RHEUMATOLOGY

doi:10.1093/rheumatology/keu280
Advance Access publication 4 August 2014

Original article

A comparative study of diagnostic and imaging techniques for osteoarthritis of the trapezium

Arianna B. Lovati[1], Alessandro Pozzi[2], Matilde Bongio[3], Camilla Recordati[4], Gianfranco Berzero[2] and Matteo Moretti[1]

Abstract

Objectives. The aims of this study were to determine whether micro-CT is a reliable investigation method to evaluate the severity of OA in the trapezium and to develop a novel micro-CT scoring system based on a quantitative assessment of the subchondral bone thickness in order to better assess OA through an objective parameter.

Methods. We compared different diagnostic and imaging techniques performed consecutively on each sample: X-ray, visual analysis, micro-CT and histology. OA and healthy trapezia were subjected to semi-quantitative and quantitative analyses to be classified in four degrees of severity in OA (control, OA-2, OA-3 and OA-4). Specifically, samples were analysed using Dell's score for X-ray, Brown's score for visual analysis and Mankin's score for histology. Micro-CT was scored using a novel quantitative scoring system based on subchondral bone thickness measurements. Results obtained with each technique were then compared and correlated.

Results. X-ray analysis showed a higher frequency of OA-2 (27%) and OA-3 (32%) compared with OA-4 (5%), whereas visual analysis, micro-CT and histology showed a lower percentage for OA-2 (18%, 18% and 14%) and OA-3 (23%) and increased frequency for OA-4 (45%, 32% and 40%). Only the micro-CT score of subchondral bone thickness correlated significantly with all the other techniques ($P < 0.05$).

Conclusion. This is the first comparison of techniques proposing a novel scoring system based on objective and quantitative micro-CT data that can be applied as a useful diagnostic tool for OA, providing a deeper comprehension of the pathophysiology of OA in trapezium.

Key words: trapezium, osteoarthritis, comparative diagnostic analyses, X-ray, micro-CT, subchondral bone thickness, stereomicroscopy, histology.

CLINICAL SCIENCE

Introduction

OA of the trapeziometacarpal joint (TMJ-OA) is a disabling condition occurring in women (20%) and men (6%) >45 years old [1, 2]. Compressive forces and repetitive loading of the thumb produce mechanical stress and factor release leading to cartilage degeneration and subchondral bone sclerosis [3–8].

Radiography is the gold standard in evaluating TMJ-OA severity and progression [9] by grading through approved radiographic scores [10, 11]. Although X-ray is a non-invasive and non-destructive technique, it offers incomplete details on subchondral bone defects [12]. The radiographic findings correlate poorly with patient discomfort and pain perception [13]. Studies have compared X-ray with other diagnostic methods—stereomicroscopy [14, 15], histology [16] and micro-CT [17]—to gain a deeper insight into the anatomy and pathophysiology of OA and bone damage. Stereomicroscopy and histology are invasive destructive techniques that, like X-ray, depend upon the evaluation of examiners using scoring systems [15, 18]. On the other hand, micro-CT is a non-invasive whole-volume imaging technique that provides high

[1]Cell and Tissue Engineering Laboratory, [2]Hand Surgery Unit, IRCCS Galeazzi Orthopaedic Institute, [3]Cell and Tissue Engineering Laboratory, Gruppo Ospedaliero San Donato Foundation and [4]Mouse and Animal Pathology Laboratory (MAP Lab), Filarete Foundation, Milan, Italy.

Submitted 15 November 2013; revised version accepted 22 May 2014.

Correspondence to: Matteo Moretti, Cell and Tissue Engineering Laboratory, IRCCS Galeazzi Orthopaedic Institute, Via R. Galeazzi 4, 20161 Milan, Italy. E-mail: matteo.moretti@grupposandonato.it

Alessandro Pozzi and Matilde Bongio contributed equally to this work.

contrast between bone and soft tissue and produces quantitative data on bone stereology [19, 20], morphology and microarchitecture [20, 21] thanks to high spatial resolution and multiplanar capacity [22]. Recently efforts have been made to translate the micro-CT application from *in vitro* to an emerging clinical tool for *in vivo* studies [23–26]. Nevertheless, a micro-CT grading system to score trapezium OA has not yet been proposed.

The aim of our study was to determine whether micro-CT could be regarded as a comprehensive and reliable approach to quantifying OA severity. Thus we compared a micro-CT-based scoring system with commonly used semi-quantitative, examiner-dependent scoring systems for X-ray, visual analysis and histology. This is the first scientific report that proposes a novel micro-CT-based quantitative scoring system to grade trapezium OA, providing a deeper comprehension of its pathophysiology by comparing different diagnostic techniques.

Methods

Sample retrieval

With the approval of the institutional review board (IRCCS Galeazzi Orthopaedic Institute, Scientific Technical Committee), trapezia were isolated *en bloc* through a dorsal approach from OA patients undergoing prosthetic implant following written informed consent. Nineteen OA samples (OA groups) were harvested from 6 men [mean age 64.7 years (S.D. 6.9)] and 13 women [mean age 66.5 years (S.D. 11)]. Three non-OA trapezia (control group) were explanted from female cadavers [mean age 75.0 years (S.D. 5)] and processed at the University of Nantes (Nantes, France) according to local institutional ethical and practical protocols.

