Arthritis Care & Research Vol. 68, No. 3, March 2016, pp 348–356 DOI 10.1002/acr.22670 © 2016, American College of Rheumatology

ORIGINAL ARTICLE

Toward Standardized Musculoskeletal Ultrasound in Pediatric Rheumatology: Normal Age-Related Ultrasound Findings

PAZ COLLADO,¹ JELENA VOJINOVIC,² JUAN CARLOS NIETO,³ DANIEL WINDSCHALL,⁴ SILVIA MAGNI-MANZONI,⁵ GEORGE A. W. BRUYN,⁶ ANNAMARIA IAGNOCCO,⁷ MARIA ANTONIETTA D'AGOSTINO,⁸ and ESPERANZA NAREDO,³ on behalf of the OMERACT ULTRASOUND PEDIATRIC GROUP

Objective. The Outcome Measures in Rheumatology Ultrasound Task Force has recently started to work on the validation and standardization of musculoskeletal ultrasound (MSUS) examination in children in order to improve its applicability to joint examination.

Methods. This was a prospective multicenter study performed by 4 experts in pediatric MSUS, who independently collected representative images using predefined scanning procedures of 4 joints (knee, ankle, wrist, and second metacarpophalangeal joint) in different predefined age groups. Researchers were allowed to use their own settings (B-mode and Doppler) in order to get the best quality image and highest sensitivity for low blood flow. Images were evaluated for quality parameters and an atlas was created with the best images. An equipment comparative study was performed by a single examiner using 2 different types of machines.

Results. Sixty-four healthy children were scanned. The quality of evaluated images, obtained by predefined scanning positions, was highly comparable among the examiners. The B-mode images clearly showed age-related variations of joint findings, while Doppler images showed the presence of blood flow, particularly within the epiphyseal cartilage of the children at a younger age. There was a high to good level of consistency between images obtained from the 2 different ultrasound machines.

Conclusion. The study shows a systematic method for ultrasound examination of children at different age groups. Additionally, a baseline collection of images was developed, showing blood vessels in the joints examined. The present study could provide a framework for ongoing MSUS studies as well as for clinical practice in pediatric rheumatology.

INTRODUCTION

Musculoskeletal ultrasound (MSUS) is a readily available, useful, and child-friendly imaging modality that has proved to be of great interest in pediatric rheumatology (1). As in adults, MSUS in children has demonstrated a higher sensitivity for detecting synovitis and tenosynovitis as compared to clinical examination (2). Nevertheless, some difficulties to correctly interpret the ultrasound (US) images might be encountered when MSUS is used in chil-

¹Paz Collado, MD, PhD: Hospital Severo Ochoa, Madrid, Spain; ²Jelena Vojinovic, MD, PhD: University Clinical Center, University of Nis, Nis, Serbia; ³Juan Carlos Nieto, MD, Esperanza Naredo, MD: Hospital General Universitario Gregorio Marañón, Madrid, Spain; ⁴Daniel Windschall, MD: Asklepios Hospital Weissenfels, Weissenfels, Germany; ⁵Silvia Magni-Manzoni, MD: IRCCS Policlinico San Matteo, Pavia, Italy; ⁶George A. W. Bruyn, MD: Medisch Centrum Leeuwarden, Leeuwarden, Friesland, The Netherlands; ⁷Annamaria Iagnocco, MD: Sapienza Università di Roma, Rome, Italy; ⁸Maria Antonietta D'Agostino, MD, PhD: Université de Paris and Ambroise Paré Hospital, Paris, France. dren. The lack of standardized definitions of gray-scale and power Doppler (PD) ultrasonography findings in different age groups is the biggest limitation to establishing its validity as an imaging tool. An additional difficulty is the age-dependent variability of normal sonoanatomy, due to maturation and ossification in children (2). For this reason, acquisition technique, interpretation, and comparison of MSUS images are completely different in children as compared to adults and should be addressed specifically. Since the validity of MSUS is linked to the quality of the equipment and the knowledge of the examiner,

Dr. Naredo has received speaking fees, consulting fees, and/or honoraria (less than \$10,000 each) from AbbVie, Roche, Bristol-Myers Squibb, Pfizer, UCB, General Electric Healthcare, and Esaote, and research support from UCB and MSD.

Submitted for publication March 30, 2015; accepted in revised form July 14, 2015.

Address correspondence to Paz Collado, MD, PhD, Calle Corazón de María 55, 2°A, 28002 Madrid, Spain. E-mail: paxcollado@yahoo.es.

Significance & Innovations

- Musculoskeletal ultrasound is becoming an important tool in the clinical management of children with juvenile idiopathic arthritis (JIA).
- Since many of the difficulties encountered in its use result from an inability to correctly interpret the images, a deep knowledge of anatomy in healthy children, both in B-mode and Doppler mode, as well as a standardized method for evaluation of children are essential.
- A description of the scanning method and sonographic findings of the 4 joints chosen in this study, the most frequently affected joints in JIA, will enhance the clinical and research use of this imaging technique in pediatric rheumatology.

clear, specific definitions of normal structures are essentials for avoiding misinterpretations, especially in children (3). Lack of clear definitions may affect the validity of the technique, and MSUS can become a challenging technique in children.

