REVIEW ARTICLE

Panoramic radiographs for identifying individuals with undetected osteoporosis

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Summary Numerous panoramic radiographs are taken annually to examine dental diseases, and using them for triaging individuals with general skeletal bone diseases, such as osteoporosis, would be economical and beneficial as dentists could refer these patients to medical professionals for further examination. Since the early 1990s, several studies have been performed regarding the utility of panoramic radiographs in triage screening for osteoporosis in dental clinics. Cortical indices of the mandible on panoramic radiographs, such as cortical width and cortical shape, are significantly associated with bone mineral density (BMD) of the general skeleton, biochemical markers of bone turnover and risk of osteoporotic fractures in postmenopausal women as well as elderly men. In prospective clinical trials, about 95% of postmenopausal women identified by trained general dental practitioners using cortical shape category on panoramic radiographs had low skeletal BMD or osteoporosis. Panoramic radiography indices may be likely useful triage screening tools for identifying individuals with an increased probability of having low skeletal BMD, osteoporosis and osteoporotic fractures. However, further investigations should be conducted worldwide to determine whether these indices are acceptable for triaging individuals with osteoporosis and referring them to medical professionals.

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KEYWORDS
Osteoporosis; Mandible; Panoramic radiograph; Menopause; Triage screening

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1. Underdiagnosed osteoporosis and triage screening tool

1.1. Background of osteoporosis

Osteoporosis is a skeletal disease characterised by low bone mass and microarchitectural deterioration with a resulting increase in bone fragility and susceptibility to fracture [1]. Increases in the size of the elderly population worldwide will likely cause a marked rise in the incidence of osteoporotic fractures. An estimated 9.0 million osteoporotic fractures occurred worldwide in 2000, of which 1.6 million were at the hip, 1.7 million were at the forearm and 1.4 million were clinical vertebral fractures [2]. The number of patients with hip fracture in Japan was about 0.05 million in 1987 and 0.15 million in 2007 [3]. Both vertebral and hip fractures contribute to an increased risk of mortality and morbidity as well as a rapid increase of medical costs in older populations, especially postmenopausal women [4,5]. A conservative estimate of the worldwide annual costs of hip fracture was US $131.5 billion in 1997 [6]. In the prospective cohort from the Dubbo Osteoporosis Epidemiology Study of community-dwelling women and men aged 60 years and older, increases in absolute mortality that were above expected for 5 years after fracture ranged from 1.3 to 13.2 per 100 person-years in women and from 2.7 to 22.3 per 100 person-years in men depending on fracture type. Subsequent fracture was associated with an increased mortality hazard ratio of 1.91 (95% confidence interval [CI], 1.54–2.37) in women and 2.99 (95% CI, 2.11–4.24) in men [7]. In a prospective study of Japanese patients with hip fracture, the survival rate decreased dramatically for 2 years after the event and the mortality risk remained higher for 10 years. This risk was approximately double that of the general population, even at 10 years after fracture [8].

The bone mass, or bone mineral density (BMD), of the general skeleton, especially of the vertebrae and proximal femur, is an important factor related to fracture risk. Several BMD assessment technologies, such as dual energy X-ray absorptiometry (DXA), have been developed and applied worldwide. Osteoporosis is defined as a BMD T-score of −2.5 or less at either the lumbar spine or the femoral neck, in accordance with the World Health Organisation classification [9]. However, many populations with an increased risk of osteoporotic fractures are still undiagnosed and undertreated [10]. Insufficient understanding of the multidimensional aspects of osteoporosis in older women may be a major cause of such underdiagnosis [11]. BMD testing for all individuals at risk, especially postmenopausal women, is preferable but not practical in many countries where the equipment for BMD assessment, especially DXA, is not widely available [12]. The US Centers for Medicare and Medicaid Services (CMS) has established BMD testing as a key preventive medical service and encouraged patients to have this test when first enrolling in Medicare. However, recent CMS actions have reduced reimbursement for DXA to levels that are below the cost of providing this service at many facilities [13]. Several clinical decision-making rules to assist in identifying postmenopausal women with low BMD or osteoporosis have been developed since the mid-1990s. Nevertheless, the clinical application of these rules to determine which patients require DXA is complicated due to a lack of consensus [14].

1.2. Triage screening for osteoporosis in dental clinics

Numerous panoramic radiographs (approximately 10 million in Japan [15], 17 million in the United States [16], and 1.5 million in England and Wales [17]) are taken yearly for examining dental diseases such as dental caries and periodontal disease. It would be both economical and beneficial if these radiographs could be used for identifying postmenopausal women with undetected osteoporosis so that dentists could refer them to medical professionals for DXA testing. Instead of panoramic radiographs, several studies have investigated the utility of intraoral radiographs in identifying individuals with undetected low skeletal BMD or osteoporosis [18–26]. Some studies have evaluated the BMD of the jaws using a reference, such as an aluminium step wedge, on intraoral radiographs [18,20,21,25,26], whilst others analysed trabecular bone pattern using customised image analysis software [19,20,23,24]. However, special equipment was required to analyse alveolar BMD or trabecular bone pattern of the jaws on intraoral radiographs. The basic concept in triage screening for osteoporosis in dental clinics is that dentists, especially general dental practitioners (GDPs), do not use special equipment. They should use simple methods in triaging individuals with undetected osteoporosis in their dental clinics without incurring additional medical costs.

