

# Condylar asymmetry in children with juvenile idiopathic arthritis assessed by cone-beam computed tomography

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**SUMMARY** The purpose of this study was to determine the degree of condylar asymmetry in children with juvenile idiopathic arthritis (JIA) using cone-beam computed tomography (CBCT) and analysis software. For 20 patients (14 girls and six boys; mean age  $11.21 \pm 3.54$  years), resultant cross-sectional images of the left and right temporomandibular joints (TMJs) were semi-automatically segmented, and exact registration of the right, with respect to the flipped left grey-level condyle, was obtained.

Visual inspection of the volume images in 360 degree rotation showed a wide variety of condylar destruction patterns, ranging from small erosions within the cortex to almost complete deformation of the condylar head. Because segmentation was restricted to the delineation of the cortical region, possible changes in the deeper zones were not reproduced. Descriptive statistics [median and interquartile range (IQR)] and diagrams (frequency distribution) were used to assess the results. Initial analysis of condylar volume (including both flipped left and right) showed a median value for volume of  $0.844 \text{ cm}^3$  (IQR 0.323), while the median value for volume difference between both condyles was  $0.051 \text{ cm}^3$  (IQR 0.098). Analysis of the degree of asymmetry showed a median value of 26.18 per cent (IQR 14.46). Using the CBCT-based method, it was shown that condylar asymmetry was a common feature in children with JIA. The degree of asymmetry was variable, but significant in the majority of the subjects.

## Introduction

Juvenile idiopathic arthritis (JIA) relates to a heterogeneous group of diseases of unknown aetiology, characterized by chronic inflammation of one or more joints, with an onset before the age of 16 years and a minimum duration of 6 weeks (Petty *et al.*, 2004). JIA is considered to be an autoimmune disorder with a complex genetic component. The prevalence is reported as 0.07–4.01 per 1000 children, while the annual incidence of JIA is 0.008–0.226 per 1000 children (Manners and Bower, 2002).

Involvement of the temporomandibular joint (TMJ) was recognized by Still (1897). The reported prevalence has ranged from 17 to 87 per cent based on the JIA subtype, the methods used for diagnosis, and the population studied (Larheim *et al.*, 1981; Ronchezel *et al.*, 1995; Pedersen *et al.*, 2001; Twilt *et al.*, 2006; Billiau *et al.*, 2007). The TMJ can be affected unilaterally or bilaterally, early or late in the course of the disease, and can even be the first joint affected (Twilt *et al.*, 2006). Regarding chronic inflammation of the joints, erosive disease may develop with destruction of the joint cartilage and the subchondral bone and affect the adjacent growth cartilage, which in turn may lead to local growth disturbances and long-term disability (Sidiropoulou-Chatzigianni *et al.*, 2001). The TMJ is particularly vulnerable to dysplasia because the centre of growth of the mandible is located below the articular surface of the condylar head instead of more distal to the joint (Twilt *et al.*, 2003). Regarding TMJ arthritis, erosion and flattening of the

condyle, varying from small lesions to complete absence of the condylar head, are the most frequent radiographic signs (Rønning *et al.*, 1974; Larheim *et al.*, 1981; Karhulahti *et al.*, 1990). The resultant abnormalities, which are present in up to 69 per cent of subjects, include micrognathia, downward and posterior growth rotation of the mandible, as well as various malocclusions (Ronchezel *et al.*, 1995). In the case of unilateral TMJ damage, additional abnormalities can be seen. Jaw asymmetries can develop with reduced growth at the affected side and the chin deviating to the same side (Stabrun *et al.*, 1988; Hu *et al.*, 1996; Kjellberg, 1998). In patients with TMJ involvement, unilateral lesions occur in 41–45 per cent (Larheim *et al.*, 1981; Pearson and Rønning, 1996).