The Outcome Measures in Rheumatology Ultrasound Task Force is an international collaborative group of experts aiming to investigate the applicability of MSUS in rheumatology and to develop its metric properties for clinical trial developments. Among the different applications of MSUS fields of validation, the pediatric field has been considered as one of the main areas. With the aim of improving the validity of MSUS for the diagnosis and management of synovitis in juvenile idiopathic arthritis (JIA), a new subtask force was included (4). This task force has developed a stepwise process: first, the development and validation, using the Delphi process, of definitions for US findings in healthy children and patients with JIA, and second, creating a consensus agreement on a precise scanning method in different age groups, with the collection of images showing the sonographic appearance of blood vessels in several joints, to be included in an atlas format. Recently, normal definitions of gray-scale US findings were published (5).

Here we present the results of the second part of our process. The aims of the study were to collect representative US images and to standardize an examination method (i.e., patient position, transducer placement, and joint positioning) for joint anatomic structures and normal vascularization that can be consistent and reproducible among different sonographers and US machines, to create an atlas of normal joint appearance during skeletal maturation, and to evaluate the effect of the quality of the machine in the assessment of vascularization in healthy joints.

SUBJECTS AND METHODS

Sonographers and US equipment. A group of experts (rheumatologists and pediatric rheumatologists) with 5–

15 years of pediatric-musculoskeletal US experience, and who previously participated in the development of grayscale US definitions for healthy pediatric joints (5), were invited to participate in the present project. Four centers agreed to participate. The sonographers used the equipment available in their own centers. Each investigator was invited to enroll 5 healthy children in 4 age ranges: toddler and preschool ages 2–4 years, young children ages 5–8 years, preadolescent ages 9–12 years, and teenagers ages 13–16 years.

US examinations were performed by 5 of the study authors, using the following real-time scanners: General Electric Ultrasound System Logiq E9 (JCN, EN), equipped with a 6–15 MHz multifrequency linear (ML) transducer, Logiq 9 (PC), equipped with 10–14 MHz ML transducer, Logiq e (PC, JCN, and EN), equipped with an 8–13 MHz ML transducer, Logiq S8 (DW), equipped with a 6–15 MHz matrix ML transducer, and Philips iU22 (SM-M), using a 5–12 MHz ML transducer. Researchers were allowed to use their own settings and to adjust the Doppler parameters to obtain the highest resolution on B-mode (gray-scale) and the highest sensitivity to low flow without artefacts on Doppler mode.

Joints. The group agreed to examine 4 joints: knee, ankle, wrist, and second metacarpophalangeal (MCP) joint. Joint selection was based mainly on the fact that these are the most common peripheral joints involved in JIA (3,6). Since many MSUS publications focused on pediatrics have included the hip joint, we decided not to include it in the present study (7,8). The children were divided into 4 groups according to age-related changes reported previously by Roth et al (5) and based on the knowledge of appearance of bone ossification as detected by radiography (9–12).

US scanning method. Consent was obtained from the parents before US evaluation. The child was encouraged to lie on the examination table in the supine position for US examination of most of the joints. The youngest children (e.g., <5 years) could sit on their parent's lap in order to be calm. Sometimes babies were fed or slept during the examination, but no sedation was required. The study was approved by the local ethics committee of the coordinator's participating center and conducted in accordance with the Declaration of Helsinki.

Since there was no examination protocol available at the time, the coordinator of the project (PC) provided all participants with a preferred US protocol for scanning children. These recommendations were based on a reference book published by the coordinator that provides information regarding patient positioning and transducer placement, as well as the sonographic appearance of several joints at various ages (13).

The 4 joint regions included were investigated with both B-mode US and Doppler US, both in longitudinal and transverse planes. Table 1 shows the US scanning method suggested for this study. In all recommended scans, specific anatomic landmarks had to be present in the image to ensure the same scanning positions in all examinations performed for the study (Table 1). For longi-