Study design

Samples were analysed by X-ray, visual analysis, micro-CT and histology, considering their advantages, disadvantages and limitations (see supplementary Table S1, available at *Rheumatology* Online). For each evaluation we defined three equal anatomical compartments within the specimens—ulnar, middle and radial—then assessed them using standard scoring systems specific for each technique. Each specimen was classified as one of four OA degrees—CTR (control), OA-2, OA-3 and OA-4—depending on the average of the two compartments with the highest values.

Conventional X-ray analysis

Conventional radiographs (45 kV, 4 mA; Bucky Diagnost CS, Philips, Amsterdam, The Netherlands) included posterior–anterior views of 14 OA patients' hands. No controls were evaluated radiographically because of their cadaveric origin. The X-ray staging of OA in the TMJ was performed by three examiners according to Dell's scoring system [11] (see supplementary Table S2, available at *Rheumatology* Online) based on joint narrowing, subluxation severity and osteophyte formation.

Visual analysis

Nineteen trapezia were examined by visual analysis using a stereomicroscope (SZX10, Olympus, Tokyo, Japan) equipped with a digital camera (DS-Fi1 5 M pixel, Nikon, Tokyo, Japan). The ulnar, middle and radial compartments were analysed by three examiners using Brown's scoring system [15] to stage the degree of cartilage degeneration.

Micro-CT analysis

Nineteen trapezia were scanned by an Explore Locus micro-CT scanner (GE Healthcare, Pewaukee, WI, USA). A micro-CT higher-resolution (Bin-1) protocol was performed (80 kV, 450 μA, 1600 ms exposure time, 400 projections over 270°). The isotropic resolution was 27 μm with a voxel size of 0.021 × 0.021 × 0.021 mm. The bone surface structure was examined after the three-dimensional (3D) image reconstruction using MicroView software version 2.1.2 (GE Healthcare), then quantified. Phantom calibration was performed for each scan to define the optimal threshold for bone, then an isosurface volume rendering function was applied. A histogram depicting the voxel distribution along the density scale expressed in Hounsfield units was computed. To classify each specimen into one of the four OA degrees, a new scoring system was developed according to the subchondral bone thickness. Eight lines (four lines on the coronal plane, four lines on the sagittal plane) were drawn through the subchondral thickness of each compartment (Fig. 1A). The measurement of the thickness was divided into four grading groups: CTR, 0–0.50 mm; OA-2, 0.50–1 mm; OA-3, 1–1.50 mm and OA-4, >1.50 mm. Next, three volumes of interest (VOIs) (2 × 1 × 1 mm) were defined within the subchondral bone of all compartments (Fig. 1B). Bone volume fraction (BV/TV), trabecular number (Tb.N), trabecular thickness (Tb.Th) and trabecular spacing (Tb.Sp) were quantified for each selected VOI.

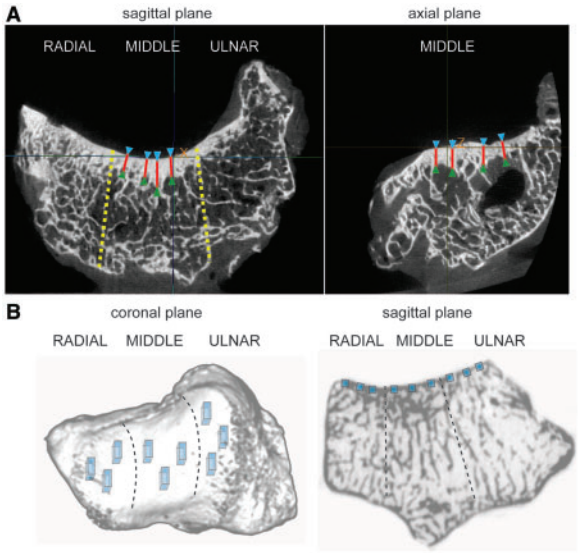
Histological analyses

Nineteen trapezia were fixed in 10% formalin and decalcified in EDTA 10% w/v. Sagittal sections of 5 μm from the radial to the ulnar compartment were obtained, embedded in paraffin and stained with haematoxylin and eosin (H&E) and safranin O–fast green. Samples were scored for the ulnar, middle and radial compartments by two examiners according to Mankin's grading system [18]. Grading was based on the aspect of cartilage (score 0–6), chondrocytes (0–3), proteoglycan content (0–4) and tidemark integrity (0–1). The total Mankin's score (range 0–14) of each sample was divided into four grades [27]. CTR included a score from 0 to 3 (normal cartilage), OA-2 from 3 to 7 (mild degeneration), OA-3 from 8 to 12 (moderate degeneration) and OA-4 from 13 to 14 (severe degeneration).

Statistical analysis

Statistical analyses between groups and compartments were performed with GraphPad Instat version 3.06 (GraphPad Software, La Jolla, CA, USA) using two- and one-way analysis of variance, respectively. For multiple

Fig. 1 Micro-CT analysis



(**A**) Representative micro-CT sections of trapezium. Four lines were designed on the sagittal and axial planes through the subchondral bone thickness of the three compartments (separated by dotted lines). (**B**) Schematic illustration of the three $2 \times 1 \times 1$ mm VOIs (boxes) within the TM articular surface of the ulnar, middle and radial compartments (divided by dotted lines) on the coronal and sagittal planes. VOI: volume of interest; TM: trapeziometacarpal.

comparisons, Bonferroni's *post hoc* test was performed. The mean (S.D.) and 95% CI were calculated and $P < 0.05$ was considered significant. The interrater reliability of the examiners' scores for each technique was calculated with intraclass correlation coefficient (ICC): ICC = 1, perfect reliability; ICC > 0.75, excellent reliability [28]. The Pearson correlation coefficient (two-tailed test) was calculated to determine the correlation between the results obtained from X-ray, visual analysis, micro-CT and histology. The significant level was set at $\alpha = 0.05$.