The aims of this review were to provide basic information and evidence regarding the appropriate panoramic radiography indices for identifying individuals, especially postmenopausal women, at risk of osteoporosis; the relationship between panoramic radiography indices and several parameters related to risk of osteoporotic fractures, such as skeletal BMD; the development of a computer-assisted diag-
nosis (CAD) system for use on digital panoramic radiography; and how many patients with undetected osteoporosis are actually identified by GDPs in their clinics using panoramic radiography indices.

2. Appropriate indices on panoramic radiographs in screening for osteoporosis

2.1. Trabecular bone of the mandible on panoramic radiographs

Trabecular bone is more susceptible to osteoporosis than cortical bone, and thus the trabecular bone pattern of the general skeleton, such as the vertebrae and proximal femur, is analysed visually or with computer-aided methods to estimate the probability of having osteoporosis and predict the risk of future fractures [27]. Although we recently suggested that trabecular bone analysis of the jaws may be useful in screening for osteoporosis on panoramic radiographs, whether trabecular bone of the jaws is markedly influenced by general bone metabolism rather than local factors, such as inflammation induced by dental infection, remains controversial [28,29]. Trabecular bone of the jaws is easily resorbed and/or sclerosed by local inflammation. The degrees of interexaminer and intraexaminer agreement of visual assessment of the trabecular pattern are also expected to be relatively low because the trabecular pattern of the jaws is more diverse than that of the general skeleton, such as the vertebrae and proximal femur [30]. Furthermore, the use of a specialised computer system for analysis of trabecular bone would be incompatible with the basic concept of screening for osteoporosis in dental clinics.

2.2. Cortical width of the mandible on panoramic radiographs

Bras et al. first described the thickness of the mandibular angular cortex as a useful diagnostic tool in patients with metabolic diseases such as renal osteodystrophy [31]. Thereafter, several researchers have evaluated whether cortical width of the mandibular angle, subsequently named the gonion index (GI) [32], is an effective screening tool for identifying elderly, especially postmenopausal women, with undetected osteoporosis [18,33–36]; however, this index was not helpful for this purpose. Four possible reasons exist as to why this index is not useful in identifying elderly subjects with undetected osteoporosis. First, the measurement error of the GI will markedly influence the results because the GI is very small. Second, unstable horizontal magnification on panoramic radiographs will probably influence the results. Third, the site of measurement of GI described by Bras et al. [31] is unclear. Finally, as the masseter and medial pterygoid muscles attach to the mandibular angle, occlusal function may influence the GI measurement. In addition to the GI, cortical width at the antegonion, named AI by Ledgerton et al., is also not useful because of problems associated with repeatability and precision of GI measurement [32].

In 1994, we and Klemetti et al. first demonstrated the possibility that the cortical width below the mental foramen, subsequently designated the mental index (MI) or mandibular cortical width (MCW) [37,38], is a useful screening tool in identifying postmenopausal women with undetected low skeletal BMD or osteoporosis. This index can overcome some of the shortcomings of GI and AI measurements. Benson et al. have already defined new radiomorphometric index, the panoramic mandibular index (PMI), calculated as the cortical width below the mental foramen (the MCW) divided by the distance between the mental foramen and inferior border of the mandible [39]; however, measurement error due to both the MCW and distance between the mental foramen and inferior border of the mandible is likely to markedly influence the results [40–45]. In addition, the recognition of accurate position of the mental foramen may differ amongst different examiners. Therefore, many studies focus on the MCW when evaluating the cortical width of the mandible on panoramic radiographs [32,34–36,42–62].

2.3. Cortical shape of the mandible on panoramic radiographs

Extended Haversian canals in the cortex of the mandible are elevated in patients with osteoporosis [63], which can be seen as several black lines parallel to the inferior cortex of the mandible on panoramic radiographs. As the Haversian canals finally grow together, the inferior cortex will disappear in patients with severe osteoporosis. In 1994, Klemetti et al. first defined cortical shape classification on panoramic radiographs for identifying postmenopausal women with osteoporosis as follows (Fig. 1) [38]:

1. Normal cortex: the endosteal margin of the cortex is even and sharp on both sides;
2. Mildly to moderately eroded cortex: the endosteal margin shows semilunar defects (lacunar resorption) or appears to form endosteal cortical residue; or
3. Severely eroded cortex: the cortical layer forms heavy endosteal cortical residue and is clearly porous.

In this classification, subsequently designated the mandibular cortical index (MCI) [32], the cortices distal from the mental foramen to the antegonial region on both sides are

![Figure 1](image-url)
As the MCI is an objective index, many studies have reported the intraobserver and interobserver agreement of the MCI (Table 1). The results of these studies were varied because of the different sample sizes and the differences in the ability of observers with regard to accurate diagnosis of the MCI. Oral radiologists may be able to perform more accurate diagnosis than other dentists. In our recent international collaborative research (Osteoporosis Screening Project in Dentistry: OSPD) with voluntary participation of 60 investigators from 15 countries, the weighted kappa value for intraobserver agreement was much better for oral radiologists compared to that for other dentists [65]. Furthermore, in this research, the intraobserver agreement was acceptable (weighted kappa values > 0.4) in most of the observers.

