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Differences between the temporal and mandibular components of the temporomandibular joint in topographic distribution of osseous degenerative features on cone-beam computerized tomography

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KEYWORDS Temporomandibular joint; Osseous features; Topographic distribution	<i>Background/purpose:</i> Temporomandibular joint osteoarthritis (TMJOA) pathology is character- ized by degenerative changes of the subchondral bone. The topographic distribution of osseous degenerative changes in TMJ is not clear. This study aimed to evaluate the topographic distri- bution of osseous degenerative features in the TMJ by using cone-beam computerized tomog- raphy (CBCT).
	Materials and methods: The CBCT images of 26 female patients diagnosed to have TMJOA were retrieved from the database of the National Taiwan University Hospital. The images of left and right TMJs were evaluated independently by 2 examiners. The evaluated degenerative features included surface erosion, subcortical cysts, subcortical sclerosis, and osteophytes in the mandibular condyle and temporal component of the TMJ. The topographic distribution at different portions in the mandibular condyle and temporal component of the TMJ was statistically analyzed.
	<i>Results:</i> Significant differences in the topographic distribution of the osseous degenerative features were observed (a) between the mandibular condyle and the temporal component and (b) between the anterior/central portion and posterior portion of the temporal component. No significant differences were observed in the topographic distribution of the TMJOA

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features in the condyle, except for surface erosion between the central and lateral portion of the condyle.

*Conclusion:* The results suggest that the mandibular condyle and temporal component react differently in TMJ osseous degeneration, with the condyle being more vulnerable than the temporal component. Mandibular activities that require the mandibular condyle to function outside the fossa may be more destructive to the health and integrity of the TMJ.

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## Introduction

A normal temporomandibular joint (TMJ) achieves appropriate distribution of mechanical loading across the joint condyle and fossa. When the balance between the mechanical loading in the joint and the adaptive capacity of the host is lost, dysfunctional remodeling of the osseous components occurs.<sup>1,2</sup> A retrospective clinical study reported that unilateral TMJ osteoarthritis (OA) is associated with asymmetry of the mandible and the increase of electromyographic activity of the masseter on the OA side.<sup>3</sup> Experimentally induced long-term disordered occlusion results in increased osteoclast activation, reduced bone mineral density, and cortical bone loss in rats.<sup>4,5</sup> Functional overload from occlusion with subsequent microtrauma is believed to cause osseous degenerative changes in the TMJ.<sup>6–8</sup>

The articular surface of the TMJ that bears the occlusal loading from the masticatory muscles is composed of a layer of fibrocartilage and the underlying subchondral bone. The articular surface is stress-sensitive and subject to extensive remodeling. TMJ OA pathology is characterized by progressive cartilage degradation, chronic inflammation in the synovial tissue, and degenerative changes of the subchondral bone.<sup>9,10</sup> Several animal studies have assessed the osseous changes associated with condylar compression and indicated direct resorptive remodeling at the site of injury as a result of local tissue disruption and impaired cellular function.<sup>11,12</sup> However, the causal relationship between TMJ osseous degeneration and occlusal loading in the masticatory system requires further elucidation.

Degenerative joint disease (DJD) is a critical subtype of temporomandibular disorders (TMDs).<sup>13</sup> It is associated with disc displacement, trauma, functional overload, and autoimmune diseases.<sup>14</sup> An increasing number of studies have focused on the remodeling changes of the subchondral bone in TMJ DJD pathogenesis. 4,10,15 The clinical diagnosis of TMJ DJD is based primarily on radiographic features of the mandibular condyle and the articular temporal component, including flattening, surface erosion, subcortical sclerosis, subcortical cyst, and osteophyte formation.<sup>16-18</sup> Conebeam computerized tomography (CBCT) can reveal more detailed changes in the TMJ bony structures than conventional radiographic modalities, which represents a unique advantage for TMJ DJD diagnosis.<sup>19-21</sup> CBCT images reveal the precise location and extent of osseous degenerative changes in the mandibular and temporal components of the TMJ.<sup>22,23</sup> The usefulness of CBCT is extensively discussed in

the literature,  $^{22,24}$  and the use of CBCT for reliable diagnosis of pathologies in osseous structures is highly recommended.  $^{16,21}$ 

