Normal sonoanatomy of small joints in healthy children: changes in cartilage and vascularisation according to age and gender

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Abstract

Objective

The metacarpophalangeal (MCP) and metatarsophalangeal (MTP) joints may be involved in juvenile idiopathic arthritis. Our goal was to describe their normal sonoanatomy in healthy children, according to age and gender.

Methods

We studied 41 consecutive healthy children (20 girls, 21 boys; age 2-15 years) divided into four age groups: 2-4 years (n=9), 5-7 years (n=11), 8-12 years (n=12), and 13-15 years (n=9). Longitudinal ultrasound axis of the MCP and MTP joints were obtained. The evolution of the cartilage thickness and vascularisation of these joints were studied according to age and gender. The MCP or MTP joints were the statistical unit.

Results

At all sites, on B-mode images, cartilage thickness was associated with age ($p<0.0001$). Cartilage thickness at different sites was significantly greater in boys than in girls ($p\leq0.05$). Blood vessels were seen within the cartilage, with differences across age groups.

Conclusion

This study provides children's age- and gender-specific sonoanatomy data of MCP and MTP and confirms the importance of using colour Doppler or Power Doppler to study cartilage vascularisation.

Key words

ultrasound, healthy children, metacarpophalangeal joints, metatarsophalangeal joints, epiphyseal cartilage, physeal cartilage

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Introduction

Musculoskeletal ultrasonography (MSUS) is useful for detecting synovitis and bone erosions in adults (1). Power Doppler ultrasonography (PD-US) can detect synovial inflammation (2) and is sensitive to changes induced by anti-inflamatory treatments (3). US is used in children with juvenile idiopathic arthritis (JIA) to assess the large joints, such as knees (4-6), hips (6, 7), and shoulders (8) and small joints with standardised MSUS measures of cartilage thickness in children reported recently (9-12). To date, there is not much known on small joints cartilage vascularisation during childhood.

Given the physiological changes of cartilage during growth, it is a challenge to assess joints cartilage in children using PD-US. As age increases, cartilage thickness decreases. The cartilage is anechoic in young children then generates scattered bright echoes, and the physeal cartilage undergoes ossification (9-12). Water is the main component of cartilage (13). The hyaline cartilage that covers the end of the epiphyses in children can generate a few echoes, in keeping with its histological structure made of blood vessels, chondrocytes, and mesenchymal stroma. The ossification centre appears as a hyperechoic dot that grows with advancing age, gradually replacing the hyaline cartilage. Once maturation is complete, only the articular cartilage is visible. Well-known differences exist between paediatric and adult inflammatory joint diseases. The interpretation of PD-US findings of joint components and joint vascularisation in healthy children requires consensual definitions of these components in normal B-mode and Doppler during growth. To date, there is a paucity of literature on these features, in particular on the normal cartilage vascularisation of the joints in healthy children.

The objective of this study was to describe physiological changes of epiphyseal cartilage in the metacarpophalangeal (MCP) and metatarsophalangeal (MTP) joints using B-mode and power Doppler during childhood. These findings were then assessed according to age and gender.

Materials and methods

This was a retrospective analysis of US-PD data collected from a paediatric population under 16 years old between 2007 and 2008 for a 6-month study period. Informed consent from the parents or legal guardians of each patient was obtained before children's inclusion and data collection (image acquisition). The study was approved by our institutional review board (CCP Ouest VI no. 495). Exclusion criteria were age younger than 2 years old, joint pain, and a history of joint injury. The 30 minutes time needed to perform an ultrasound evaluation of the MCP and MTP joints seemed to be too long for children under 2 years old.

Population

A sample of 41 consecutive healthy children (20 girls, 21 boys; age 2–15 years) of colleagues and families in our institution were invited to participate in our study requiring a rheumatologist consultation visit for US-PD of their joints. Data collection was done over 6 months. In line with the results (*i.e.* age-related changes in cartilage thickness during childhood) by Roth *et al.* (11) and those radiographically detecting the appearance of bone ossification (9–12), retrospectively, we divided our sample into four age groups: 2-4 years old (yo) (n=9), 5-7 yo (n=11), 8-12 yo (n=12), and 13-15 yo (n=9).

Ultrasound and power Doppler evaluation

The children groups were seen at our unit and one round of US-PD acquisition of their joints was performed. These images were then evaluated for reproducibility in two rounds by two US experts. This static image evaluation was chosen *versus* a second round of US-PD acquisition to avoid volunteer children's return to the hospital.