Results

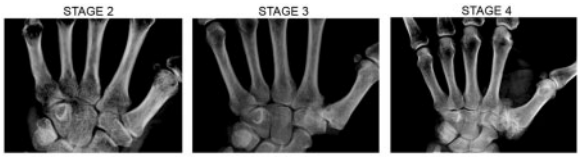
X-ray analysis

The Dell score system detected a narrowed TMJ space and moderate osteophytosis (stage 2) in 43% of OA patients; a mild trapezium subchondral sclerosis, osteophytes and TMJ subluxation greater than one-third of the joint space (stage 3) in 50% and a pantrapezium OA with complete destruction of the joint space, bone loss, early ankylosis and osteophytes, marked subluxation of the TMJ and a compensatory hyperextension of the interphalangeal joint (stage 4) in 7% (Fig. 2).

Visual analysis

For the Brown's score, 14% of trapezia presented a smooth and shiny cartilage on the TM articular surface

Fig. 2 X-ray scoring



Representative panel of preoperative anteroposterior X-ray views of the hand and TMJ classified according to Dell's scoring system. TMJ: trapeziometacarpal joint.

(stage 1); 18% exhibited early signs of cartilage degeneration as mild fibrillation and focal erosions (stage 2); 23% showed advanced cartilage degeneration with partial subchondral bone exposition and fissures (stage 3) and 45% showed marked cartilage degeneration with subchondral cysts, bone eburnation and osteophytes marginally to the radial and ulnar compartments (stage 4) (Fig. 3A). The progressive subchondral bone eburnation was centrally located in the middle compartment coupled with centrifugal cartilage degeneration and subchondral bone exposition. The residual cartilage was irregular and located in the dorsal area of the trapezium bones. In stage 4, the presence of subchondral bone cysts represents a typical sign of severe OA.

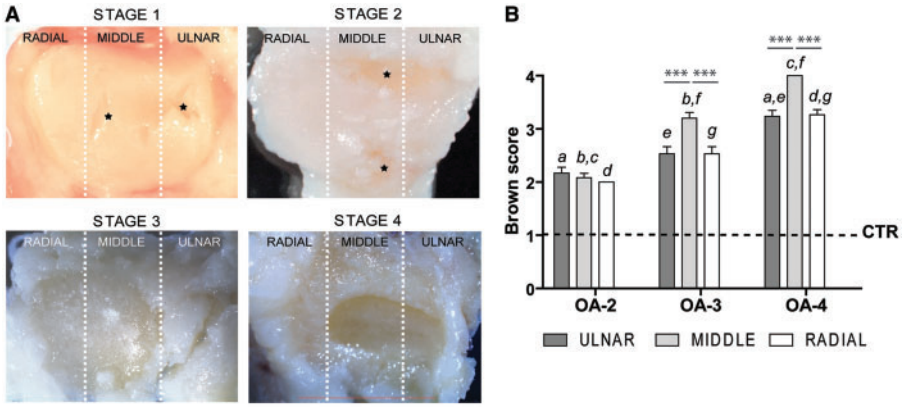
Semi-quantitative evaluation of visual analysis of the proximal articular surface of the trapezia showed that all compartments had a progressive increase in cartilage degeneration from OA-2 to OA-4 (Fig. 3B). All degenerative stages showed a highly significant difference compared with CTR ($P < 0.001$). No differences between regions were detected in OA-2. In OA-3 and OA-4, the middle compartment significantly increased compared with both the ulnar ($P = 0.0001$, $P = 2.3E-07$) and radial ($P = 0.0001$, $P = 5.0E-07$) compartments.

Micro-CT analysis

Fig. 4A shows a 3D reconstruction of a control and OA trapezium. The volumetric rendering revealed a smooth and biconcave–convex saddle-shaped articular surface for the control. OA trapezium showed a complete loss of the saddle shape with irregularities of the subchondral bone and exposition of the trabecular bone in the articular surface.

An overall increasing trend of the subchondral bone thickness was observed from CTR to OA-4 in all compartments, with a preference for the radial (Fig. 4B). OA-2 (16%) did not show a difference with CTR (16%). OA-3 (47%) differed from CTR with respect to the ulnar (95% CI −1.35, −0.08, $P < 0.05$) and radial (95% CI −1.64, −0.16, $P < 0.01$) compartments. OA-4 (21%) differed from CTR with respect to the ulnar (95% CI −1.80, −0.35) and radial (95% CI −2.14, −0.50) compartments for $P < 0.001$ and with respect to the middle for $P < 0.05$ (95% CI −1.52, −0.07). The ulnar and radial compartments in OA-4 differed significantly from the respective compartments in OA-2 for $P < 0.05$ (95% CI −1.53,

Fig. 3 Stereomicroscopic visual analysis



(**A**) Stereomicroscopic visual analysis of representative trapezia for the four stages according to Brown's scoring system. Stars indicate cartilage damage caused by the harvest procedure. (**B**) Quantitative evaluation of visual analysis. The histogram shows the Brown's score for all compartments in OA-2, OA-3 and OA-4. Statistical significance for $P < 0.001$ in OA groups *vs* controls (CTR) (black dotted line), among different OA groups (a–g) and compartments (***).