Oral parafunctional activity is regarded as one of the risk factors for TMD.<sup>25,26</sup> Research has suggested that compressive stress during oral parafunction, such as clenching, is localized at the lateral portion of the TMJ condyle.<sup>27,28</sup> If parafunctional overloading of the TMJ plays a role in the development of TMJ DJD, the topographic distribution of osseous degenerative changes in TMJ should be consistent with this finding. This study evaluated the topographic distribution of TMJ osseous degenerative features by using CBCT. The study was approved by the Research Ethics Committee at the National Taiwan University Hospital in Taipei, Taiwan (201904088RINA).

### Materials and methods

#### Participants

This retrospective cross-sectional study used TMJ CBCT images from patients with TMD who sought treatment at the National Taiwan University Hospital during the period from October 2018 to January 2019. Clinical examinations were performed on all patients who visited the Orofacial Pain Clinic (Department of Dentistry at the National Taiwan University Hospital in Taipei, Taiwan) by a clinician who has specifically focused on TMD and orofacial pain for 29 years. Diagnoses of TMD followed the recommendations in the Diagnostic Criteria for Temporomandibular Disorders.<sup>13</sup> A special examination sheath adopted from the Diagnostic Criteria for Temporomandibular Disorders and approved by the National Health Insurance Administration of Taiwan was used as a standardized step-by-step examination protocol during the clinical examination. The first part of the examination sheath was for documentation of the patient's subjective description of his or her chief complaints, including the location, quality, frequency, duration, and intensity (in 0-10 scale) of the pain or headaches, the noises from the TMJ during mandibular functioning, and any other dysfunctions of the masticatory system. The second part of the examination sheath was for documentations of the objective examinations by the clinicians. The examinations included measurements of horizontal incisal overjet, vertical incisal overlap, tracing of mandibular midline deviation, pain free mouth opening, maximal unassisted and assisted mouth opening, lateral excursion and

protrusion of the mandible (all in mm). Whether these mandibular movements were associated with pain familiar to the patient's pain complaints were also documented. Any palpable or audible noises, clicking or crepitus, during mouth opening, closing or reciprocal were marked. TMJ locking while opening mouth or at mouth wide open position and whether the locking can be reduced by the patient or by the clinician was noted. Palpation pain at the TMJ, temporalis, masseter, medial pterygoid, and neck muscles, the referral of the pain, and whether the pain is familiar to the patient's pain or headache were all documented. A panoramic radiograph was routinely taken as a screening for osseous and odontogenic pathologies in the maxilla and mandible that might contribute to the patient's complaints. With the information from above-mentioned examinations, the diagnoses were checked from the most common TMDs, i.e. arthralgia, local myalgia, myofascial pain with or without referral, headache attributed to TMD, degenerative joint disease, subluxation, disc displacement with reduction and with or without intermittent locking, and disc displacement without reduction and with or without limited mouth opening. Diagnoses different from the most common TMDs were written down at the area for special comments. Those patients who were diagnosed to have TMJ arthralgia and degenerative joint disease were asked to take a CBCT examination for evaluation of the osseous degenerative changes in the TMJs. The CBCT images of these patients were used for analysis. Patients with a history of cleft or other congenital syndromes, TMJ injury, facial osteotomy or genioplasty, or autoimmune diseases were excluded from this study.

## CBCT image acquisition

A 3DX Accuitomo (J Morita Mfg. Corp, Kyoto, Japan) was used in accordance with standardized scanning protocol (90 kVp, 5 mA, 30.8 s, FOV  $6 \times 6$  cm, with a high resolution of 0.125 mm voxel size, approximate effective dose = 114  $\mu$ Sv1). From the raw scans, 2-dimensional reconstructions were obtained using i-Dixel 3DX Vision 2.2.1.3 software (J Morita Mfg. Corp, Kyoto, Japan).