Image acquisition

All US-PD evaluations were performed by two senior rheumatologists who had over 7 years of experience with MSUS (SJJ and CC).

The same ATL-HDI 5000 (Philips, Andover, MA, USA) US machine with an L12-5 linear probe was used for imaging

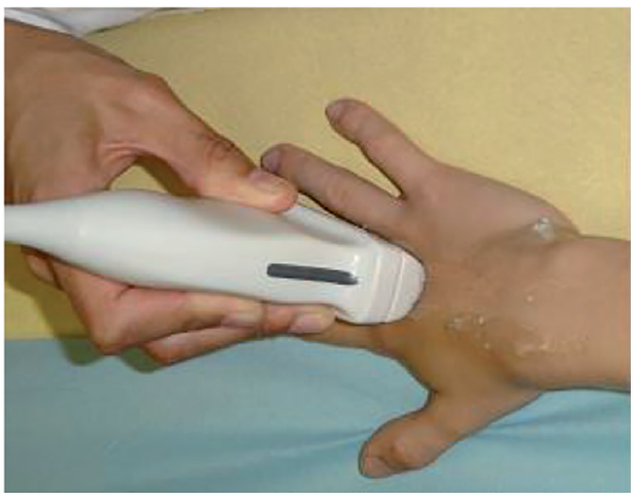

Fig. 1. Position of the probe to assess in B mode and PD-US the metacarpophalangeal joint.

assessment of all of the children except two for whom technical difficulties due to US machine led to the use of another machine, *i.e.* Technos MPX (Esaote, Genoa, Italy) machine with an L14-8 linear probe. The B-mode US was used to assess the thickness of MCP and MTP joint cartilages and power Doppler was used to detect normal vascularisation of these joints. The power Doppler settings were standardised: repetition frequency was set at 750 Hz and colour gain was set just below the level at which colour noise appeared (no flow was visualised at the body surface). The Doppler box was placed over the entire joint to reach the epiphyseal cartilage of the MCP or MTP and also the proximal and distal physis of MCP2 and MTP5 cartilage, including the feeding vessel channels. The Doppler box was enlarged to the top of the image to avoid reverberation artifacts. Vascular flow region of interest (ROI) was assessed in longitudinal and transversal planes at the proximal and distal MCP2, MTP5 physeal cartilage and at the epiphyseal cartilage of each joint, including the feeding vessel channels. Vascular flow ROI was then confirmed by pulsed wave Doppler to exclude artifacts. Low wall filters were used. Given the lack of anatomic knowledge or definition of normal joint vascularisation available at the time, the presence of 1 or more Doppler signals located within the ROI of the joint was taken into account as long as the signals were reproducible in both planes of scanning.