As mentioned above, the MCW and the MCI defined by Klemetti et al. [38] are appropriate in triaging individuals with underdiagnosed low skeletal BMD or osteoporosis.

3. Relationships among cortical indices, skeletal BMD and bone quality

From the viewpoint of the definition of osteoporosis, the positive relationship between cortical indices detected on panoramic radiographs, general skeletal BMD and bone quality should be confirmed to demonstrate whether cortical indices are effective indicators for identifying individuals with an increased likelihood of osteoporosis.

3.1. Cortical width of the mandible and skeletal BMD

In 1994, we and Klemetti et al. first reported the significant moderate association between the MCW and skeletal BMD measured by quantitative computed tomography (QCT) in postmenopausal women [37,38]. We suggested the utility of MCW measurements in identifying postmenopausal women with an increased likelihood of osteoporosis [37], but Klemetti et al. concluded that panoramic radiographs should not be used to assess the patient’s status regarding osteoporosis [38]. Thereafter, several studies reported significant relationships between the MCW and skeletal BMD in postmenopausal women as well as elderly men [34,35,43,44,46,51,53,54,57,61,62] (Table 2). In triage screening for osteoporosis, neither sensitivity nor specificity becomes high because of trade-off phenomena. Klemetti et al. [38] denied the usefulness of the MCW because of high sensitivity and low specificity or low sensitivity and high specificity when using the MCW with different cut-off points; however, from the viewpoint of triage screening for osteoporosis, high sensitivity (about 90%) and relatively low specificity (about 40–60%) are considered acceptable in medical applications [66].

Cadarette et al. reported that the sensitivity of simple decision rules, such as the Osteoporosis Self-Assessment Tool (OST), calculated using the patient’s age and weight, and the Osteoporosis Risk Assessment Instrument (ORAI) to identify postmenopausal women with osteoporosis ranged from 92% to 95% and specificity ranged from 35% to 46% [67]. They concluded that these data confirmed the validity of the ORAI, the OST chart and the OST equation as triage screening tools for BMD testing. In postmenopausal Asian women, the OST...
had a sensitivity of 91% and specificity of 45%, with an area under the receiver operating characteristic (ROC) curve of 0.79 [68]. In a systematic review, Rub et al. noted that summary estimates of the diagnostic odds ratio (DOR) for OST and the other clinical decision rules, such as ORAI and Simple Calculated Osteoporosis Risk Estimation (SCORE), did not differ significantly in white women [69]. In another systematic review, Liu et al. reported that the OST had sensitivity of 81% and specificity of 68% in identifying DXA-determined osteoporosis in men [70].

### Table 1  Intra- and interobserver agreement of mandibular cortical index (MCI).

<table>
<thead>
<tr>
<th>Authors (year) [Ref.]</th>
<th>Number of observers</th>
<th>Number of observed radiographs</th>
<th>Observer agreements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Klemetti et al. (1994) [38]</td>
<td>1</td>
<td>352</td>
<td>No described</td>
</tr>
<tr>
<td>Taguchi et al. (1996) [46]</td>
<td>3</td>
<td>100</td>
<td>Mean intraobserver agreement 92%; Mean interobserver agreement 82%</td>
</tr>
<tr>
<td>Horner and Devlin (1998) [42]</td>
<td>2</td>
<td>40</td>
<td>Intraobserver agreement, kappa value = 0.54, 0.38; Interobserver agreement, kappa value = 0.30</td>
</tr>
<tr>
<td>Ledgerton et al. (1999) [32]</td>
<td>2</td>
<td>No described</td>
<td>Interobserver agreement, Weighted kappa value = 0.78</td>
</tr>
<tr>
<td>Devlin et al. (2001) [47]</td>
<td>9 GDPs, 1 expert</td>
<td>10</td>
<td>Interobserver agreement (for 1 expert), mean weighted kappa values = 0.57, 0.44 (for 1st and 2nd observation)</td>
</tr>
<tr>
<td>Bollen et al. (2000) [48]</td>
<td>2</td>
<td>30</td>
<td>Mean intraobserver agreement, Kendall’s tau = 0.582; Interobserver agreement, Kendall’s tau = 0.764</td>
</tr>
<tr>
<td>Zlataric et al. (2002) [49]</td>
<td>No described</td>
<td>136</td>
<td>Intraobserver agreement, excellent</td>
</tr>
<tr>
<td>Drozdzowska et al. (2002) [35]</td>
<td>2</td>
<td>28</td>
<td>Intraobserver agreement, kappa value = 0.75, 0.66; Interobserver agreement, kappa value = 0.70</td>
</tr>
<tr>
<td>Nakamoto et al. (2003) [71]</td>
<td>27 GDPs</td>
<td>100</td>
<td>Intraobserver agreement, untrained 19 (70%) GDPs had kappa values &gt; 0.6</td>
</tr>
<tr>
<td>Halling et al. (2005) [72]</td>
<td>2</td>
<td>70</td>
<td>Interobserver agreement, kappa value = 0.77</td>
</tr>
<tr>
<td>Yasar and Akgünül (2006) [43]</td>
<td>1</td>
<td>48</td>
<td>Intraobserver agreement, weighted kappa value = 0.85</td>
</tr>
<tr>
<td>Horner et al. (2007) [61]</td>
<td>5</td>
<td>653</td>
<td>Interobserver agreement, weighted kappa values 0.16–0.75; Interobserver agreement, weighted kappa values 0.19–0.78</td>
</tr>
<tr>
<td>Uysal et al. (2007) [64]</td>
<td>No described</td>
<td>No described</td>
<td>Interobserver agreement, weighted kappa value = 0.86</td>
</tr>
<tr>
<td>Taguchi et al. (2008) [65]</td>
<td>60</td>
<td>100</td>
<td>Interobserver agreement, weighted kappa values &gt; 0.6 for 36 (60%)</td>
</tr>
</tbody>
</table>