# Image analysis

After the CBCT images were retrieved from the database, each patient was assigned a code to replace their personal identification to keep the radiographic examiners blinded from the participants' clinical history and diagnosis. To avoid bias, an oral surgeon and a radiologist reviewed and diagnosed each CBCT image independently. Right and left TMJs of the same participant were examined independently. The analysis criteria for TMJ osseous degenerative features followed the guidelines published by Ahmad et al.<sup>16</sup> In brief, the degenerative features of the osseous component in the TMJ were recorded as the following: (1) surface erosion, defined as reduced density or disrupted continuity of the articular cortical bone; (2) subcortical cyst, defined as a radiolucent cavity beneath the articular surface that appeared distinct from surrounding normal trabecular bone patterns; (3) subcortical sclerosis, defined as an increased calcification density relative to adjacent trabecular bone; and (4) osteophyte, defined as beak-like exophytic and sclerotic objects that stand out from the smooth cortical surface of the joint surface. Our previous study demonstrated fair to good inter-examiner agreement and reliability and acceptable sensitivity and specificity when the 2 examiners used CBCT to identify TMJ osseous degenerative features.<sup>21</sup>

We intended to address the topographic distribution of these TMJ osseous degenerative features on the mandibular condyle and temporal component of the TMJ. The images of the condyle were oriented in front view and divided into mesial, central, and lateral portions. The sagittal view of the temporal component was divided into anterior (eminence), posterior (fossa), and central (transition) portions. A yes/no scoring criterion was used to evaluate the presence of each TMJ osseous degenerative feature at each of the 3 portions on the temporal and mandibular components of the TMJ. The scores of the 2 examiners were subsequently compared. For inconsistent diagnoses, the images were reviewed again and discussed until a consensus was reached between the 2 examiners.

# Statistical analysis of the data

Cohen's  $\kappa$  was calculated to determine the inter-examiner agreement on the presence or absence of TMJ osseous degenerative features in all 1248 data points (see the Results section). Statistical comparisons were made using the nonparametric McNemar test (P < 0.05) to compare the probabilities of each feature between the condyle and fossa as well as among the 3 portions of the condyle or fossa. Statistical analyses were conducted using SPSS version 20 (IBM Corp. Armonk, NY, USA).

# Results

A total of 35 cases of patients met the diagnostic criteria of TMJ arthralgia and degenerative joint disease and underwent CBCT examination. Among the 35 patients, 2 were male, 5 had a history of facial trauma, 1 had been diagnosed with rheumatoid arthritis, and 1 had received a CBCT examination for a reason unrelated to TMJ DJD. These nine patients were excluded from the final evaluation list. Thus, 26 female participants were included in this study. The youngest participant was 15 years old, and the oldest was 66 years old. The mean age of the participants was  $37.7 \pm 16.1$  years. In total, 11 (42%) of the participants were younger than 25 years old, 9 (35%) were between the ages of 26 and 50 years, and the remaining 6 (23%) were older than 51 years. The left and right TMJs were analyzed independently; thus, a total of 52 joints were studied.

After the CBCT images were evaluated, we combined the clinical examination information and image evaluation to finalize a diagnosis for each TMJ. Among the 52 TMJs examined, 6 (11.5%) were painless and exhibited no osseous degenerative changes on the CBCT images and were diagnosed as "normal." Another 6 (11.5%) TMJs exhibited no osseous degeneration but pain was present, either selfreported by the patient or induced by palpation during the clinical examination; these 6 joints were diagnosed with arthralgia. The other 7 (13.5%) TMJs were painless but

Table 1     Diagnosis of the 52 TMJs.						
		Pain				
		No	Yes	Sum		
TMJ osseous Degeneration	No	6 (11.5%)Normal	6 (11.5%)Arthralgia	12 (23.0%)		
	Yes	7 (13.5%)Osteoarthrosis	33 (63.5%)Osteoarthritis	40 (77.0%)		
	Sum	13 (25.0%)	39 (75.0%)	52(100%)		

Note. A total of 52 TMJs from 26 female patients were retrieved from the data base.

Six joints were diagnosed to be normal, 6 arthralgia, 7 osteoarthrosis, and 33 osteoarthritis.

exhibited at least one TMJ osseous degenerative feature on the CBCT image; they were classified as osteoarthrosis. In the remaining 33 (63.5%) TMJs, pain and at least one TMJ osseous degenerative feature were present; they were categorized as osteoarthritis (Table 1).