In general, it is difficult to examine the TMJ radiographically. Despite the fact that various imaging techniques have been developed over the years, no single technique exists that provides accurate imaging of all components of the joint. Recently, improvements in technology have led to cone-beam computed tomography (CBCT), which can provide high-resolution images (i.e. with an isotropic resolution ranging from 0.4 mm to as low as 0.125 mm), short scanning times (10–70 seconds), and reduced radiation dose (reportedly up to 15 times lower than that of medical CT scans; Scarfe *et al.*, 2006). CBCT therefore provides the opportunity for multiplanar imaging and three-dimensional (3D) information.

The purpose of this study was to determine the degree of condylar asymmetry in children with JIA using CBCT. Cross-sectional images in digital format were semi-automatically segmented, and the resultant grey-level condyles (i.e. from left and right) were registered after horizontally flipping the left piece. Analysis of the degree of condylar asymmetry was performed using custom-made software.

### Subjects and methods

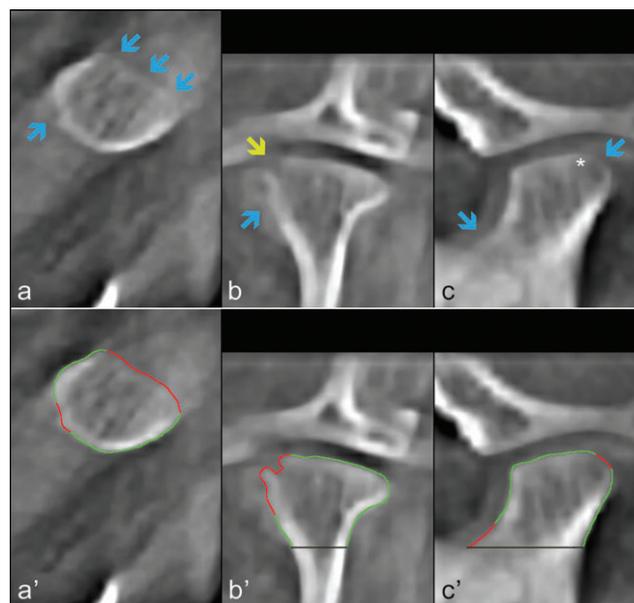
In the multidisciplinary Paediatric Rheumatology outpatient clinic at the University Hospitals Leuven, children with JIA are also examined by an orthodontist. In view of the severity of the TMJ affection and insufficient information on the anatomy of the joint with conventional radiography, a CBCT investigation of the TMJs at the Oral Imaging Centre (University Hospital St Rafaël, Leuven, Belgium) is performed for complete diagnosis. In this report, the first 20 patients with JIA examined with this CBCT technique are reviewed. The group consisted of 14 girls and six boys with a mean age of  $11.21 \pm 3.54$  years, while JIA subtype, severity, and duration of the disease were variable. Prior to each radiographic examination, the patients were informed about the aims of the procedure and informed consent was obtained according to the Declaration of Helsinki.

The cone-beam device used for this study was the 3D Accuitomo® (J. Morita, Kyoto, Japan). The patients were positioned with one strap placed over the forehead and another around the chin, while critical positioning of the head was undertaken after 'scouting' the region of interest. All left and right condyles were captured by the same operator according to a fixed clinical protocol (80.0 kV, 4.0 mA). During reconstruction (1.0 mm slice interval), the data, stored as projections through the acquisition phase, were transformed into subsets of two-dimensional images (cross-sections) along the axial ( $n = 31$ ), frontal ( $n = 41$ ), and sagittal ( $n = 41$ ) axis. Each cross-section (DICOM; approximately 100 kB) had a pixel size of  $0.125 \times 0.125$  mm and a slice thickness of 1.0 mm along the respective axis (1:1:8 voxel proportion). All data were saved on an external hard disk.