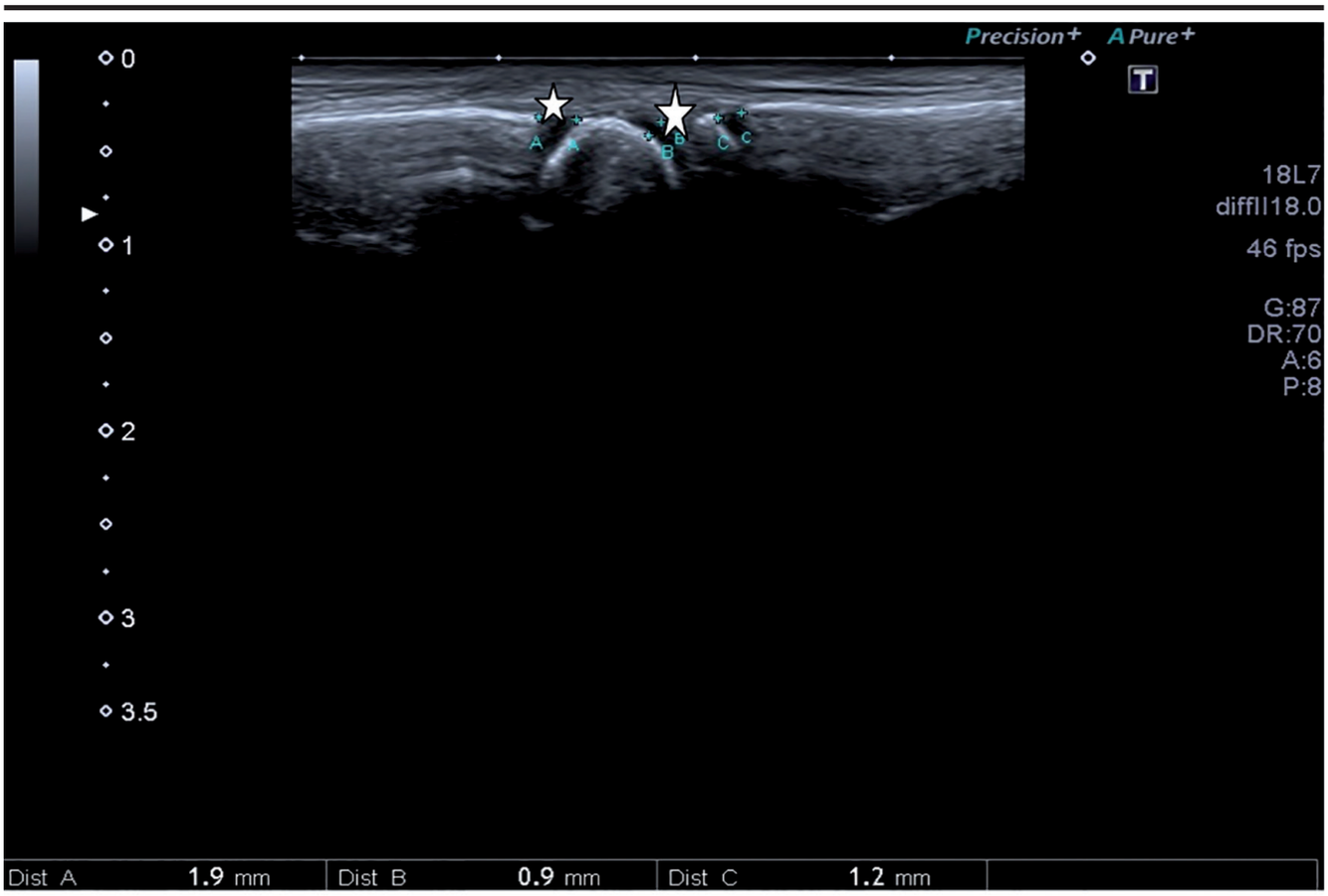

Fig. 2. Dorsal B-mode ultrasound view of the second metacarpophalangeal (MCP) and cartilage measurement.
MCP2 joint of a 7-year-old boy. The proximal (**A**) and distal (C) physeal cartilage is anechoic (the stars on the left is between the metacarpal bone and epiphyseal ossification centre in the MCP head (A) and the stars on the right is between the ossification centre in the base of the first phalanx (**C**) and the phalangeal bone.The epiphyseal cartilage (**B**) overlies the head of the metacarpal bone.