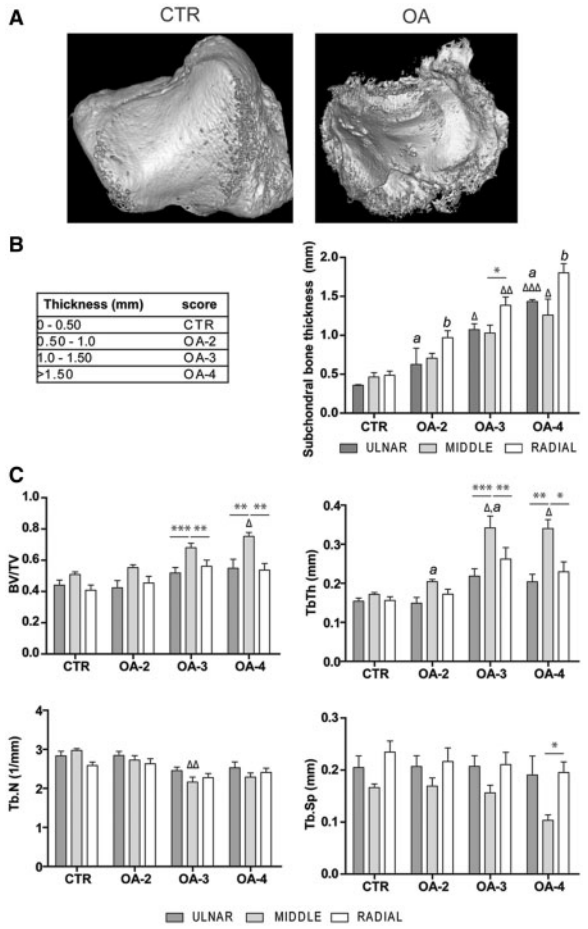
−0.08 and −1.65, −0.01, respectively). Regarding the comparison between compartments within the same score, no statistical difference was detected in CTR and OA-2. In OA-3 the radial compartment showed a significant increase compared with the middle ($P = 0.02$). Fig. 4C shows the stereological parameters. An increasing trend of BV/TV among grades was observed for the middle compartment, although only OA-4 differed significantly from CTR (95% CI −0.48, −0.01, $P < 0.05$). CTR and OA-2 showed no significant difference between the three compartments. The middle compartment of OA-3 and OA-4 was significantly different compared with the ulnar ($P = 0.0007$, $P = 0.008$) and radial ($P = 0.008$, $P = 0.005$). A similar trend in the middle compartment was observed for Tb.Th. Specifically, OA-3 and OA-4 showed an increased Tb.Th compared with CTR (95% CI −0.31, −0.03, $P < 0.01$ and −0.32, −0.01, $P < 0.05$). Furthermore, the middle compartment in OA-3 and OA-4 differed from the ulnar ($P = 0.0001$, $P = 0.008$) and radial ($P = 0.009$, $P = 0.02$). Equal distribution in Tb.N was observed between groups. Only in OA-3 did the middle compartment show a significant lower Tb.N than CTR (95% CI −0.18, −1.43, $P < 0.01$). Similarly for Tb.Sp, only the middle compartment of OA-4 was lower compared with the radial ($P = 0.03$).

Histological analysis

Fig. 5A shows sagittal sections of H&E-stained trapezia. CTR samples (15%) presented a normal, slightly convex contour. The articular surface was preserved, viable chondrocytes were uniformly distributed in the superficial, mid and deep zones and the proteoglycan content ranged from normal to moderately reduced. The tidemark was intact. An increasing concavity was observed with progression of the histological grading. In grade 1 samples (OA-2; 15%) the cartilage thickness showed multifocal irregularities and vertical clefts (fibrillations) extending into the mid zone. Chondrocytes increased in number and the proteoglycan content was slightly to markedly reduced. The tidemark was intact. In grade 2 samples (OA-3; 10%) the cartilage was most affected in the middle compartment, with complete erosion of the cartilage and increased density and thickness of the exposed subchondral bone. The less affected ulnar and radial compartments had fibrillations extending from the mid to the calcified zone. Clusters of chondrocytes and hypocellular areas were found. The proteoglycan content was overall markedly reduced. The tidemark, where cartilage was still present, was intact or crossed by blood vessels. In grade 3 samples (OA-4; 60%) the articular cartilage was completely eroded, although the ulnar compartment was occasionally less severely affected and retention of the cartilage was observed. The exposed subchondral bone was affected by osteosclerosis, microfractures with fibrocartilaginous repair and bone cysts, resulting in bone remodelling and marked deformation of the joint surface with compensatory osteophyte formation.

An increasing trend in the Mankin score was observed related to the increase in OA severity stage (Fig. 5B). There was no significant difference between CTR and OA-2. OA-3 showed significantly higher scores compared with CTR (95% CI −17.94, −6.39, $P < 0.001$) and OA-2 (95% CI −16.28, −4.723, $P < 0.001$) with respect to the middle compartment, whereas OA-4 showed significantly higher scores in the ulnar, middle and radial compartments compared with CTR (95% CI −11.50, −3.33; −16.38, −8.21; −12.33, −4.16, $P < 0.001$) and OA-2 (95% CI −10.33, −2.16; −14.71, −6.54, $P < 0.001$; −8.50, −0.33, $P < 0.05$). Regarding the differences between compartments within the same stage, in OA-3 only the middle compartment had a higher score compared with the radial ($P = 0.03$); in OA-4 the middle compartment had a higher score than both the ulnar ($P = 0.0002$) and radial ($P = 0.002$) compartments.