Five types of software were used to complete the analysis. Baris Sumengen's Matlab Toolbox implementing Level Set Methods (Vision Research Lab., University of California, Santa Barbara, USA) was employed on all three subsets for both the left and right condyles. In this way, image smoothing, based on a mean curvature flow algorithm, was obtained. Curvature-based forces were chosen due to their ability to smooth similar regions of the image, while preserving their edges. Smoothed data from related subsets were upsampled onto a 1:1:1 grid (i.e. isotropic voxels) using trilinear interpolation. In order to combine all the information present in the smoothed axial, frontal, and sagittal subsets, the three data sets were rigidly registered using multimodality image registration using information

theory (MIRIT; Maes *et al.*, 1997) and trilinearly interpolated. The resulting data set was then resliced perpendicular to the axial ( $n = 241$ ), frontal ( $n = 326$ ), and sagittal ( $n = 329$ ) axes, with an inter-slice distance of 0.125 mm. For delineation purposes, all reslices (1:1:1 voxel proportion) were saved in BMP format.

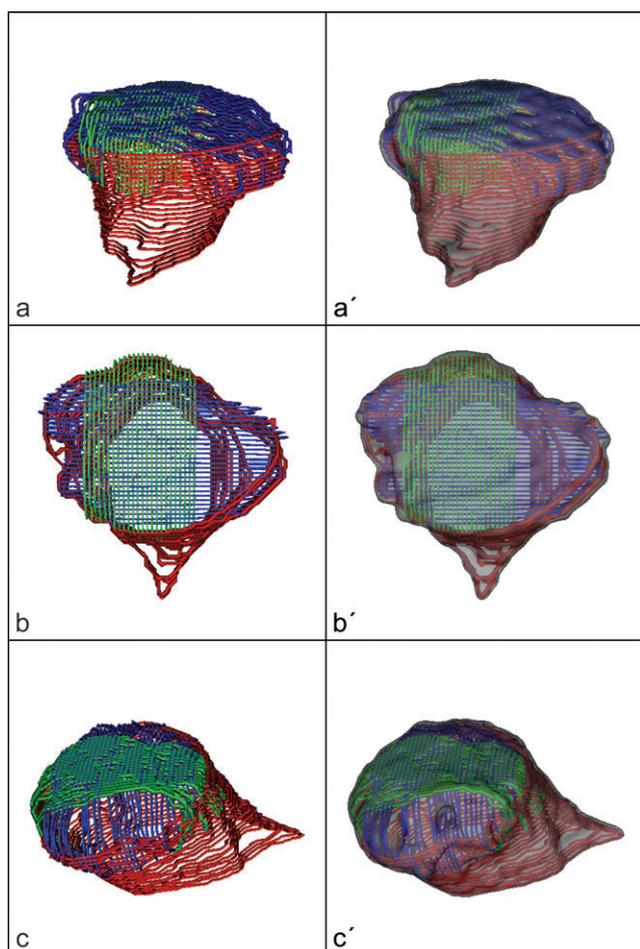
To delineate the grey-level condyle on each cross-section, image analysis software (Image-Pro Plus Version 4.0, Media Cybernetics, Silver Spring, Maryland, USA) was used. The program allowed semi-automatic segmentation (i.e. operator input was only required when the computer experienced difficulties due to a vague border) of the condylar contour. Because redundant information was generated by upsampling, only cross-sections with even numbers (axis step 2) were used. This measure to reduce the work load was found to be reasonable in a pilot study. All delineation was performed by the same operator (EH). In practice, three situations could occur due to the variable degree of condylar destruction (Figure 1). In two of these, partial intervention by the operator was required to obtain a closed contour. To maximize the automated function of the program, however, the condylar necks were delineated in the axial subsets starting from the mandibular incisor, while both the frontal and sagittal subsets were used to segment the parts of the cranium. In this way, each part of the surface presented was the most reliable (as confirmed in a pilot study) and therefore there was no need for inter- and intraoperator reliability tests. Each contour line was saved as a binary image in TIFF format.



**Figure 1** Representative axial (a), frontal (b), and sagittal (c) cross-sections and respective delineation results (a', b', and c') illustrating the three possible situations during the procedure: automatic segmentation of the condylar contour (green), operator input required (red) in case of a vague border (blue arrows), or a discontinuity (yellow arrow) both caused by erosion. Note that the cyst (indicated by \* in c) was not taken into account.