GDPs: general dental practitioners.

### Table 2  Relationship between cortical width of the mandible and skeletal bone mineral density (BMD).

<table>
<thead>
<tr>
<th>Authors (year) [Ref.]</th>
<th>Number of subjects</th>
<th>Sites of BMD assessment</th>
<th>BMD equipments</th>
<th>Significant correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taguchi et al. (1994) [38]</td>
<td>44 postmenopausal Japanese women</td>
<td>Lumbar spine</td>
<td>QCT</td>
<td>Yes (r = 0.48)</td>
</tr>
<tr>
<td>Klemetti et al. (1994) [38]</td>
<td>353 postmenopausal Finnish women</td>
<td>Lumbar spine</td>
<td>QCT</td>
<td>Yes</td>
</tr>
<tr>
<td>Taguchi et al. (1996) [46]</td>
<td>29 pre- and 95 postmenopausal Japanese women</td>
<td>Lumbar spine</td>
<td>QCT</td>
<td>Yes (Kendall’s tau = 0.36)</td>
</tr>
<tr>
<td>Devlin and Horner (2002) [34]</td>
<td>74 postmenopausal British women</td>
<td>Lumbar spine</td>
<td>DXA</td>
<td>Yes (r = 0.52)</td>
</tr>
<tr>
<td>Drozdzowska et al. (2002) [35]</td>
<td>30 postmenopausal edentulous Polish women</td>
<td>Hip, calcaneus, hand phalanges</td>
<td>DXA, QUS</td>
<td>No</td>
</tr>
<tr>
<td>Yasar and Akgünül (2006) [43]</td>
<td>48 postmenopausal Turkish women</td>
<td>Lumbar spine</td>
<td>DXA</td>
<td>No</td>
</tr>
<tr>
<td>Vlasiadis et al. (2007) [44]</td>
<td>133 postmenopausal Greek women</td>
<td>Lumbar spine</td>
<td>DXA</td>
<td>Yes</td>
</tr>
<tr>
<td>Taguchi et al. (2007) [57]</td>
<td>450 postmenopausal Japanese women</td>
<td>Lumbar spine</td>
<td>DXA</td>
<td>Yes (r = 0.44)</td>
</tr>
<tr>
<td>Devlin et al. (2007) [60]</td>
<td>671 postmenopausal European women</td>
<td>Lumbar spine, hip</td>
<td>DXA</td>
<td>Yes</td>
</tr>
<tr>
<td>Okabe et al. (2008) [62]</td>
<td>659 Japanese men and women</td>
<td>Heel</td>
<td>QUS</td>
<td>Yes (r = 0.44)</td>
</tr>
</tbody>
</table>

QCT: quantitative computed tomography; DXA: dual energy X-ray absorptiometry; QUS: quantitative ultrasound.
Devlin and Horner reported that the MCW was significantly correlated with the BMD T-score at the lumbar vertebrae ($r = 0.52, P < 0.01$) in 74 postmenopausal British women aged 43–79 years (mean age, 62 years) [34]. Okabe et al. also reported the significant correlation between the MCW and heel bone density measured by ultrasound ($r = 0.44, P < 0.001$) in 659 Japanese subjects (262 men and 397 women) [62]. Yaşar and Akgünlu found no significant association between the MCW and spine BMD measured by DXA in 48 postmenopausal Turkish women aged 40–64 years, although a marginally significant relation was noted on binary regression analysis [43]. Drozdowska et al. also failed to find a significant association between the MCW and hip BMD and ultrasound measurements of calcaneus and hand phalanges in 30 healthy postmenopausal edentulous Polish women aged from 48 to 71 years old (mean age, 59 years) [35]. The small sample sizes may have contributed to the lack of significant associations in these two studies.