Fig. 4 Micro-CT volume rendering and scoring system



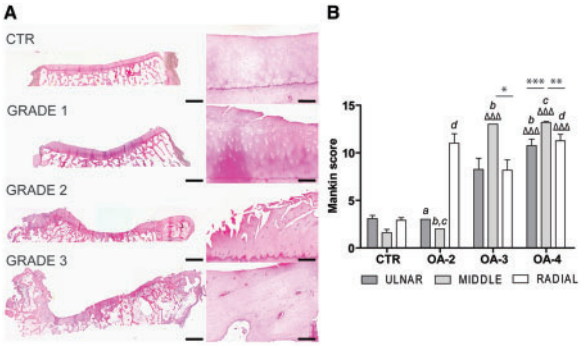
(**A**) Micro-CT volumetric rendering of a healthy (CTR) and osteoarthritic trapezium (OA grade 4). (**B**) Quantitative scoring system evaluating the thickness of subchondral bone and analysis of subchondral bone thickness for the ulnar, middle and radial compartments. (**C**) Analysis of the stereological parameters, including bone volume fraction (BV/TV), trabecular thickness (Tb.Th), trabecular number (Tb.N) and trabecular spacing (Tb.Sp). Triangles (Δ) represent the difference *vs* CTR. $P < 0.05$ (*, Δ, a, b); $P < 0.01$ (**, ΔΔ) and $P < 0.001$ (***, ΔΔΔ).

ICC and correlation analysis

Overall interrater reliability was excellent [ICC 0.87 (95% CI 0.69, 0.96) for X-ray, 0.96 (95% CI 0.91, 0.98) for visual analysis and 0.99 (95% CI 0.99, 1) for histology].

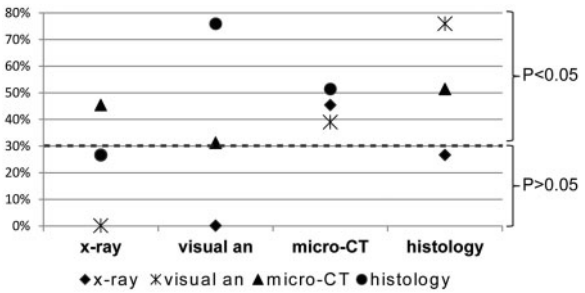
Except for X-ray, CTR showed the same frequency (14%) in all the diagnostic methods. According to the X-ray score, the majority of patients were OA-2 (27%) and OA-3 (32%), whereas only 5% were OA-4. In contrast, according to visual analysis, micro-CT and histological scores, a lower percentage of patients were OA-2 (18%, 18% and 14%, respectively) and OA-3 (all at 23%), whereas an increased frequency was observed for OA-4 (45%, 32% and 40%, respectively). For the Pearson correlation (Fig. 6), only the micro-CT subchondral thickness score was significantly correlated with all the other scores, including Dell's X-ray score [coefficient of determination (R^2) = 0.45, $P = 0.02$], visual analysis Brown's score ($R^2 = 0.39$, $P = 0.004$) and histological Mankin score ($R^2 = 0.51$, $P = 0.001$). X-ray showed no significant correlation with visual analysis ($R^2 = 0.0$, $P = 0.88$) and histology ($R^2 = 0.27$, $P = 0.10$). Visual analysis and histology showed the highest correlation, with $R^2 = 0.76$ ($P < 0.0001$).

Fig. 5 Histological analysis of trapezia



(**A**) Representative images of histological grades according to Mankin's system (H&E). Left panels—deeper articular surface with increasing grade (scale bar 2 mm). Right panels—CTR: normal cartilage, viable chondrocytes, intact tidemark; grade 1: surface irregularities, vertical clefts (fibrillations) in the mid zone; grade 2: fibrillations extending to the radial and calcified zone, articular cartilage erosion; grade 3: exposed and thickened subchondral bone (sclerosis) (scale bar 0.2 mm). (**B**) Mankin's score histogram among compartments and groups. Triangles (Δ) represent the difference *vs* CTR. $P < 0.001$ (***, ΔΔΔ, a, b, c), $P < 0.01$ (**) and $P < 0.05$ (*, d).

Fig. 6 Correlation analysis



Pearson correlations with two-tailed *P*-values. Only micro-CT significantly correlated with all the other diagnostic techniques ($P < 0.05$).

Discussion

Incongruity of the TMJ due to ligament laxity, trauma or cartilage degeneration increases compressive forces on

the trapezium and leads to TMJ-OA. X-ray is the primary analysis for the diagnosis of TMJ-OA in clinical practice and is usually coupled with visual analysis [14, 15], micro-CT [17, 29] or histology [27]. A single study that combines multiple analyses (qualitative and quantitative) of the TMJ has never been described. Here, each trapezium was subjected to four different diagnostic methods—X-ray, visual analysis, micro-CT and histology—to obtain a more comprehensive overview of the pathology and advancement of TMJ-OA based on their correlation. Only an earlier study on dental carious lesions described the comparison of different diagnostic techniques [30]. For each analysis, trapezia were classified into four OA stages according to semi-quantitative scoring systems supported by high interrater reliability, except for micro-CT, for which we developed a quantitative scoring system based on subchondral bone thickness. The results showed the highest correlation of our novel scoring system for micro-CT with all the already approved grading systems, indicating the accuracy and reliability of such a method to classify trapezium OA. Subchondral bone sclerosis was the first parameter of OA degeneration mainly localized in the radial compartment, shifting to the middle compartment at later stages because of changes in the mechanical properties of articular cartilage.