Each TMJ had 2 components: the mandibular condyle and the temporal component. Each component was topographically divided into 3 portions, and 4 features were examined for the presence or absence of TMJ osseous degenerative features at each portion. In total, examiners compared judgments on 1248 data points (26 participants  $\times$  2 TMJs  $\times$  2 joint components  $\times$  3 portions in each component  $\times$  4 osseous degenerative features). The 2 examiners agreed on the diagnosis of 90.94% (1135/1248) of the CBCT images (Table 2), with a Cohen's  $\kappa$  of 0.756 (P < 0.001). With Fleiss et al. as a reference,<sup>29</sup> the interexaminer agreement was considered to be excellent.

We tested the incidence of TMJ osseous degenerative features between the osteoarthrosis group and the osteoarthritis group with a  $\chi^2$  test and observed no significant differences between the 2 groups in the TMJ osseous features of the 2 components of the TMJ, with the exception of sclerosis in the temporal component (P = 0.008, Table 3). Data of these 40 joints from these 2 groups were pooled together for further analysis.

In the mandibular condyle, surface erosion appeared to have the highest incidence (38 out of the 40 TMJs examined, 95%) among the 4 osseous degenerative features. Osteophytes had the second highest incidence (32 joints, 80%). Subcortical sclerosis and subcortical cysts were identified in 20 (50%) and 10 (25%) of the TMJs, respectively. In the temporal component, surface erosion also had the highest incidence (26 joints, 65%) compared with the other 3 features. Subcortical sclerosis had the second highest incidence in the fossa (5 joints, 12.5%). Osteophytes (1 joint, 2.5%) and subcortical cysts (none) were rare in the temporal component of the TMJ. A comparison between the 2 components of the TMJ in terms of the incidence of each TMJ osseous degenerative feature revealed significant differences in surface erosion, subcortical sclerosis, and osteophytes (P < 0.001, McNemar test; see Fig. 1). No comparison was conducted with respect to the incidence of subcortical cysts between the 2 components because no cysts were discovered in the temporal component, which violated the assumption of the McNemar test.

We further analyzed the topographic distribution of each osseous degenerative feature in the temporal and mandibular components of the TMJ. No statistical differences were observed in the topographic distribution of different osseous degenerative features among the mesial, central, and lateral portions in the condyle (P > 0.05, McNemar test). The only exception was the incidence of surface erosion at the central portion (37 joints, 92.5%) of the condyle, which was significantly higher than that at the lateral portion (28, 70%, P = 0.012; see Fig. 2). In the temporal component, the incidences of subcortical sclerosis (5, 12.5%), osteophytes (1, 2.5%), and subcortical cysts (0) were too low to compare their topographic distributions (Fig. 1). However, statistical analysis did reveal a significantly higher incidence of surface erosion at the eminence (22, 55%) and transition portion (21, 52.5%) of the temporal component than at the fossa (8, 20%; both P < 0.01, McNemar test). No significant difference was observed between the eminence and transition portion in the temporal component (Fig. 3).

### Discussion

This study investigated the topographic distribution of various osseous degenerative features in TMJs diagnosed with DJD. Our study revealed that patients with TMJ DJD who visited the TMD/Orofacial Pain Clinic at National Taiwan University Hospital were predominantly female, with 26 female participants included in this study. Their ages varied widely, and the number of patients with TMJ

Table 2 Inter-examiner agreement.

		Exam	Examiner 1	
		No	Yes	Sum
Examiner 2	No	884	57	941
	Yes	56	251	307
	Sum	940 308 1248	940 308 1248	940 308 1248

Note. A total of 1248 data points were compared for the judgement of the appearance of each TMOA feature on the three portions of each TMJ condyle and fossa. The agreement between the two examiners were 90.94%. The inter-examiner agreement was considered excellent,  $\kappa = 0.756$ , P < 0.001 ( $\chi$ 2 test, kappa statistics).

