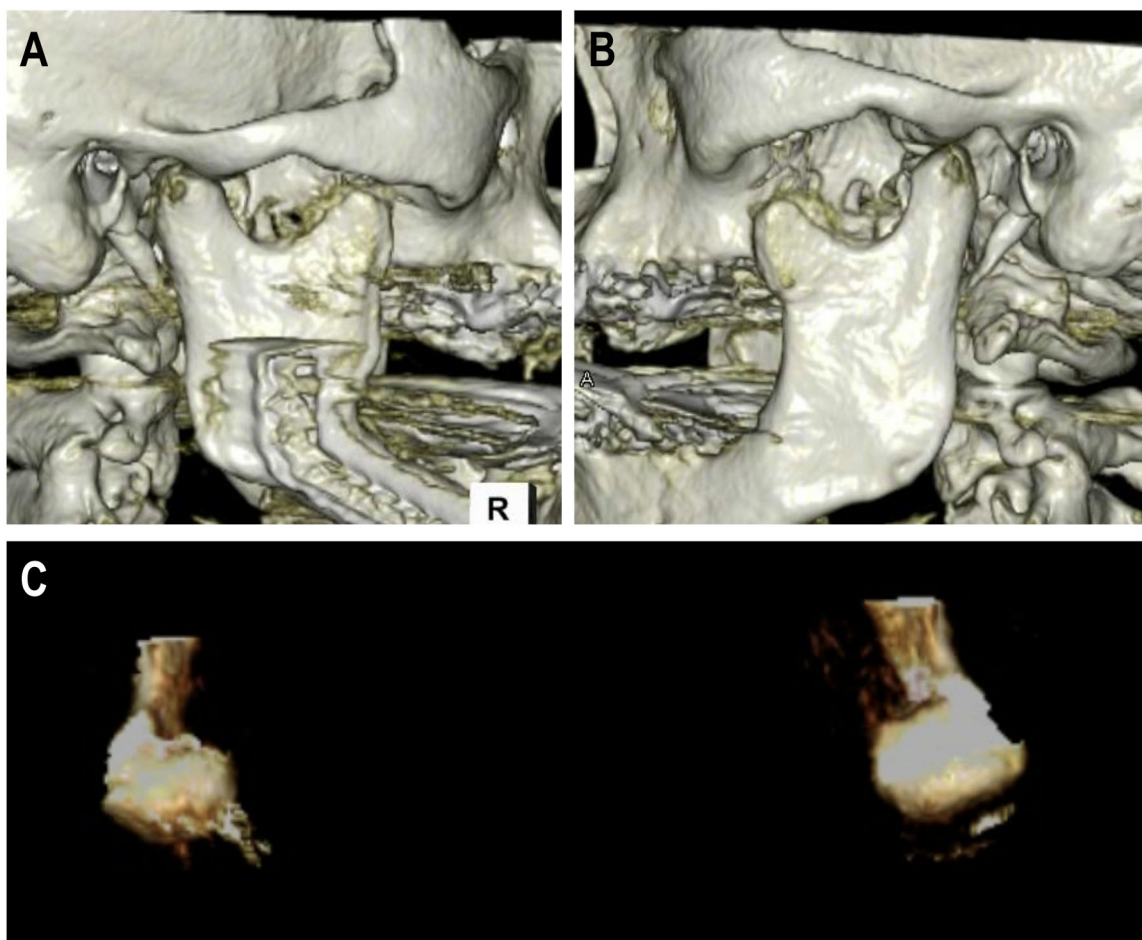


Figure 3

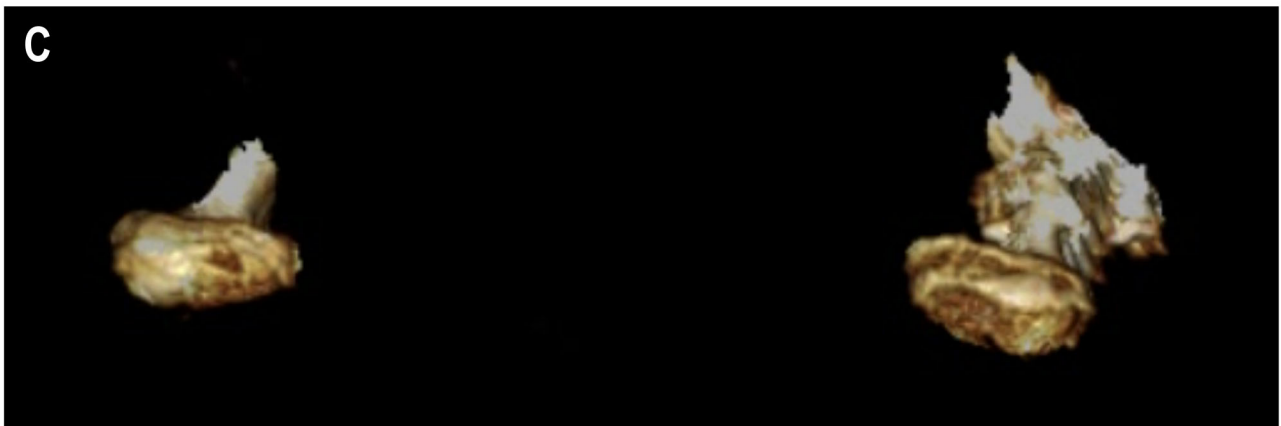
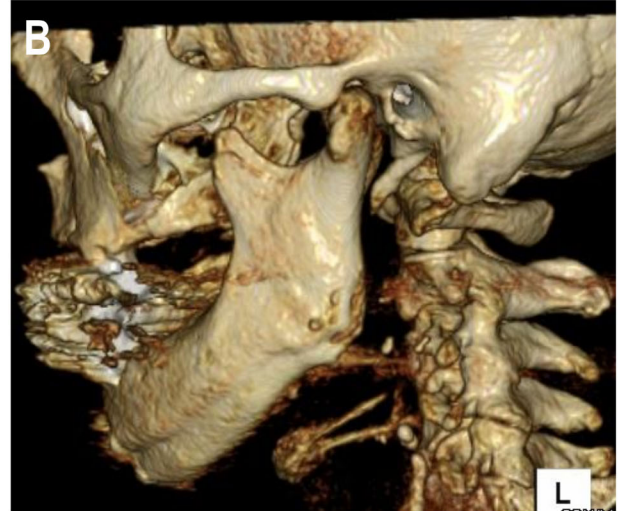
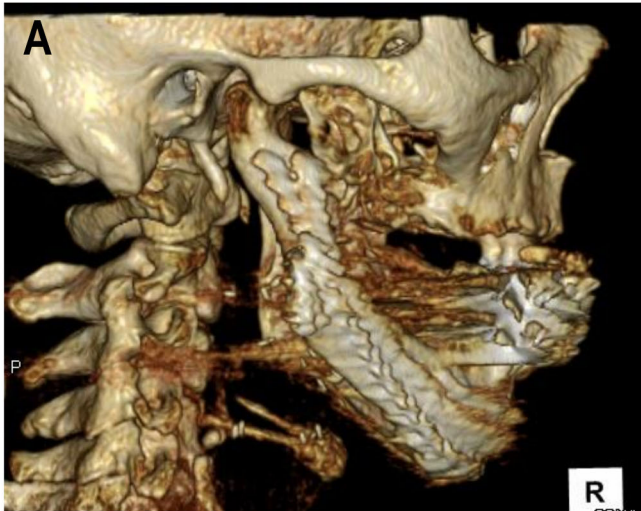


Figure 4

Table 1. Measurement of condylar protrusive movement

	Observer 1			Observer 2		
	Right/diseased side ^a	Left/nondiseased side	Crosswise difference ^b	Right/diseased side ^a	Left/nondiseased side	Crosswise difference ^b
Control	8.6	8.4	0.2	12.4	11.3	1.1
	8.3	7.9	0.4	13	12.3	0.7
	6.6	7.1	0.5	6.9	7	0.1
	6	6.1	0.1	5.5	4.6	0.9
	6.8	7.4	0.6	7.1	6.8	0.3
	5.8	6.1	0.3	7	5.8	1.2
	4.8	5.2	0.4	4.7	5.2	0.5
Median	6.6	7.1	0.4	7	6.8	0.7
(range)	4.8 – 8.6	5.2 – 8.4	0.1 – 0.6	4.7 – 13	4.6 – 12.3	0.1 – 1.2
Patient	2.6	6.1	3.5	3	6.3	3.3
	4.9	3.5	1.4	3.2	1.6	1.6
	7.6	8.6	1	8.2	7.8	0.4
	5	10.3	5.3	5.7	10.4	4.7
	2.6	3	0.4	4.1	2.1	2
	2.6	5.7	3.1	3.1	5.2	2.1
	3.5	7.8	4.3	4.4	8.7	4.3
Median	3.5	6.1	3.1	4.1	6.3	2.1
(range)	2.6 – 7.6	3 – 10.3	0.4 – 5.3	3 – 8.2	1.6 – 10.4	0.4 – 4.7
<i>p</i> values			0.006			0.013

All measurements are expressed in millimeters

a: values are from the right side in the control, and diseased side in the surgical group,

b: in surgical patients, the numerical differences between the diseased and non-diseased side were calculated.