Studies have demonstrated the low rate of reliability and specificity of radiology for the OA diagnosis due to deficiency in detecting signs of cartilage degeneration and the extension of subchondral bone sclerosis [22, 31]. Similarly, in our study the results obtained from the X-ray showed a higher frequency of trapezium bones in stage 2 and 3 compared with stage 4, while the other techniques produced opposite outcomes. Although X-ray is quick, non-invasive, painless and low cost, its main limit is based on its two-dimensional (2D) character, which leads to the overlapping of anatomical structures. Additionally, X-ray evaluates the entire articular joint, thus losing the spatial separation of adjacent bones and details of different compartments of the trapezia [32].

In order to properly classify the specimens into four OA grades, three equal compartments were defined for each trapezium [17] and they were analysed separately using visual analysis, micro-CT and histology. Visual analysis offers an examination of the cartilage and bone surface and blood vessel invasion of the subchondral bone. However, the invasive surgical procedure and 2D observation are the main drawbacks of this technique [15]. Our visual examination showed a predominance of cartilage degeneration and subchondral bone damage in the middle compartment. This result agrees with a previous study in which the late stages of OA (stages 3 and 4) were characterized by eburnation in the central area followed by a centrifugal spread of cartilage degeneration [14]. When joint stability is lost, the altered movements of the metacarpal on trapezium and the compressive forces leave imprints on the subchondral bone within the central area [14]. According to other research on early OA stages, the dorsoradial region is affected first and is more damaged by OA than the others [33–35]. Specifically, during opposition, palmar or radial abduction of the thumb, the radial segment receives the highest compressive forces against the metacarpal bone [33]. Thanks to the high spatial resolution and sensitivity, micro-CT is an excellent tool for detecting early changes in BMD, bone stereology and microarchitecture, but it is insensitive in detecting articular cartilage and soft tissues [22]. To score TMJ-OA severity, we developed a micro-CT scoring system for subchondral bone thickness because of its exposure to the initial mechanical stress during the OA degeneration [6, 7]. Accordingly, others have suggested that changes in the density and architecture of the subchondral bone have a relevant effect on the beginning and progression of cartilage degeneration [36, 37]. The progressive thickening of the subchondral bone (sclerosis) influences the mechanical stress on the articular cartilage, which leads to cartilage thinning and eburnation of the subchondral bone [37]. In our study, the thickness of the subchondral bone in OA trapezia showed an increase in all compartments with OA progression. Nevertheless, subchondral bone thickness was predominant at the radial compartment, suggesting that this region absorbs the compressive forces in both healthy and OA trapezia. The subchondral bone remodels to compensate for the loss of cartilage and to stabilize the joint, leading to altered subchondral bone remodelling (sclerosis) [38]. The BV/TV and Tb.Th significantly increased in the middle compartment with higher grades (3 and 4), whereas the Tb.Sp decreased. Similar observations were supported by previous studies performed in human OA trapezium [17], femur head [5, 39] and knee [40]. Thus it can be supposed that the subchondral bone in OA remodels quickly with rapid turnover, which influences the bone's ability to mineralize, and that the higher Tb.Th in OA groups corresponds to a diminished stiffness of the subchondral bone [41]. Tb.N remained unchanged in the OA groups, differing from findings in another study [17]. However, in that study, they measured the stereological parameters by drawing the VOIs within the trabecular bone of the trapezia, whereas we restricted the analyses to subchondral bone thickness excluding the underlying trabecular bone.

Histology provides a detailed evaluation of cartilage and bone, cell type and morphology, blood vessels and inflammation. Nevertheless, the invasiveness and 2D analyses are the main disadvantages [42]. In our study, the radial compartment was mainly affected by primarily degenerative changes in early grade OA (OA-2). In the later grades (OA-3 and OA-4), the entire articular surface was involved in the degenerative process and joint instability and metacarpal translation induced severe pathological patterns in the middle compartment. In fact, this compartment showed the highest grade of degeneration—cartilage loss, subchondral bone eburnation and cyst formation. As supported by others, trapezium OA occurred primarily in the radial compartment because of degeneration of the palmar beak ligament, which contributes to radial deviation, followed by a conflict between the metacarpal and the middle compartment of the trapezium [43].

The comparison between techniques showed changes in subchondral bone closely associated with cartilage damage, as also demonstrated by others [44, 45], suggesting the ability of the periarticular bone to stabilize the damaged joint by a remodelling process [46]. Histology is the most accurate but destructive method to investigate TMJ-OA, providing a qualitative assessment of the structure and composition of osteochondral tissue [47]. Micro-CT is a non-invasive analysis, can provide 3D reconstruction and quantitatively assesses sclerosis thickness through the entire articular surface [12]. Our results showed that the novel micro-CT scoring system is an appropriate predictor to stage OA severity and was the only technique that significantly correlates with all other diagnostic scores, as also stated by others [30]. Other studies have used different compartmentalization of the trapezia, e.g. no partition [14, 15], three compartments [17] and four [29] compartments, making the results difficult to compare. In the current study, the partition of trapezia in three equal compartments offered, for the first time, a direct comparison among several techniques within the same sample. The intrinsic inability of micro-CT to depict soft tissues and cartilage degeneration could represent a limitation in the diagnosis of OA [12]. Nevertheless, studies are focusing on the use of micro-CT for OA investigations [39, 48] and clinical micro-CT scanners are being optimized for use in clinical practice and trials [26].