In our recent study in 450 postmenopausal Japanese women (mean age, 57 years), spine BMD measured by DXA was significantly correlated with the MCW ($r = 0.44, P < 0.001$) [57]. The adjusted odds ratios for low spine BMD (T-score $\leq -1.0$) associated with the second, third and lowermost quartiles of cortical width were 1.71, 2.30 and 5.43, respectively, compared to the uppermost quartile. The odds ratios for osteoporosis according to cortical width category were similar to those for low BMD. In this study, the lowermost quartile was below 2.9 mm (corrected for vertical magnification error). In our other study of 157 healthy younger postmenopausal women less than 65 years old, the respective likelihood ratios for identifying women with low BMD (at the spine or proximal femur) and osteoporosis were 13.90 and 6.40 for thin cortical width (<3.0 mm) [54]. Devlin et al. reported that for three observers, a MCW of <3 mm (corrected for magnification error) provided diagnostic odds ratios of 6.51, 6.09 and 8.04 in screening of osteoporosis in 671 postmenopausal European women aged 45–70 years old. They concluded that only dental patients with a thinner MCW (i.e., <3 mm) should be referred for further osteoporosis investigation [60]. Considering the results of our Japanese studies and their European study, asymptomatic dental patients with a MCW of less than about 3 mm may be candidates for DXA measurement.

### 3.2. Cortical shape of the mandible and skeletal BMD

Since Klemetti et al. [38] proposed MCI classification on panoramic radiographs, some studies have reported significant associations between MCI and skeletal BMD in postmenopausal women as well as elderly men [29,35,43,44,46,51–54,57,61,62,65,71–75] (Table 3). In our previous study, the sensitivity and specificity for identifying spine osteoporosis by MCI were 86.8% and 63.6%, respectively, in 159 healthy postmenopausal Japanese women and 80.0% and 64.1%, respectively, in 157 postmenopausal Japanese women with histories of hysterectomy, oophorectomy or oestrogen use [53]. In this study, women with eroded cortex (mild to moderate and severe) were considered to have an increased likelihood of spinal osteoporosis. The area under the ROC curves in identifying women with osteoporosis by MCI was 0.771 in the former group. In another study of 158 healthy postmenopausal Japanese women younger than 65 years old, the sensitivity and specificity in identifying those with osteoporosis were 86.7% and 65.6%, respectively [54]. This diagnostic performance was better than simple decision rules, such as OST, used in clinical practice.

However, in a European multicentre study (OSTEODENT project), Horner et al. concluded that the MCI has limited value for diagnosing osteoporosis [61]. In their study, in which five observers participated, the sensitivity and specificity for identifying osteoporosis at any one of the three skeletal sites (total hip, femoral neck and lumbar spine) by MCI were 87.2–95.0% and 7.8–35.4%, respectively, in 653 postmenopausal European women when those with an eroded cortex (mild to moderate and severe) were considered to have an increased probability of osteoporosis. In addition, the sensitivity and specificity for identifying osteoporosis at any one of the three skeletal sites by MCI were 19.1–24.8% and 91.2–93.2%, respectively, when women with only a severely eroded cortex were considered to have an increased probability of osteoporosis. Their diagnostic performances were relatively low compared to those in our study. In the OSTEODENT project, the weighted kappa statistics for intraobserver agreement were <0.4 in three of five observers (0.30, 0.33 and 0.15), suggesting that the low levels of intraobserver agreement may have contributed to the low diagnostic ability. The sensitivity and specificity in the original paper by Klemetti et al. were 16% and 96%, respectively [38], which were similar to the results of the OSTEODENT project; however, Klemetti et al. [38] did not use the osteoporosis definition based on the WHO classification but the original Finnish osteoporosis definition. Horner et al. recommended a combination of the simple clinical risk index, OSIRIS, with the MCI to increase the diagnostic performance in identifying postmenopausal women in dental clinics [61]; however, the main work of GDPs is dental practice and not triage osteoporosis screening and thus this combination would not be acceptable in general dental practice.

Horner et al. also recommended that women with only severely eroded cortex should be screened in dental clinics because of the high specificity and high likelihood ratio for a positive risk result [61]. Halling et al. also mentioned that low sensitivity and high specificity were necessary in triage screening for osteoporosis in dental clinics [72]. Moreover, whether we should use only severely eroded cortex or both mildly to moderately and severely eroded cortices to detect osteoporosis risk remains controversial in clinical dental practice. Given the high sensitivity of the latter, we can identify most postmenopausal women at risk for osteoporosis, whereas we may also identify many postmenopausal women who do not require DXA (false-positive fraction). This false-positive fraction would likely lead to unnecessary medical costs for BMD examinations. In the case of high specificity (low sensitivity), however, a small false-positive fraction rate would ensure minimal unnecessary medical costs but would also not identify a large proportion of women at risk for osteoporosis. The treatments related to osteoporotic fractures in these undetected women at risk for osteoporosis may also lead to higher medical costs. Several simple clinical decision rules for osteoporosis recommend high sensitivity (approximately 90%) to identify most women at risk for osteoporosis who would be candidates for further testing with DXA. This may result in the reduction of osteoporotic...
fractures, related medical costs and the subsequent high mortality rate. Both approaches may be valid, but the approach implemented would likely be influenced by local health care facilities (availability of DXA) and regional/national guidelines on therapeutic intervention.