Table 3	Incidence of	of the osseous	degenerative	features.
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		Osteoarthrosis $(n = 7)$		Osteoarthritis (n = 33)		p-value
		n	%	n	%	
Mandibular Condyle	Surface erosion	7	100	31	93.9	0.504
	Subcortical cyst	3	42.9	7	21.2	0.230
	Subcortical sclerosis	4	57.1	16	48.5	0.677
	Osteophyte	4	57.1	28	84.8	0.096
Temporal Component	Surface erosion	5	71.4	21	63.6	0.695
	Subcortical cyst	0	0.0	0	0.0	N/A
	Subcortical sclerosis	3	42.9	2	6.1	0.008*
	Osteophyte	0	0.0	1	3	0.641

The  $\chi^2$  test showed no significant difference in most TMJ osseous degenerative features between osteoarthrosis and osteoarthritis groups, except for sclerosis in the temporal component (P = .008). Since no subcortical cysts were found in the temporal component, the comparison between the two groups was not implemented.

DJD seemed to decline with age. The inter-examiner agreement regarding CBCT diagnosis was excellent. Among the 52 TMJs, 40 joints (77%) exhibited osseous degenerative changes and were used to further analyze the topographic distribution of the osseous degenerative features in the temporal and mandibular components of the TMJ. Statistical analysis revealed highly significant differences between the mandibular condyle and the temporal component in terms of the incidences of surface erosion, subcortical sclerosis, and osteophytes. Generally speaking, no significant differences were observed for the 4 osseous degenerative features in the topographic distribution among the mesial, central, and lateral portions of the mandibular condyle. Notably, subcortical cysts, subcortical sclerosis, and osteophytes were relatively infrequently observed in the temporal component of the TMJ. Surface

erosion, however, was identified in 65% of the temporal component in the TMJs diagnosed with DJD. When surface erosion occurs, it appears significantly more often in the anterior portion (the eminence) and the central portion (the transition between the concave and convex portion) of the temporal component than in the posterior portion (the fossa).

The osseous degenerative changes in the mandibular condyle and temporal component of the TMJ differed in 2 respects. First, TMJ osseous degenerative features were more frequently observed in the condyle than in the articular fossa/eminence, which aligns with the results of other studies (20, 22). Second, among the 4 types of osseous degenerative features, surface erosion, subcortical sclerosis, and osteophytes were significantly more prevalent in the condyle than in the temporal component. In



**Figure 1** Differences in surface erosion, subcortical sclerosis and osteophytes between the mandibular condyle and the temporal component were also highly significant (\*\*\*P < 0.001, McNemar test). No comparison was implemented because of violation of the assumption for McNemar test.

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Figure 2 Topographic distribution of osseous degenerative features in mandibular condyle. Comparisons for the topographic distribution of different TMJ osseous degenerative features in the mandibular condyle showed a significant difference only in surface erosion between the central portion and the lateral portion (\*P < 0.05).

addition to these differences, we noted the rare occurrence or absence of osteophytes and subcortical cysts in the temporal component of the TMJ. Several factors may have contributed to these differences. First, the mandibular condyle and the temporal component exhibit different patterns of growth and development. The mandibular condyle undergoes endochondral bone formation, whereas the temporal bone develops through intramembranous bone formation. Second, the load bearing manner differs between the temporal and mandibular components of the TMJ. The loading of the condyle during jaw movement centers on a small area of the condyle head, whereas the loading of the temporal component is distributed on the considerably wider slope and eminence of the fossa. Whether any differences exist in the cellular or biochemical composition of the upper and lower components of the TMJ is unclear. More research is necessary to confirm and explain this finding.

For some time now, efforts have been focused on elucidating the relationship between the development of TMD and dental occlusion classification, occlusal interferences in the centric occlusion/centric relation, or oral parafunctions that occur mostly when the mandibular condyle is located posteriorly in the fossa. Nevertheless, evidence has indicated that the TMJ is more heavily loaded during jaw opening than during jaw closing.<sup>30,31</sup> During jaw



**Figure 3** Topographic distribution of surface erosion in temporal component. Comparisons for the topographic distribution of surface erosion in the temporal component showed a significantly lower incidence at the fossa than the eminence and transition portion (\*\* P < 0.01, McNemar test); there was no significant difference between the eminence and the transition portion.