Our study provides a comprehensive overview of TMJ-OA and proposes a reproducible and objective OA scoring method for subchondral bone thickness. This innovative standardized score along with micro-CT volume rendering could be good indicators for treatment options in TMJ-OA.

Rheumatology key messages

- To detect OA, standard diagnostic techniques are not quantitative or invasive.
- Micro-CT subchondral bone thickness quantification is a reproducible and objective method to classify OA.
- Micro-CT significantly correlated with approved techniques for OA diagnosis.

Acknowledgements

The authors thank Dr P. Bellemere (Clinique St Jeanne d'Arc, Faculty of Medicine, University of Nantes, Nantes, France) for the explantation and processing of the healthy samples. The authors also thank Dr S. Previdi (Istituto Farmacologico Mario Negri, Milan, Italy) for technical assistance in carrying out the micro-CT scans.

Funding: The entire work was funded by the Italian Ministry of Health, which contributed solely in terms of financial support.

Disclosure statement: The authors have declared no conflicts of interest.

Supplementary data

Supplementary data are available at *Rheumatology* Online.

References

1 Boughton O, Mackenzie H. Osteoarthritis of the trapeziometacarpal joint (TMJ): a review of the literature. In: Chen Q, ed. Osteoarthritis: Diagnosis, Treatment and Surgery. Rijeka, Croatia: InTech, 2012:203–10.

2 Bettinger PC, Linscheid RL, Cooney WP III *et al*. Trapezium tilt: a radiographic correlation with advanced trapeziometacarpal joint arthritis. J Hand Surg Am 2001; 26:692–7.

3 Radin EL, Paul IL, Rose RM. Role of mechanical factors in pathogenesis of primary osteoarthritis. Lancet 1972;1: 519–22.

4 Hulth A. Does osteoarthrosis depend on growth of the mineralized layer of cartilage? Clin Orthop Relat Res 1993; 287:19–24.

5 Li B, Aspden RM. Composition and mechanical properties of cancellous bone from the femoral head of patients with osteoporosis or osteoarthritis. J Bone Miner Res 1997;12: 641–51.

6 Lajeunesse D, Hilal G, Pellettier J *et al*. Subchondral bone morphological and biochemical alterations in osteoarthritis. Osteoarthritis Cartilage 1999;7:321–2.

7 Lajeunesse D. The role of bone in the treatment of osteoarthritis. Osteoarthritis Cartilage 2004;12(Suppl A): S34–8.

8 Buckland-Wright C. Subchondral bone changes in hand and knee osteoarthritis detected by radiography. Osteoarthritis Cartilage 2004;12(Suppl A):S10–9.

9 Rovati LC. Radiographic assessment. Introduction: existing methodology. Osteoarthritis Cartilage 1999;7: 427–9.

10 Eaton RG, Littler JW. Ligament reconstruction of the painful thumb carpometacarpal joint. J Bone Joint Surg Am 1973;55:1655–66.

11 Dell PC, Brushart TM, Smith RJ. Treatment of trapeziometacarpal arthritis: results of resection arthroplasty. J Hand Surg 1978;3:243–49.

12 Stach CM, Bäuerle M, Englbrecht M *et al*. Periarticular bone structure in rheumatoid arthritis patients and healthy individuals assessed by high-resolution computed tomography. Arthritis Rheum 2010;62:330–9.

13 Dahaghin S, Bierma-Zeinstra SM, Ginai AZ *et al*. Prevalence and pattern of radiographic hand osteoarthritis and association with pain and disability (the Rotterdam Study). Ann Rheum Dis 2005;64:682–87.

14 Pelligrini VD Jr. Osteoarthritis of the trapeziometacarpal joint: the pathophysiology of articular cartilage degeneration. II. Articular wear patterns in the osteoarthritic joint. J Hand Surg Am 1991;16:975–82.

15 Brown GD, Roh MS, Strauch RJ *et al*. Radiography and visual pathology of the osteoarthritic scaphotrapeziotrapezoidal joint, and its relationship to trapeziometacarpal osteoarthritis. J Hand Surg 2003;28A:739–43.

16 O'Driscoll SW, Marx RG, Beaton DE *et al*. Validation of a simple histological-histochemical cartilage scoring system. Tissue Eng 2001;7:313–20.

17 Nufer P, Goldhahn J, Kohler T *et al*. Microstructural adaptation in trapezium bone due to subluxation of the thumb. J Orthop Res 2008;26:208–16.

18 Mankin HJ, Dorfman H, Lippiello L *et al*. Biochemical and metabolic abnormalities in articular cartilage from osteoarthritic human hips: correlation of morphology with biochemical and metabolic data. J Bone Joint Surg Am 1971; 53:523–37.

19 Burghardt AJ, Kazakia GJ, Majumdar S. A local adaptive threshold strategy for high resolution peripheral quantitative computed tomography of trabecular bone. Ann Biomed Eng 2007;35:1678–86.

20 Goulet RW, Goldstein SA, Ciarelli MJ *et al*. The relationship between the structural and orthogonal compressive properties of trabecular bone. J Biomech 1994;27:375–89.