### 3.3. Cortical indices of the mandible and bone quality

Although the definition of bone quality remains controversial, it is thought to encompass both structural and material properties of bone. The proposed determinants of the material properties of bone are the degree of secondary mineralisation, accumulation of microdamage and collagen cross-link formation that is affected by the bone turnover rate. Biochemical markers of bone turnover, such as serum bone-specific alkaline phosphatase (BAP) and serum or urinary N-telopeptide cross-links of type I collagen (NTx), corrected for creatinine, are widely and easily used to estimate the degree of bone turnover rate in the medical field. Postmenopausal women with a high bone turnover rate have an increased risk of osteoporosis and/or subsequent osteoporotic fractures [76]. Demonstrating a significant association between biochemical markers of bone turnover and cortical indices of the mandible on panoramic radiographs would provide important insight regarding whether cortical indices of the mandible on panoramic radiography indices may be useful in identifying individuals, especially postmenopausal women, with an increased probability of osteoporosis.

We first reported the significant association between serum total alkaline phosphatase (ALP) and urinary NTx and MCI on panoramic radiographs in 82 postmenopausal Japanese women aged 46—68 years [53]. Mandibular cortical erosion was significantly associated with increased NTx

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**Table 3** Diagnostic efficacy in identifying individuals with osteoporosis by cortical shape (cortical erosion) of the mandible.

<table>
<thead>
<tr>
<th>Authors (year) [Ref.]</th>
<th>Number of subjects</th>
<th>Sites of BMD assessment</th>
<th>BMD equipments</th>
<th>Diagnostic efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Klemetti et al. (1994) [38]</td>
<td>353 postmenopausal Finnish women</td>
<td>Lumbar spine</td>
<td>QCT</td>
<td>Sensitivity 16%, specificity 96%</td>
</tr>
<tr>
<td>Taguchi et al. (1996) [46]</td>
<td>29 pre- and 95 postmenopausal Japanese women</td>
<td>Lumbar spine</td>
<td>QCT</td>
<td>Correlation with BMD Kendall’s tau = −0.49 (P &lt; 0.001)</td>
</tr>
<tr>
<td>Drozdzowska et al. (2002) [35]</td>
<td>30 postmenopausal edentulous Polish women</td>
<td>Hip, calcaneus, hand phalanges</td>
<td>DXA, QUS</td>
<td>Sensitivity 93%, specificity 31%</td>
</tr>
<tr>
<td>Nakamoto et al. (2003) [71]</td>
<td>100 postmenopausal Japanese women</td>
<td>Lumbar spine, femur</td>
<td>DXA</td>
<td>Sensitivity 77%, specificity 38%</td>
</tr>
<tr>
<td>Taguchi et al. (2004) [53]</td>
<td>316 postmenopausal Japanese women</td>
<td>Lumbar spine</td>
<td>DXA</td>
<td>Sensitivity 80—87%, specificity 64%</td>
</tr>
<tr>
<td>Halling et al. (2005) [72]</td>
<td>211 elderly men and women</td>
<td>Heel</td>
<td>DXA</td>
<td>Sensitivity 99%, specificity 8% or sensitivity 50%, specificity 89%</td>
</tr>
<tr>
<td>White et al. (2005) [29]</td>
<td>200 postmenopausal Japanese women</td>
<td>Hip</td>
<td>DXA</td>
<td>83% of women with low BMD were identified</td>
</tr>
<tr>
<td>Yaşar and Akgünlu (2006) [43]</td>
<td>48 postmenopausal Turkish women</td>
<td>Lumbar spine</td>
<td>DXA</td>
<td>Sensitivity 96%, specificity 38%</td>
</tr>
<tr>
<td>Taguchi et al. (2006) [54]</td>
<td>158 postmenopausal Japanese women younger than 65 years</td>
<td>Lumbar spine, hip</td>
<td>DXA</td>
<td>Sensitivity 87%, specificity 66%</td>
</tr>
<tr>
<td>Sutthiprapaporn et al. (2006) [73]</td>
<td>100 postmenopausal Japanese women</td>
<td>Lumbar spine, hip</td>
<td>DXA</td>
<td>Sensitivity 73%, specificity 49%</td>
</tr>
<tr>
<td>Vlasiadis et al. (2007) [44]</td>
<td>133 postmenopausal Greek women</td>
<td>Lumbar spine</td>
<td>DXA</td>
<td>No described</td>
</tr>
<tr>
<td>Taguchi et al. (2007) [57]</td>
<td>450 postmenopausal Japanese women</td>
<td>Lumbar spine</td>
<td>DXA</td>
<td>Odds ratio 4.73—14.73</td>
</tr>
<tr>
<td>Horner et al. (2007) [61]</td>
<td>671 postmenopausal European women</td>
<td>Lumbar spine, hip</td>
<td>DXA</td>
<td>Sensitivity 87—95%, specificity 8—35% or sensitivity 19—25%, specificity 91—93%</td>
</tr>
<tr>
<td>Okabe et al. (2008) [62]</td>
<td>659 Japanese men and women</td>
<td>Heel</td>
<td>QUS</td>
<td>Correlation with BMD r = 0.231 (P &lt; 0.001)</td>
</tr>
<tr>
<td>Taguchi et al. (2008) [65]</td>
<td>100 postmenopausal Japanese women</td>
<td>Lumbar spine, hip</td>
<td>DXA</td>
<td>Sensitivity 83%, specificity 43%</td>
</tr>
</tbody>
</table>

QCT: quantitative computed tomography; DXA: dual energy X-ray absorptiometry; QUS: quantitative ultrasound.
needed to clarify the true associations between them. turnover, further investigations in larger populations are examined the association between cortical indices on eroded cortex [78]. As only three studies to date have found a significant association between increased ALP level increased risk of osteoporosis. In contrast, Vlasiadis et al. radiographs have a high bone turnover rate, resulting in an increased risk of osteoporosis. In contrast, Vlasiadis et al. found a significant association between increased ALP level and likelihood of eroded cortex in 141 postmenopausal white women 38–81 years of age but not between urinary NTx and eroded cortex [78]. As only three studies to date have examined the association between cortical indices on panoramic radiographs and biochemical markers of bone turnover, further investigations in larger populations are needed to clarify the true associations between them.