opening, the mandibular condyle travels forward along the anterior slope of the fossa and closer to the eminence. The mechanical stress in the TMJ is the lowest during the initial phase of jaw opening, increases dramatically during the translating phase, and reaches its peak when the jaw opens to its maximal range.<sup>31</sup> The location of the mandibular condyle relative to the temporal component in these 3 phases of jaw opening matches the topographical structure of the fossa, transition portion, and eminence of the temporal bone. Our findings that the eminence and transition portion exhibited significantly higher incidence of surface erosion than the fossa corroborates the results of the aforementioned studies. In addition, prolonged maximal mouth opening induces increased proteoglycan deposition, cytokine expression, hypertrophic chondrocyte and macrophage formation in the mandibular condyle, and persistent orofacial mechanical allodynia and TMJ dysfunction in rodents.<sup>32,33</sup> It is not uncommon for patients to experience initiation or exaggeration of pain in the TMJ or masticatory muscles following prolonged mouth opening during dental treatment. This study and the abovementioned studies seem to indicate that mandibular activities requiring the mandibular condyle to function outside the fossa may be more damaging to the health and integrity of the TMJ.

Excessive mechanical loading is considered a key factor for inducing cartilage degradation in the TMJ.<sup>14</sup> Studies have suggested that compressive stress during clenching is concentrated in the lateral portion of the mandibular condyle.<sup>27,28</sup> Our study observed no significant difference among the mesial, central, and lateral portions in the condyle for all 4 osseous degenerative features, except the incidence of surface erosion in the central portion, which was higher than in the lateral portion of the condyle. However, our results do not refute the findings of other research because other studies have focused on the episodic physical loading of the TMJ, whereas we studied the pathological changes following long-term overloading of the TMJ. Repeated or long-term mechanical overloading results in the destruction of tissues and necrosis of cells. leading to the release of proteases, cytokines, and growth factors in a joint and the activation of nociceptive C fibers in the TMJ.<sup>34,35</sup> The induced pain further releases substance P and calcitonin gene-related peptide and vasoactive intestinal peptide from C fiber nerve endings and triggers neurogenic inflammation.<sup>36,37</sup> The inflammatory chemicals are diffused throughout the joint cavity through the flow of synovial fluid, causing extensive chondrocyte or synovial cell breakdown, the release of more proteolytic enzymes, and worsened tissue degradation.<sup>38</sup> Such a vicious and cyclic process of joint inflammation causes progressive and diffuse cartilage degradation, subchondral bone remodeling, and chronic inflammation in synovial tissue.<sup>39,40</sup> Most patients seeking help from TMJ specialists have already experienced symptoms for some time. What we observe in the CBCT images most likely reflects wellestablished destructive changes in the TMJs. More wellcontrolled longitudinal studies are required to verify the progress of osseous degeneration in the TMJ.

Our study raises some critical concerns that merit further consideration, including (1) whether the variations in probability of the 4 TMJ osseous degenerative features are attributed to any specific order of occurrence; (2) whether the 4 features reflect different progressive stages of TMJ osteoarthritis; (3) whether any particular order exists for the features to transform from one to the other during the patients' life span; and (4) what inflammatory chemicals or cell activities are specifically involved in each of the features. CBCT can aid in the investigation of these matters.

TMJ osseous degenerative changes are more frequently observed in the mandibular condyle than in the temporal component, suggesting that the two components behave differently in the development of osseous degeneration. No significant differences in the topographic distribution of TMJ osseous degenerative features were observed among the mesial, central, and lateral portions of the condyle, suggesting that TMJ DJD cannot always be attributable to mechanical overloading. Surface erosion was more frequently observed in the eminence and transition portion than the fossa in the temporal component, indicating that mandibular activities that demand the condyle to function outside the fossa may play a crucial role in the development of TMD DJD. New therapeutic modalities should include biological processes associated with cellular reactions and molecular mechanisms. Intra-TMJ therapeutic strategies should consider the two components independently and target a specific component when treatment is delivered inside the TMJ.

# Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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# References

- 1. Arnett WG, Milam SB, Gottesman L. Progressive mandibular retrusion—idiophatic condylar resorption. Part I. *Am J Orthod Dentofacial Orthop* 1996a;110:8–15.
- 2. Arnett WG, Milam SB, Gottesman L. Progressive mandibular retrusion—idiophatic condylar resorption. Part II. *Am J Orthod Dentofacial Orthop* 1996b;110:117–27.
- **3.** Matsumoto R, Ioi H, Goto TK, et al. Relationship between the unilateral TMJ osteoarthritis/osteoarthrosis, mandibular asymmetry and the EMG activity of the masticatory muscles: a retrospective study. *J Oral Rehabil* 2010;37:85–92.
- 4. Jiao K, Niu LN, Wang MQ, et al. Subchondral bone loss following orthodontically induced cartilage degradation in the mandibular condyles of rats. *Bone* 2011;48:362–71.
- 5. Zhang J, Jiao K, Zhang M, et al. Occlusal effects on longitudinal bone alterations of the temporomandibular joint. *J Dent Res* 2013;92:253–9.
- 6. Kuang B, Dai J, Wang QY, et al. Combined degenerative and regenerative remodeling responses of the mandibular condyle to experimentally induced disordered occlusion. *Am J Orthod Dentofacial Orthop* 2013;143:69–76.

- 7. Li H, Zhang XY, Wu TJ, et al. Endoplasmic reticulum stress regulates rat mandibular cartilage thinning under compressive mechanical stress. *J Biol Chem* 2013;288:18172–83.
- **8.** Zhang M, Zhang J, Lu L, et al. Enhancement of chondrocyte autophagy is an early response in the degenerative cartilage of the temporomandibular joint to biomechanical dental stimulation. *Apoptosis* 2013;18:423–34.
- Gynther GW, Dijkgraaf LC, Reinholt FP, et al. Synovial inflammation in arthroscopically obtained biopsy specimens from the temporomandibular joint: a review of the literature and a proposed histologic grading system. J Oral Maxillofac Surg 1998;56:1281-6.
- **10.** Wang XD, Kou XX, He DQ, et al. Progression of cartilage degradation, bone resorption and pain in rat temporomandibular joint osteoarthritis induced by injection of iodoacetate. *Plos One* 2012;7:e45036.
- 11. Asano T. The effects of mandibular retrusive force on the growing rat mandible. *Am J Orthod* 1986;90:464–74.
- Ellis III E, Hinton RJ. Histologic examination of the temporomandibular joint after mandibular advancement with and without rigid fixation: an experimental investigation in adult Macaca mulatta. J Oral Maxillofac Surg 1991;49:1316–27.
- **13.** Schiffman E, Ohrbach R, Truelove E, et al. Diagnostic criteria for temporomandibular disorders (DC/TMD) for clinical and research applications: recommendations of the international RDC/TMD consortium network and orofacial pain special interest group. *J Oral Facial Pain Headache* 2014;28:6–27.
- Tanaka E, Detamore MS, Mercuri LG. Degenerative disorders of the temporomandibular joint: etiology, diagnosis, and treatment. J Dent Res 2008;87:296-307.
- Embree M, Ono M, Kilts T, et al. Role of subchondral bone during early-stage experimental TMJ osteoarthritis. J Dent Res 2011;90:1331-8.
- Ahmad M, Hollender L, Anderson Q, et al. Research diagnostic criteria for temporomandibular disorders (RDC/TMD): development of image analysis criteria and examiner reliability for images. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;107:844–60.
- Kalladka M, Quek S, Heir G, et al. Temporomandibular joint osteoarthritis: diagnosis and long-term conservative management: a topic review. J Indian Prosthodont Soc 2014;14:6–15.
- 18. Zhao YP, Zhang ZY, Wu YT, et al. Investigation of the clinical and radiographic features of osteoarthrosis of the temporomandibular joints in adolescents and young adults. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;111:e27–34.
- **19.** dos Anjos Pontual ML, Freire JS, Barbosa JM, et al. Evaluation of bone changes in the temporomandibular joint using cone beam CT. *Dentomaxillofacial Radiol* 2012;41:24–9.
- Krisjane Z, Urtane I, Krumina G, et al. The prevalence of TMJ osteoarthritis in asymptomatic patients with dentofacial deformities: a cone-beam CT study. Int J Oral Maxillofac Surg 2012;41:690-5.
- 21. Tsai CM, Wu FY, Chai JW, et al. The advantage of using conebeam computerized tomography over panoramic radiography and temporomandibular joint quadruple radiography in assessing temporomandibular joint osseous degenerative changes. J Dent Sci 2020;15:153–62.
- Alexiou KE, Stamatakis HC, Tsiklakis K. Evaluation of the severity of temporomandibular joint osteoarthritic changes