To reconstruct the condylar surface starting from the previously obtained cross-section contours, custom-made software written on top of the Matlab FastRBF Toolbox (FarField Technology Limited, Christchurch, New Zealand) was used. For illustration purposes, the original contour lines from the axial, frontal, and sagittal subsets were plotted onto a combined volume (Figure 2). When multiple contours were available for a certain part, the best fit was preferred. Starting with the generated surface (also called mask), the grey-level condyle was extracted from the original volume file (1:1:1 grid). In case of the left condyle, the extracted volume was horizontally flipped in order to match its right counterpart.

For quantitative analysis of the degree of condylar asymmetry between the flipped left and right entity, exact registration of the latter with respect to the former is required. Therefore, software for image registration MIRIT (Maes *et al.*, 1997) was employed to geometrically register the image volumes resulting from both extraction procedures (Figure 3). Subsequent registration of the masks was also obtained.



**Figure 2** The original contour lines from the axial (red), frontal (blue), and sagittal (green) subsets plotted onto a combined volume (different views in a, b, and c). The generated surface (grey transparent) represents the best fit (a', b', and c').

Finally, a code was written on top of the public domain Visualisation Toolkit package (Schroeder *et al.*, 1998) to undertake quantitative measurements and to provide some qualitative information on the registered flipped left and right generated image volumes. In that way, both condylar surfaces were assessed through a 360 degree rotation, while numerical values for the volume parts (expressed as voxel counts) were obtained. Resultant volume parts were colour coded as follows: red, flipped left condyle only; blue, right condyle only; and green, common (Figure 4). To calculate the various volumes and to determine the degree of condylar asymmetry, the following formulas were used:

$$\text{Volume flipped-left} = (n_{\text{green voxels}} + n_{\text{red voxels}}) \times (0.125 \text{ mm} \times 0.125 \text{ mm} \times 0.125 \text{ mm})$$

$$\text{Volume right} = (n_{\text{green voxels}} + n_{\text{blue voxels}}) \times (0.125 \text{ mm} \times 0.125 \text{ mm} \times 0.125 \text{ mm})$$

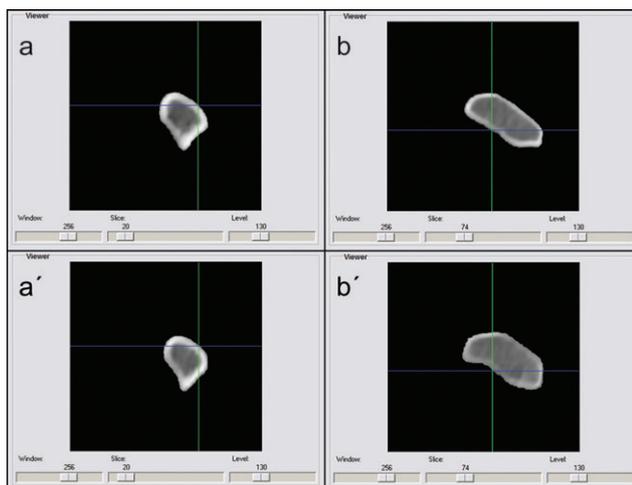
$$\text{Asymmetry (in\%)} = [(n_{\text{blue voxels}} + n_{\text{red voxels}}) / (n_{\text{blue voxels}} + n_{\text{green voxels}} + n_{\text{red voxels}})] \times 100$$

Descriptive statistics [median and interquartile range (IQR)] and diagrams (frequency distribution) were used to report the results.