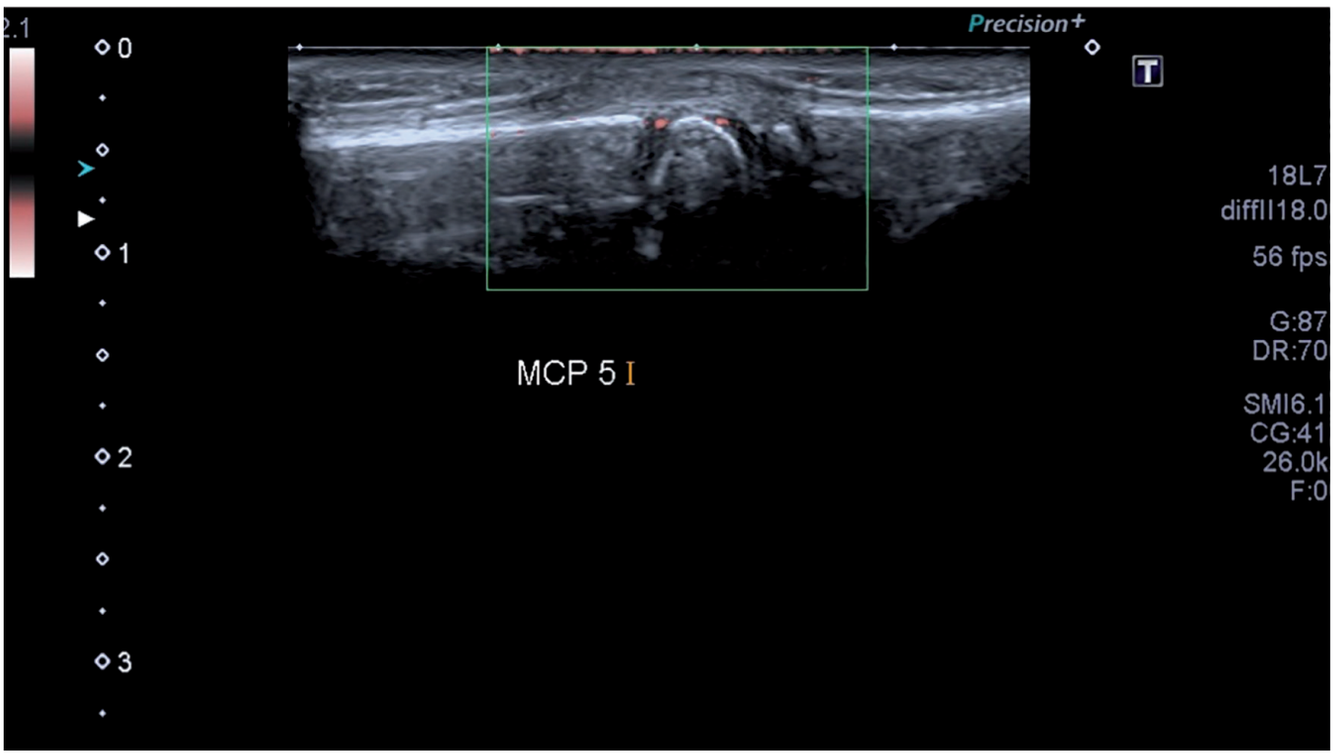

Fig. 3. Dorsal B-mode ultrasound view of the fifth metacarpophalangeal (MCP5) and its vascularisation using PD-US. MTP5 joint of a 7-year-old boy. The proximal and distal physeal cartilage is anechoic. A signal is visualised in the proximal physeal cartilage and in the epiphyseal cartilage.

Eight MCP and all ten MTP joints were assessed in each participant. Given our US-PD experience, there are machine and anatomy-related difficulties in obtaining image acquisition of first MCP joint (MCP1). This difficulty could lead to an inaccurate measurement of joint's thickness due to an inaccurate insonation angle (oblique *vs*. orthogonal) (15). The child was supine, with the hands lying on the examination table for the MCP joints (Fig. 1) and the knees flexed at 90° and the feet flat on the table for the MTP joints.

For US examination, we decided arbitrarily to choose dorsal B-mode axis of each joint to identify each cartilage structure of the joints (*i.e*. epiphyseal cartilage for MCP and MTP joints, proximal and distal physeal cartilage for MCP2 and MTP5 joints).

Cartilage thickness was measured in B-mode at orthogonal insonation angle including the white band (when visible) caused by the synovial-cartilage interface and the second white band caused by the cartilage-bone interface at the MCP2 (Fig. 2), MCP3, MCP4, MCP5 and all five MTP epiphyses. Proximal and distal MCP2, MTP5 physeal cartilages (*i.e*. growth plate) were measured by tracing a horizontal line defining the cartilage distance between two points (Fig. 2).

Power Doppler was used to assess vascularisation of the epiphyseal cartilages of the MCP and MTP epiphyseal cartilage and also MCP2, MTP 5 proximal and distal physeal cartilages (Fig. 3). Vascularisation was defined as at least one signal in the ROI (*i.e*. proximal and distal physeal cartilage in MCP2 and MTP5 and epiphyseal cartilage for the other joints, including the feeding vessel channels). The duration of US examination was 30 minutes.

Image interpretation

The intra- and inter-observer reliability was done on 50 US static images (obtained from different childhood ages, *i.e*. with different cartilage maturation) in two rounds.

Statistical analysis

We divided the participants into four age groups: 2–4 years, 5–7 years, 8–12 years, and 13–15 years. The MCP or MTP joint was the statistical unit. We computed descriptive statistics for the US components of MCP and MTP joints (measurement of cartilage thickness). We then looked for associations linking ultrasound features to age and gender. Finally, we conducted analyses in subgroups defined based on parameters that influenced the ultrasound findings.

Continuous variable, thickness of epiphyseal cartilage, was assessed using the Mann-Whitney test. For dichotomous data (vascularisation presence or absence), we chose the chi-square test. Correlation between cartilage thickness and age was evaluated using the Spearman correlation coefficient. Inter- and intra-observer agreements were calculated usingintra class coefficient correlation. Statistical tests were performed with SPSS 23.0, 2012 (SPSS Inc., Chicago, IL, USA).