21 Buchman SR, Sherick DG, Goulet RW *et al*. Use of microcomputed tomography scanning as a new technique for the evaluation of membranous bone. J Craniomaxillofac Surg 1998;9:48–54.

22 Batiste DL, Kirkley A, Laverty S *et al*. High-resolution MRI and micro-CT in an ex vivo rabbit anterior cruciate ligament transection model of osteoarthritis. Osteoarthritis Cartilage 2004;12:614–26.

23 Burghardt AJ, Link TM, Majumdar S. High-resolution computed tomography for clinical imaging of bone microarchitecture. Clin Orthop Relat Res 2011;469: 2179–93.

24 Burghardt AJ, Lee CH, Kuo D *et al*. Quantitative in vivo HR-pQCT imaging of 3D wrist and metacarpophalangeal joint space width in rheumatoid arthritis. Ann Biomed Eng 2013;41:2553–64.

25 Nishiyama KK, Shane E. Clinical imaging of bone microarchitecture with HR-pQCT. Curr Osteoporos Rep 2013; 11:147–55.

26 Wang G, Zhao S, Yu H *et al*. Design, analysis and simulation for development of the first clinical micro-CT scanner. Acad Radiol 2005;12:511–25.

27 Doerschuk SH, Hicks DG, Chinchilli VM *et al*. Histopathology of the palmar beak ligament in trapeziometacarpal osteoarthritis. J Hand Surg 1999;24:496–504.

28 Fleiss JL. Statistical Methods for Rates and Proportions. New York, NY, USA: John Wiley & Sons, 1981:218.

29 Lee AT, Williams AA, Lee J *et al*. Trapezium trabecular morphology in carpometacarpal arthritis. J Hand Surg Am 2013;38:309–15.

30 Soviero VM, Leal SC, Silva RC *et al*. Validity of microCT for in vitro detection of proximal carious lesions in primary molars. J Dent 2012;40:35–40.

31 Feydy A, Pluot E, Guerini H *et al*. Osteoarthritis of the wrist and hand, and spine. Radiol Clin North Am 2009;47: 723–59.

32 Wolf JM, Oren TW, Ferguson B *et al*. The carpometacarpal stress view radiograph in the evaluation of the trapeziometacarpal joint laxity. J Hand Surg Am 2009;34: 1402–6.

33 Momose T, Nakatsuchi Y, Saitoh S. Contact area of the trapeziometacarpal joint. J Hand Surg 1999;24:491–5.

34 Kovler M, Lundon K, McKee N *et al*. The human first carpometacarpal joint: osteoarthritic degeneration and 3-dimensional modeling. J Hand Ther 2004;17:393–400.

35 Shi Q, Hashizume H, Inoue H *et al*. Finite element analysis of pathogenesis of osteoarthritis in the first carpometacarpal joint. Acta Med Okayama 1995;49: 43–51.

36 Radin EL, Rose RM. Role of subchondral bone in the initiation and progression of cartilage damage. Clin Orthop Rel Res 1986;213:34–40.

37 Radin EL, Swann DA, Paul IL *et al*. Factors influencing articular cartilage wear in vitro. Arthritis Rheum 1982;25: 974–8.

38 Guzman RE, Evans MG, Bove S *et al*. Mono-iodoacetate-induced histologic changes in subchondral bone and articular cartilage of rat femorotibial joints: an animal model of osteoarthritis. Toxicol Pathol 2003;31:619–24.

39 Zhang ZM, Li ZC, Jiang LS *et al*. Micro-CT and mechanical evaluation of subchondral trabecular bone structure between postmenopausal women with osteoarthritis and osteoporosis. Osteoporos Int 2010;21:1383–90.

40 Bobinac D, Spaniol J, Zoricic S *et al*. Changes in articular cartilage and subchondral bone histomorphometry in osteoarthritic knee joints in humans. Bone 2003;32: 284–90.

41 Grynpas MD, Alpert B, Katz I *et al*. Subchondral bone in osteoarthritis. Calcif Tissue Int 1991;49:20–6.

42 Pritzker KPH, Gay S, Jimenez SA *et al*. Osteoarthritis cartilage histopathology: grading and staging. Osteoarthritis Cartilage 2006;9:13–29.

43 Bettinger PC, Linscheid RL, Berger RA *et al*. An anatomic study of the stabilizing ligaments of the trapezium and trapeziometacarpal joint. J Hand Surg Am 1999;24: 786–98.

44 Burr DB. The importance of subchondral bone in the progression of osteoarthritis. J Rheumatol Suppl 2004;70: 77–80.

45 Buckland-Wright C. Subchondral bone changes in hand and knee osteoarthritis detected by radiography. Osteoarthritis Cartilage 2004;12(Suppl A):S10–9.

46 Sharma AR, Jagga S, Lee SS, Nam JS. Interplay between cartilage and subchondral bone contributing to pathogenesis of osteoarthritis. Int J Mol Sci 2013;14: 19805–30.

47 Mainil-Varlet P, Van Damme B, Nesic D *et al*. A new histology scoring system for the assessment of the quality of human cartilage repair: ICRS II. Am J Sports Med 2010;38: 880–90.

48 Chappard C, Peyrin F, Bonnassie A *et al*. Subchondral bone micro-architectural alterations in osteoarthritis: a synchrotron micro-computed tomography study. Osteoarthritis Cartilage 2006;14:215–23.