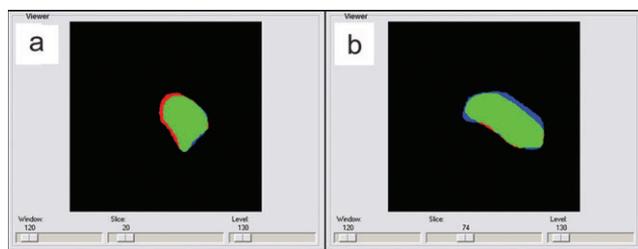
**Results**

*Qualitative analysis*

Surface rendering revealed detailed images of the flipped left and right condyles based on the processed and registered CBCT data. Visual inspection of the volume images in 360 degree rotation showed a wide variety of condylar destruction patterns, ranging from small erosions within the cortex (Figure 5a–c) to almost complete deformation of the

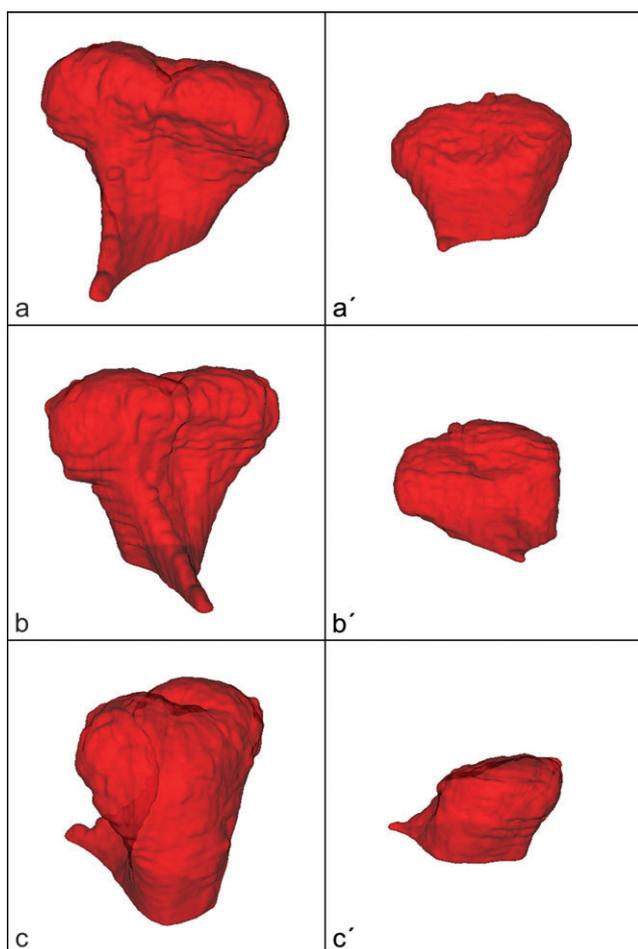


**Figure 3** Two representative axial cross-sections of the flipped left (a, b) and right (a', b') volume files showing the exact registration of the latter with respect to the former. The blue and green lines indicate corresponding positions in frontal and sagittal orientation, respectively.



**Figure 4** Volume parts colour coded as follows: red, flipped left condyle only; blue, right condyle only; and green, common. Note that the same axial levels as in Figure 3 are depicted.

condylar head (Figure 5a'–c'). Because segmentation was restricted to the delineation of the cortical region, possible changes in the deeper zones (e.g. cysts) were not reproduced.



**Figure 5** Representative views illustrating visual inspection of the volume images in 360 degree rotation. Divergent condylar destruction patterns are shown: small erosions within the cortex (a, b, and c) versus complete deformation of the condylar head (a', b', and c').

*Quantitative analysis*

Initial analysis of condylar volume (including both flipped left and right) showed a median value for volume of 0.844 cm<sup>3</sup> (IQR 0.323), while the median value for differences in volume between both condyles was 0.051 cm<sup>3</sup> (IQR 0.098).

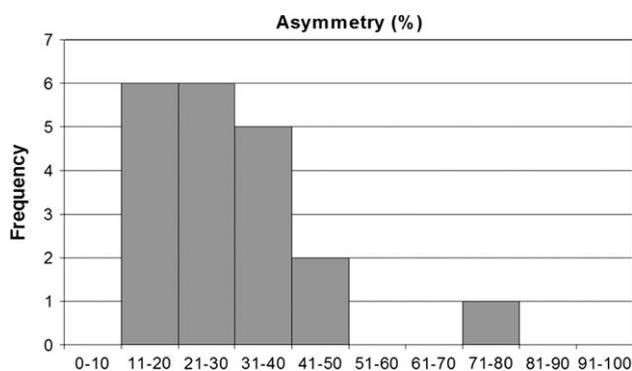
Analysis of the degree of asymmetry showed a median value of 26.18 per cent (IQR 14.46). A histogram of the frequency distribution is shown in Figure 6. Based on the qualitative information, four situations (Figure 7) could be defined.