Results

Patient characteristics

We studied 41 children, 20 girls and 21 boys. The girls ranged in age from 3 years to 15 years 8 months (median, 8 years 11 months) and the boys from 2 years 7 months to 14 years 2 months (median, 8 years 11 months). The distribution among the four age groups was

as follows: 2–4 yo (n=9); 5–7 yo (n=11); 8–12 yo (n=12); and 13–15 yo (n=9). In each child, we studied the MCP joints 2 through 5 and all 5 MTP joints.

Ultrasound findings at the metacarpophalangeal (MCP) joints

In all cases, the epiphyseal cartilage was seen as an anechoic or hypoechoic band distal to the hyperechoic epiphyseal bone of the MCP head. Our measurements of the physeal cartilage (anechoic or hypoechoic band located in the proximal and/or distal physeal of MCP2 and MTP5). Indeed, the physeal cartilage is open at a younger age and closes gradually with age. When still open, the physeal cartilage was an anechoic or hypoechoic band located in the proximal and/or distal physeal of MCP2 and MTP5.

The thickness of the epiphyseal cartilage of the MCP joints 2 through 5 and of the proximal and distal physeal cartilage of MCP2, MTP5 decreased significantly with increasing age (Table I). Of 264 MCP joints evaluated using power Doppler data, 11 generated signals in epiphyseal cartilages indicating the presence of blood flow (Table II).

Ultrasound findings at the MTP joints

The epiphyseal cartilages of the MTP joints showed the same features as those of the MCP joints in the different age groups. The thickness of the epiphyseal cartilage and of the proximal and distal physeal cartilage decreased with increasing age.

Of 332 MTP joints evaluated using power Doppler data, 23 generated signals in epiphyseal cartilages indicating the presence of blood flow (Table II).

Cartilage thickness according to gender

At both the MCP and the MTP joints, the epiphyseal cartilage was thicker in boys than in girls (Table I). There was a significant difference between all MCP and MTP joint cartilage thicknesses according to gender (Table III).

Cartilage thickness according to age groups

Epiphyseal cartilage thickness decreased with increasing age (Table III). However, proximal and distal physeal cartilage was present in the oldest age group. Besides, epiphyseal cartilage was still visible in the oldest age group (13–15 yo). In all four age groups, the epiphyseal cartilage thickness was greater at the MTP than at the MCP joints. Epiphyseal cartilage thickness was greater at the MTP5 joint than at the other MTP joints (mean, 2.45 mm). A substantial layer of epiphyseal cartilage was still present in the oldest age group.

Table IV showed that the correlation between thickness of the epiphyseal cartilage in MCP (3 to 5), all MTP (2 to 5) and the proximal and distal physeal cartilage of MCP2 joint according to age was negative indicating that the thickness of cartilage decreased when the age increased.

Vascularisation according to age groups

At the MCP joints, power Doppler signals indicating the presence of blood flow in epiphyseal cartilage were seen in all four age groups (Table IV). The MCP epiphysis signals were present more among the oldest age groups: 2–4 yo (0% of children); 5–7 yo (18% of children) ; 8–12 yo (33% of children); 13–15 yo (55% of children).

The MTP Doppler results showed a high degree of vascularisation in 8-12 yo age group (50% of children) compared to other age groups. MTP1 signal distributions were the highest in the 5–7 yo and 8–12 yo age groups.

Static image reliability results

The intraclass coefficient correlation was 0.997 and 0.965 (SJJ and CC respectively). The inter-observer reliability was 0.949.

Table I. Mean cartilage thickness (millimeters) at the metacarpophalangeal (MCP) and metatarsophalangeal (MCP) joints according to the four age groups.

Cartilage thickness	2-4 years (n=9)	5-7 years (n=11)	8-12 years (n=12)	13-15 years (n=9)
MCP2 epiphysis	2.2	1.7	1.4	1.0
proximal physis	1.6	1.5	1.3	0.4
distal physis	1.3	1.2	1.1	0.3
MCP3 epiphysis	2.3	1.7	1.3	0.9
MCP4 epiphysis	2.4	1.7	1.4	0.9
MCP5 epiphysis	2.3	1.7	1.4	0.9
MTP1 epiphysis	3.2	2.6	1.9	1.0
MTP2 epiphysis	3.7	2.6	1.9	1.3
MTP3 epiphysis	3.7	2.5	1.8	1.2
MTP4 epiphysis	3.8	2.4	1.7	1.2
MTP5 epiphysis	4.3	2.6	1.8	1.1

Table II. Vascularisation of the cartilage at the metacarpophalangeal (MCP) joints and metatarsophalangeal (MTP) joints according to the four age groups.