3.4. Cortical indices of the mandible and risk of osteoporotic fractures

Cortical indices of the mandible (the MCW and MCI) on panoramic radiographs may indeed be associated with osteoporosis status based on skeletal BMD assessment (T-score ≤ −2.5) and increased high bone turnover rate measured by biochemical markers of bone turnover; however, whether individuals with an eroded cortex and/or thinned cortex of the mandible on panoramic radiographs have an increased future risk of osteoporotic fractures remains unclear. In a large cohort study named NORA, which was conducted by Siris et al. using peripheral measurement devices, 82% of postmenopausal women with fractures had T-scores better than −2.5 [79]. The possibility exists that women identified by cortical indices of the mandible on panoramic radiographs and referred to medical professionals for further investigations do not have an increased probability of having future osteoporotic fractures.

In 2000, we first reported the association between cortical indices of the mandible detected on panoramic radiographs and self-reported osteoporotic fracture status in a well designed case–control study conducted in Washington State in the United States [28]. Four hundred and eighty-seven individuals more than 60 years old participated in this study with informed consent. Of these participants, 56.9% were postmenopausal women. Cases (n = 93) were individuals reporting osteoporotic fractures (fractures occurring after minor impact). Controls (n = 394) were individuals reporting traumatic fractures (n = 105) or no fractures (n = 289). In this study, the adjusted odds ratios for osteoporotic fractures associated with moderately eroded and severely eroded mandibular cortices were 2.0 and 8.0, respectively. After adjusting for all potentially confounding factors, the MCW was 0.54 mm (or 12%) thinner in subjects with an osteoporotic fracture compared to controls (95% CI, 0.25–0.84 mm). Persson et al. also found a significant association between the MCI and self-reported history of osteoporosis in 1084 subjects aged 60–75 years (mean age, 67.6 years) [80]. The likelihood of an association between osteoporosis and the MCI was 2.6.

The diagnostic efficacy in identifying women with osteoporosis based on skeletal BMD assessment is similar in both simple screening tools such as OST and cortical indices of the mandible detected on panoramic radiographs; however, our recent study suggested that the MCI detected on panoramic radiographs had better diagnostic performance than OST in identifying women with both a low skeletal BMD and high bone turnover rate [75]. As women with both low BMD and high bone turnover rate have a higher probability of future risk of osteoporotic fractures, the MCI may be a useful indicator in identifying women with higher risk of osteoporotic fractures than simple screening tools, such as the OST index.

Okabe et al. performed a longitudinal study in 262 Japanese men and 397 Japanese women aged 80 years old and reported that cortical measurements on panoramic radiographs were not significantly associated with the occurrence of fractures within 5 years after baseline examination [62]. However, their results should be analysed and interpreted with caution. First, they did not evaluate the occurrence of spine fractures by lateral X-ray examination. In our recent clinical trial, a considerably higher percentage (20.5%) of women who were screened based on the MCI on panoramic radiographs had spine fractures that were not diagnosed previously [81]. Second, individuals with osteoporotic fractures may have died before they reached the age of 80 years because osteoporotic fractures are strongly associated with mortality rate. Sampling bias may influence their negative results. Further longitudinal studies in large numbers of individuals aged 50 years or older are necessary to determine conclusively whether cortical indices are useful in identifying individuals with an increased probability of future osteoporotic fractures.

4. Computer-assisted diagnosis system on digital panoramic radiography

Digital panoramic radiography has recently been developed and is now used worldwide. In Japan, about 20% of GDPs have changed their panoramic radiography unit to a digital system. Most GDPs are expected to use digital systems because they are filmless and cost-effective. Although the basic concept of triage screening for osteoporosis in dental clinics is to avoid using special equipment for screening, computer-assisted diagnosis (CAD) systems would be helpful in determining the cortical indices of the mandible on digital panoramic radiography.

In 2003, we developed a CAD system to determine the MCI on panoramic radiographs (Japanese patent no. 3964795) [74]. In this system, normal and eroded cortices are automatically distinguished by setting a rectangular region of interest (ROI) on digitised panoramic radiographs. When using this CAD system, the sensitivity and specificity for identifying women with low skeletal BMD (T-score ≤ −1.0) were 76.8% and 61.1%, respectively. The respective values for identifying women with osteoporosis (T-score ≤ −2.5) were 94.4% and 43.8%, respectively. Consequently, in 2004, we developed an additional new CAD system in which we can easily measure the MCW on digitised panoramic...
radiographs by assigning the mental foramen of the mandible [55]. In this CAD system, sensitivity and specificity for identifying postmenopausal women with spinal osteoporosis were about 88.0% and 58.7%, respectively. Those for identifying postmenopausal women with femoral osteoporosis were about 87.5% and 56.3%, respectively. Finally, we developed an advanced CAD system by combining both the MCW and MCI with a neural network [82]. In this system, the sensitivity and specificity for identifying postmenopausal women with osteoporosis were 91.7–100% and about 61.8–68.7%, respectively.