**Discussion**

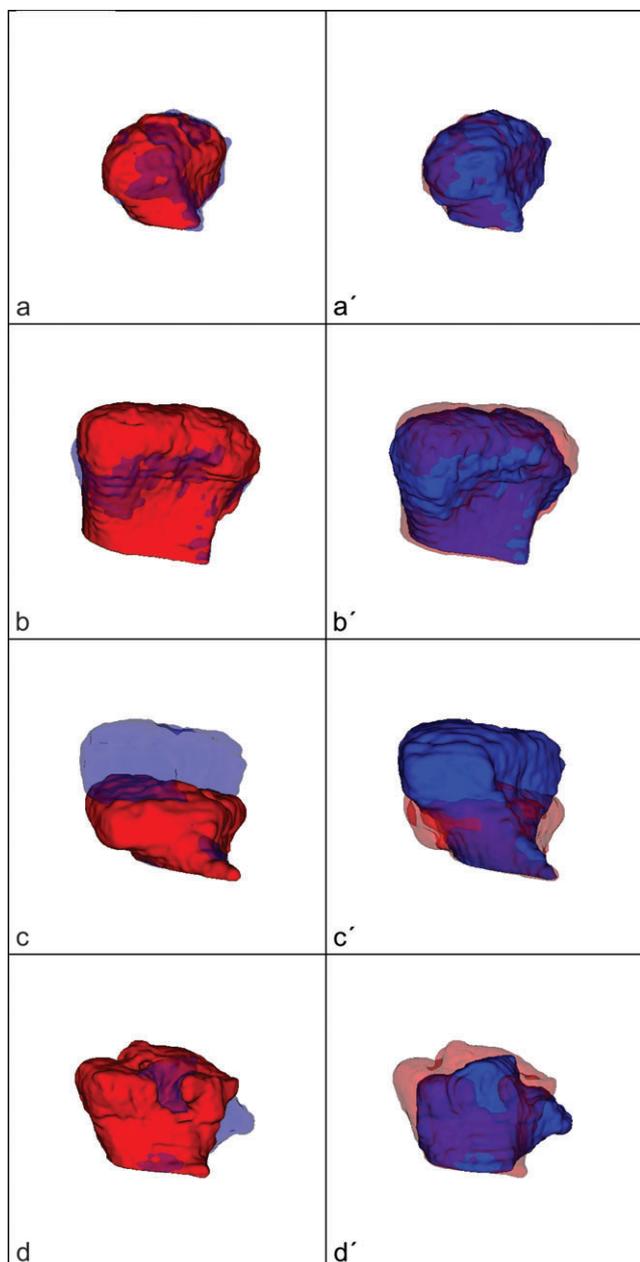
This study is the first to demonstrate an important degree of condylar asymmetry in children with JIA using CBCT and analysis software. With this method, median values of 0.051 cm<sup>3</sup> (IQR 0.098) and 26.18 per cent (IQR 14.46) were found for differences in volume and degree of asymmetry, respectively.

Regarding mandibular asymmetry, most articles report on the vertical dimension of the condyle and ramus as measured on panoramic radiographs taken of healthy subjects. Liukkonen *et al.* (2005) measured vertical dimensions on panoramic radiographs of healthy children at 7 and 16 years of age. A significant side difference was found for condylar height at the age of 7 years (about 4.6 per cent of the total height), while for ramus height measurements, a significant side difference was found at both ages. This fluctuation during growth may indicate that functional forces to the TMJs and mandibular gonial regions are not necessarily in balance, which may lead to unequal growth of the condyle and ramus heights on the right and left sides. Thus, facial asymmetry in the lower jaw region would appear to be a naturally occurring phenomenon in healthy young subjects, which, however, is only seldom clinically significant.