Vascularisation	2-4 years (n=9)	5-7 years (n=11)	8-12 years (n=12)	13-15 years (n=9)
MCP2 epiphysis	0	0	2	0
proximal physis	0	1	0	0
distal physis	2	3	0	1
MCP3 epiphysis	0	0	1	3
MCP4 epiphysis	1	0	1	0
MCP5 epiphysis	1	0	1	1
MTP1 epiphysis	3	5	6	0
MTP2 epiphysis	1	0	1	1
MTP3 epiphysis	3	0	0	0
MTP4 epiphysis	1	0	0	0
MTP5 epiphysis	2	0	0	0

Discussion

US is a particularly attractive imaging technique in paediatric rheumatology to assess several joints simultaneously and at the same time distinguishing structures such as bones, cartilage and joints. Radiography lacks sensitivity for detecting synovial and cartilaginous abnormalities in children and adults with inflammatory joint disease. Nevertheless, radiography is sensitive in detection

Table III. Mean cartilage thickness (millimeters) of metacarpophalangeal (MCP) and metatarsophalangeal (MCP) joints according to the gender.

Thickness of epiphyseal cartilage	Girls	Boys	*p*-value
MCP2	1.2 ± 0.3	1.7 ± 0.6	<0.001
MCP3	1.2 ± 0.4	1.6 ± 0.7	0.003
MCP4	1.3 ± 0.4	1.6 ± 0.7	0.018
MCP5	1.2 ± 0.4	1.6 ± 0.7	0.012
MTP1	1.7 ± 0.7	2.2 ± 0.8	0.004
MTP2	1.8 ± 0.6	2.4 ± 1	0.001
MTP3	1.7 ± 0.7	2.2 ± 0.9	0.012
MTP4	1.7 ± 0.8	2.3 ± 1.2	0.006
MTP5	1.6 ± 0.7	2.4 ± 1.2	0.001

Table IV. Correlation between joints cartilage thickness (millimeters) [metacarpophalangeal (MCP) and metatarsophalangeal (MTP)] and age.

	Correlation coefficient with age
Cartilage thickness at the MCPs	
MCP2 epiphysis	-0.71 (p<0.001)
proximal physis	-0.486 (p<0.001)
distal physis	-0.476 (p<0.001)
MCP3 epiphysis	-0.803 (p<0.001)
MCP4 epiphysis	-0.839 (p<0.001)
MCP5 epiphysis	-0.79 (p<0.001)
Cartilage thickness at the MTPs	
MTP1 epiphysis	-0.816 (p<0.001)
MTP2 epiphysis	-0.812 (p<0.001)
MTP3 epiphysis	-0.852 (p<0.001)
MTP4 epiphysis	-0.844 (p<0.001)
MTP5 epiphysis	-0.865 (p<0.001)
proximal physis	-0.431 (p<0.001)
distal physis	-0.576 (p<0.001)

of accelerated bone maturation (16), a JIA abnormality caused by hyperaemia. MRI has excellent sensitivity for synovial abnormalities, cartilaginous alterations, and erosions. In JIA, chronic inflammation impairs growth by destroying the ossification centres, accelerating bone maturation, and inducing premature closure of the growth plates. Thus, patients with JIA may have small fingers and toes (17). Ultrasonography is still under a step validation process but several studies have shown US usefulness for detecting early evidence of arthritis and the subsequent cartilage erosion and loss both in children and adults (18-20). Nevertheless, US components of JIA in children have not yet been accurately identified, standardised and validated (*i.e*. OMERACT process). In the light of the above, we believe that accurate knowledge of normal sonoanatomy of small-joints cartilage, *i.e*. thickness and vascularisation, should be the mandatory step before diagnosis of JIA in children. A diagnosis based on validated and consensual US-PD components of JIA.