In the OSTEODENT project, Devlin et al. had also developed a CAD system in which they could easily measure the MCW on digitised panoramic radiographs [59]. For the diagnosis of osteoporosis at the femoral neck, the MCW derived from the manually initialised fit gave an area under the ROC curve $[A(z)] = 0.805$. GDPs may be able to apply CAD systems for identifying individuals with osteoporosis on digital panoramic radiography in the near future.

5. Prospective clinical trials in screening for osteoporosis in dental clinics

Many investigations have been performed regarding cortical indices of the mandible and skeletal BMD or osteoporosis. However, most of these studies were “experimental” and not “practical”. Observers who should use cortical indices such as the MCW and MCI are GDPs and not investigators in universities or other institutions. To date, only two prospective studies in Japan have used clinical trials to clarify how many patients with undetected low BMD or osteoporosis are identified in general dental practice by GDPs using their own panoramic radiographs.

In the study of the Hiroshima Dental Association in Japan, of 453 women aged 50 years and older who visited the dental clinics of 22 trained GDPs and had panoramic radiographic assessment for examination of dental diseases, 168 postmenopausal women were diagnosed as having low skeletal BMD based on the MCI. Of these women, 39 aged 50–84 years (mean age, 64.8 years) with no previous diagnosis of osteoporosis participated in this study. These women had BMD assessment at the lumbar spine and femoral neck using DXA. Spine fractures were assessed on lateral radiographs obtained at the time of DXA assessment. Of these women, 2 (5.1%) had normal BMD (BMD T-score $> -1.0$), 21 (53.9%) had osteopenia (BMD T-score $-2.5$ to $-1.0$) and 16 (41.0%) had osteoporosis (BMD T-score $< -2.5$) [81]. Eight women (20.5%) had fractures at the thoracic spine, lumbar spine or both. This study suggested that most women with low skeletal BMD as well as undiagnosed spine fractures may be identified by GDPs using the MCI on panoramic radiographs. In a study by the Aichi Dental Association in Japan, about 123 (95%) of 130 women who were identified by trained GDPs in their clinics had osteopenia (24%) or osteoporosis (71%) [83]. Investigators in the Aichi Dental Association recommend that women with a severely eroded cortex should be identified and referred to medical professionals for further investigation.

In these prospective clinical trials, the question arose regarding whether the prevalence rates of osteopenia and osteoporosis were similar between postmenopausal women who were and were not diagnosed as having low BMD based on identification of cortical erosion by GDPs. Prior to the study by the Hiroshima Dental Association, a pilot study including 61 women aged 50 years and older (mean age, 62.8 years) was conducted [84]. In this study, only 2 (9%) of 22 women who were not diagnosed as having low skeletal BMD based on cortical erosion findings by 14 trained GDPs in their clinics had osteoporosis, whereas 14 (36%) of 39 women who were diagnosed as having low BMD had osteoporosis. This pilot study indicated a significant difference in the prevalence rates of osteopenia or osteoporosis between postmenopausal women who were and were not diagnosed by GDPs based on the panoramic radiography index.

For GDPs to undergo training with regard to reading of cortical indices of the mandible on panoramic radiographs and understanding the concept of screening for osteoporosis would be very difficult in dental clinics. We have already constructed a self-learning system via a website to allow GDPs to learn how to use panoramic radiography indices in triage screening of osteoporosis and take training about the reading of cortical indices, especially the MCI (unpublished data). Further clinical trials in Japan as well as other counties are necessary to determine whether women diagnosed by trained GDPs using panoramic radiography indices have an increased probability of osteopenia or osteoporosis as well as undetected spinal fractures.

6. Conclusions

Cortical indices of the mandible, such as the MCW and MCI, are associated with BMD of the general skeleton, biochemical markers of bone turnover and risk of osteoporotic fracture. Evidence is still accumulating worldwide, but one can reasonably postulate that panoramic radiography indices may be useful triage screening tools for identifying individuals with underdiagnosed low skeletal BMD, osteoporosis and increased probability of osteoporotic fracture. However, several important problems still remain to be resolved. To promote evidence-based clinical dental practice, further worldwide investigations are required to determine whether panoramic radiography indices are useful tools for triaging individuals with osteoporosis and referring them to medical professionals for further investigation. After this basic confirmation, I would like to recommend the following two future researches. First is to clarify whether trained GDPs worldwide can accurately identify individuals with osteoporosis in their own clinics by panoramic radiographs and refer them to medical professionals. Second is to determine whether this intervention actually contribute to reduced rates of osteoporotic fractures. Randomized controlled trial would be necessary to evaluate the difference in rates of osteoporotic fractures between intervention and non-intervention groups in future.

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References


[43] Horner K, Devlin H. The relationships between two indices of mandibular bone quality and bone mineral density measured by
Osteoporosis and panoramic radiographs