The degree of mandibular asymmetry was examined by Turp *et al.* (1998) by measuring the full dimensions of the condyle and ramus on the right and left sides on 25 dry skulls. The relative absolute differences  $(|R - L| / |R + L|) \times$



**Figure 6** Histogram showing the frequency distribution for the degree of condylar asymmetry.



**Figure 7** Representative views illustrating the initial classification: (a, a') relatively low degree of asymmetry and relatively small condylar volumes, (b, b') relatively low degree of asymmetry and relatively large condylar volumes, (c, c') relatively high degree of asymmetry and relatively large differences in volume, and (d, d') relatively high degree of asymmetry and relatively large differences in shape. In the left column, the flipped left condyle is shown opaque with its right counterpart transparent and *vice versa* for the right column.

100 showed that the asymmetries were of a similar magnitude (between 1.20 and 2.58 per cent) for all variables except condylar height (11.06 per cent), while 60–88 per cent of the absolute differences  $|R - L|$  were due to 'real' individual asymmetries. Those authors concluded that asymmetries of the mandibular condyles and rami are part of the biological variation in humans. However, it still

remains unclear, the extent to which such asymmetries can be considered physiological. Quantitative information on condylar asymmetry did not correlate well with asymmetry in the patient's facial appearance (Figure 8). This variability in association between clinical and radiological symptoms may complicate correct diagnosis and treatment planning.

Kjellberg *et al.* (1994) measured condylar height bilaterally and relative to ramus height in three groups of children, with either normal or post-normal occlusion, or with JIA, on panoramic radiographs. They showed that the JIA group had a significantly shorter relative condylar height, and asymmetries were more common than in the other groups.

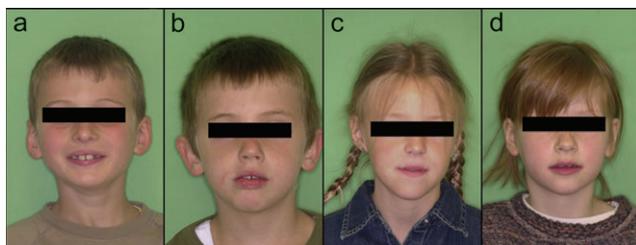
In the present study, condylar asymmetry was examined in 3Ds using CBCT.

All subjects were relatively young (mean age  $11.21 \pm 3.54$  years), while JIA subtype, severity, and duration of the JIA disease were variable. Owing to ethical constraints, it was not possible to include a control group of healthy subjects or to schedule another CBCT procedure over time. For both reasons, interpretation of the results was rendered more difficult. Absolute observations such as the amount of damage, the shape or deformation of the condyle, and condylar volume should be interpreted with some caution. On the other hand, correct interpretation of the registered flipped left versus right image volumes is straightforward because relative measures were used.

Visual inspection of the volume images in 360 degree rotation showed a wide variety of condylar destruction patterns ranging from small erosions within the cortex to almost complete deformation of the condylar head. Moreover, because of image registration, it was justified to show the degree of asymmetry (i.e. difference in shape and/or volume) between the registered flipped left and right condyles in 3Ds. Four situations are defined in Figure 7. Together, they represent an initial classification, which is not supported by the literature.

CBCT is a recent technique for dentomaxillofacial imaging. For the study of bony changes of the TMJ, CBCT may be considered as the imaging technique of choice (Ludlow *et al.*, 2007). Regarding arthritis, CBCT is, however, not suitable for imaging inflammatory reactions (e.g. marrow oedema) or the affected synovium and/or cartilage. For the latter purpose, magnetic resonance imaging and sonography are superior (Johnson, 2006).