To our knowledge, we report the first systematic evaluation of epiphyseal and physeal cartilage and its vascularisation in normal MCP and MTP joints in healthy children under 16 yo. In our study of healthy children under 16 yo, the cartilage of small joints was thicker in boys compared to girls in all age groups. All MTP cartilages were thicker than MCP joints. In the oldest age group, cartilage thickness remained greater than 2 mm at the MTP joints but was less than 2 mm at the MCP joints. Consistent with the literature, cartilage thickness decreased with growth. A study of 394 healthy children aged 7 to 16 years included assessments of the MCP2 joint and produced results similar to ours (9). Another study by the same group, which included 11 healthy children aged 9.3 to 10 years, showed greater cartilage thickness in boys than in girls at the hips, knees, ankles, MCP2, and second interphalangeal joint (10). Cartilage thickness results were the greatest in all MTP joints in the 2–4 yo. Among MTP joints, MTP5 showed the greatest thickness and reduction of healthy cartilage. If we hypothesised that cartilage and particularly physeal cartilage represents a weak area this finding may explain the greater frequency of erosions at MTP5 in rheumatoid arthritis compared to the other MTP joints. This suggests that the epihyseal cartilage sites such as MTP5 may be more vulnerable to joint erosion in adulthood.

There is a paucity of literature on cartilage vascularisation of normal small joints in children. Recent publications reported that the joint cartilage is sometimes vascularised in normal children (21-24). Vascularisation of small joints cartilage was difficult to assess. Previous results by Karmazin *et al*. (25), reported 14% of children with pannus vascularisation on US demonstrated marked increased vascularisation of the epiphyseal cartilage. Consequently, during growth, the inflammation of epiphyseal cartilage might not protect the ossification centre from erosion abnormalities. We observed the highest epiphyseal vascularisation (*i.e*. number of PD signals observed at the feeding vessel channels ROI) in MTP joints may be due to the amount of cartilage in these joints. Additionally, the MTP1 joints seemed more vascularised in 5–7 yo and 8–12 yo age groups compared with the MCP joints. Curiously, we expected in our healthy children epiphyseal cartilage vascularisation results more epiphyseal vascularisation in the 2–4 yo group because of the abundance of open feeding vessel channels in the younger children. However, Collado *et al*. (26) described in a population of healthy children no US-PD signal in MCP, and proximal interphalangeal joint or recesses. In this study, the US-PD box was focused on the joint and joint recesses and not on the normal physeal and epiphyseal cartilage. Additional more sensitive technology such as Contrast-enhanced colour PD and MRI (27) can be used for more accurate detection of such sites to better distinguish synovial inflammation from feeding vessel channel blood flow.

This study had several limitations. Its single-centre design and the small sample of children were the main limitations. Other limitations were as follows. We only measured 8 MCP joints over 10 due to technical and anatomical

difficulties in US-PD image acquisition. The use of a gold standard MRI acquisition method would have helped at accuracy assessment of our study's US-PD procedure. Nevertheless, the use of MRI would have required sedation of the children. Other cartilage vascularisation detection technology such as intravenous microbubble contrast enhanced US could have led to better images. Once again, we precluded the use of such invasive techniques.

Our results set forth the following US-PD components of MCP and MTP cartilage joints to be used as the preliminary identification step to development of a standardised guideline to be endorsed by OMERACT criteria (*i.e.* truth, discrimination, and feasibility) in paediatric rheumatology.

We showed that cartilage vascularisation at the sites of epiphysis and physis of MCP joints is a common feature and evenly distributed across age groups under 16 yo. but that of MTP joints seems more significant in particular at the MPT1. The youngest age group showed the highest MTP vascularisation.

Cartilage vascularisation of MTP1 seems highly and evenly distributed in all age groups.

MTP5 cartilage vascularisation and thickness seem to be the highest in the youngest age group and disappear with age following the closure of the feeding vessel channels and the reduction in thickness of epiphyseal MTP5 cartilage.

Further work using contrast-enhanced colour US-PD is warranted to determine whether the cartilage of joints affected by JIA contain normal feeding vessels or, instead, neovessels coming from the synovial membrane or the bone (*i.e.* cartilage).

In the footsteps of this study, long term cohort evaluations of healthy children can help at better identification of JIA high risk small joints in children under 16 yo by using the emerging novel technology such as super micro-vascular imaging which could permit to better identify cartilage vascularisation.

Key messages

- Small joints (metacarpophalangeal and metatarsophalangeal) may be involved in JIA: sonoanatomy and vascularisation of epiphyseal and physeal cartilage.
- MCP and MTP joint cartilage thicknesses decrease with age and vary with gender.

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