related to age using cone beam computed tomography. *Dentomaxillofacial Radiol* 2009;38:141–7.

- Cevidanes LHS, Hajati A-K, Paniagua B, et al. Quantification of condylar resorption in temporomandibular joint osteoarthritis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2010;110: 110-7.
- 24. Honda K, Larheim TA, Maruhashi K, et al. Osseous abnormalities of the mandibular condyle: diagnostic reliability of cone beam computed tomography compared with helical computed tomography based on an autopsy material. *Dentomaxillofacial Radiol* 2006;35:152–7.
- **25.** Ohrbach R, Bair E, Fillingim RB, et al. Clinical orofacial characteristics associated with risk of first-onset TMD: the OPPERA prospective cohort study. *J Pain* 2013;14:T33–50.
- 26. Winocur E, Littner D, Adams I, et al. Oral habits and their association with signs and symptoms of temporomandibular disorders in adolescents: a gender comparison. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2006;102:482–7.
- Koolstra JH, van Eijden TM. Combined finite-element and rigidbody analysis of human jaw joint dynamics. *J Biomech* 2005;38: 2431–9.
- Kopp S. Topographical distribution of sulfated glycosaminoglycans in the surface layers of the human temporomandibular joint. J Oral Pathol 1978;7:283–94.
- 29. Fleiss JL, Levin B, Paik MC. Statistical methods for rates and proportions, 3rd ed. Hoboken (NJ): John Wiley & Sons, 2003: 598–626.
- **30.** Huddleston Slater JJR, Visscher CM, Lobbezoo F, et al. The intra-articular distance within the TMJ during free and loaded closing movements. *J Dent Res* 1999;78:1815–20.
- **31.** Tuijt M, Koolstra JH, Lobbezoo F, et al. Differences in loading of the temporomandibular joint during opening and closing of the jaw. *J Biomech* 2010;43:1048–54.
- **32.** Hawkins JL, Durham PL. Prolonged jaw opening promotes nociception and enhanced cytokine expression. *J Oral Facial Pain Headache* 2016;30:34.
- **33.** Wang GY, Shi XQ, Wu W, et al. Sustained and repeated mouth opening leads to development of painful temporomandibular disorders involving macrophage/microglia activation in mice. *Pain* 2018;159:1277–88.
- **34.** Alstergren P. Cytokines in temporomandibular joint arthritis. *Oral Dis* 2000;6:331-4.
- **35.** Lobbezoo F, Drangsholt M, Peck C, et al. Topical review: new insights into the pathology and diagnosis of disorders of the temporomandibular joint. *J Orofac Pain* 2004;18:181–91.
- **36.** McDougall JJ. Arthritis and Pain. Neurogenic origin of joint pain. *Arthritis Res Ther* 2006;8:220.
- **37.** Sessle BJ. Peripheral and central mechanisms of orofacial inflammatory pain. *Int Rev Neurobiol* 2011;97:179–206.
- 38. De Bont LGM. Temporomandibular joint degenerative diseases: pathogenesis. In: Stegenga B, de Bont LGM, eds. Management of temporomandibular joint degenerative diseases: biologic basis and treatment outcome. Basel: Birkh~user, 1996. p3-11.
- **39.** Vernal R, Velasquez E, Gamonal J, et al. Expression of proinflammatory cytokines in osteoarthritis of the temporomandibular joint. *Arch Oral Biol* 2008;53:910–5.
- Wang X, Zhang JN, Gan YH, et al. Current understanding of pathogenesis and treatment of TMJ osteoarthritis. J Dent Res 2015;94:666–73.