The cone-beam device used for this study (3D Accuitomo®), one of the first cone-beam devices on the market, has a relatively small imaging volume (a cylinder 40 mm in diameter and 30 mm high). As a result, the left and right areas were captured consecutively, while the region of interest was restricted (i.e. starting from the mandibular incisor to the most coronal part of the condylar head). The latter is in contrast with most studies that use panoramic radiographs and/or posteroanterior (PA) cephalograms to include both the condyle and the ramus (Stabrun, 1985; Habets *et al.*, 1988; Kjellberg *et al.*, 1994).



**Figure 8** Variability in association between clinical and radiological symptoms: (a) 18.57 per cent condylar asymmetry with the left condyle being smaller and no (or little) facial asymmetry, (b) 49.37 per cent condylar asymmetry with the right condyle being smaller and moderate facial asymmetry, (c) 21.31 per cent condylar asymmetry with the right condyle being smaller and severe facial asymmetry, and (d) 73.41 per cent condylar asymmetry with the left condyle being smaller and no (or little) facial asymmetry.

Due to the relatively small imaging volume of the cone-beam device, both condyles had to be captured separately resulting in an increase in radiation dosage when compared with the smaller imaging volume. Because of this, the positioning of the head was also critical; the condyle just fits in the volume without an excess of space. An advantage of the small-field CBCT, especially in the present study, is the higher resolution in comparison with large-field CBCT. This greater resolution results in increased accuracy for bone measurements (Loubele *et al.*, 2008). In turn, a higher resolution results in more noise and therefore less segmentation possibilities to reproduce 3D images. Since the start of this study, there has been a significant evolution in CBCT regarding resolution, image quality, imaging volume, analysis software, radiation dose, compactness, and price. New devices even have the possibility to undertake volumetric measurements by scanning DICOM images into SimPlant software.

As mentioned previously, panoramic radiography has been widely used to assess the degree of mandibular asymmetry, and especially vertical measurements have been considered reliable (Liukkonen *et al.*, 2005). Some authors, however, advocate caution in making absolute linear measurements or relative comparisons on panoramic radiographs, while they emphasize the importance of ideal positioning of the head i.e. without rotation or shift (Laster *et al.*, 2005; Kamblyafkas *et al.*, 2006). Regarding the use of PA cephalograms, 4 degrees of canting has been reported as the threshold for recognition of an occlusal plane inclination by 90 per cent of observers (Bonnie *et al.*, 1997). Major disadvantages of this approach are possible image distortion and errors in landmark identification (Ahlqvist *et al.*, 1986).

In this study, CBCT data were optimized to allow semi-automatic segmentation. First, image smoothing was applied to reduce the impact of acquisition noise, while preserving edges between different anatomical components. Next, data were upsampled, registered,

trilinearly interpolated, and resliced to obtain optimal estimates for the isotropic voxels (0.125 mm per side) starting from slice thicknesses of 1.0 mm (along the respective axes) as imposed by the fixed clinical acquisition protocol. As pointed out in a pilot study (Maki *et al.*, 2000), segmentation based on thresholding, which is a more practical approach, was not sufficiently accurate because of image characteristics. In general, two conditions complicated both segmentation procedures: the presence of condylar destruction and the fact that the cortex of growing individuals had not yet reached its final maturity and density. Therefore, segmentation was restricted to delineating the cortical region, without taking possible changes in the deeper zones into account.

When comparing multiple data sets that are related in some way, the implementation of a registration step is fundamental. Throughout this study, software for image registration, MIRIT, was repeatedly applied on the 3D CBCT data to find a transformation in 3D by mathematical operations based on the total image contents (i.e. the characteristics of the histogram rather than the outer object contour) and statistical concepts. The registration software has been shown to allow such alignments of the image volumes with subvoxel accuracy (Maes *et al.*, 1997).

## Conclusion

In the present study, using the CBCT-based method, it was shown that condylar volume and shape could be measured accurately. In this group of children with JIA, condylar asymmetry was found to be a common feature. The degree of asymmetry was variable, but significant in the majority of the subjects. How this asymmetry relates to the 3D facial appearance requires further investigation.

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