Table 1. Description of standard scans for evaluating the 4 joints selected in the study*		
Joint	Scan approach	
Knee	 Anterior suprapatellar recess The knees should be flexed ~30° on the examination table. Transducer should be placed at the sagittal midline of the leg with the distal end of transducer positioning just cranial to the superior edge of the patella. The longitudinal scanning plane should provide anatomic landmarks: 1) the superior edge of patella and 2) the distal portion of the femur. Lateral parapatellar recesses The knee should be straightened with the patella lying in a central position over the femoral condyles. Transducer should be placed at the cagittal midline of the leg user cranial to the superior edge of the patella and 	
	then rotated 90° for transverse scanning. The transverse scanning plane should provide anatomic landmarks: 1) the superior edge of the patella and 2) the femoral condyle.	
Wrist	Lateral/midline/medial dorsal ⁺ With the palm facing downwards, the wrist should be positioned flat in neutral position. Transducer should be longitudinally placed at the sagittal midline of the wrist with the proximal end of transducer positioning just distal to the radius diaphysis.	
	The longitudinal scanning plane should provide anatomic landmarks: 1) the distal end of diaphysis and epiphyseal cartilage of radius (proximal), 2) dorsal recess of the radiocarpal and midcarpal joints and over them, and 3) a compartment of the extensor tendons according to the area imaged (i.e., the extensor pollicis longus tendon in lateral [radial] aspect, the extensor digitorum tendon in midline aspect, and the extensor carpi ulnaris tendon in medial [ulnar] aspect).	
MCP2	Dorsal/lateral/volar With the palm facing downwards, laterally, or upwards, the finger should be positioned flat in neutral position. Transducer should be longitudinally placed at the sagittal midline of finger just at the MCP joint (dorsal/lateral/ volar).	
Ankle	 The longitudinal scanning plane (performed for each approach) should provide anatomic landmarks: 1) the head of metacarpal bone (proximal) and 2) the base of proximal phalanx (distal). Medial/midline/lateral/dorsal The ankle should be dorsally extended ~120° with sole resting on the examination table. Transducer should be placed at the sagittal midline of the ankle with the distal end of transducer positioned on the dome of talus. The longitudinal scanning plane should provide anatomic landmarks: 1) the distal end of tibia (proximal) and 2) the talus (distal). 	
* Medial er should transduc digitorur † As the dorsal re	aspect: the transducer should be longitudinally placed on the tibialis anterior tendon (used as a landmark). Midline aspect: the transduc- d be placed at the sagittal midline of the ankle on the extensor hallucis longus and extensor digitorum tendons with the distal end of the er positioned on the talar dome (used as a landmark). Lateral aspect: the transducer should be longitudinally placed on the extensor n tendon (used as a landmark). MCP = metacarpophalangeal. dorsal approach allows an excellent view of the anechoic/hypoechoic profile of unossified epiphyseal cartilage of bones forming the cess of radiocarpal and midcarpal joints, the volar approach is not usually included in children.	

tudinal B-mode US scanning, all investigators were encouraged to sweep the transducer from the medial to lateral side of the joint, providing anatomic information, and similarly from proximal to distal in transverse scanning.

As Doppler is a technique that supplements the traditional B-mode imaging, it was used to supply any further information about the presence of blood flow in healthy joints. Blood flow was written down as present or absent in each approach. Its localization in the joint (epiphyseal cartilage, growth plate, or intraarticular connective tissue) was also reported. Once the anatomic landmarks of the investigated joint were identified in each approaching position, the Doppler mode was activated. Each participant chose between color Doppler (CD) and PD, depending on the equipment (14). The Philips iU22 used CD and the Logiq equipment used PD, but one center used Logiq e with both CD and PD to evaluate the most sensitive modality. Doppler imaging was performed by selecting a region of interest. The Doppler box was placed to cover the entire joint and extended to the top of the image to be aware of reverberation artifacts. The region of interest should be examined in 2 planes (longitudinal and transverse) for detecting reproducible Doppler signals at different insonation angles. Since there was no anatomic knowledge or definition of normal joint vascularization available at the time, the presence of 1 or more Doppler signals located within or near the joint was considered as present, as long as the signals were reproducible in at least 2 planes of scanning.

Image evaluation and atlas development. Each investigator recorded B-mode and Doppler images according to the proposed scanning method. Images were included in a PowerPoint presentation with detailed information about the child's age, structure visualized, and scanning procedure (longitudinal or transverse) used to obtain the image. Additionally, other details such as the machine type, the main setting for B-mode (i.e., frequency, gain, and dynam-



Figure 1. Transverse ultrasound scan of parapatellar knee recess, with the knee joint in full extension in a 5-yearold child. The image provides anatomic information about the recess, the epiphyseal cartilage of the patella (white asterisk), the patellar retinaculum, and the femoral condyle. The patellar retinaculum is lying anterior to the lateral recess. Note the presence of a vessel out of the epiphyseal cartilage of the patella, under the patellar retinaculum, as well as minimum fluid shown as an anechoic line. Color figure can be viewed in the online issue, which is available at http://onlinelibrary.wiley.com/journal/doi/10.1002/acr.22670/abstract.

ic range), and the setting for Doppler (i.e., PD or CD mode, frequency, gain, and pulse repetition frequency [PRF]) were also reported. A low gain and a low PRF were chosen by all investigators as the study Doppler settings to detect any blood flow. Participants' names and sex remained anonymous in all images.

The collected images were sent to the coordinator of the project for evaluation of the image quality. The evaluation included the 2 following items: 1) whether the image clearly fulfilled the validated B-mode US definitions for normal joint components (5) and whether it presented the agreed anatomic landmarks, including scanning position and image orientation (left-right), and 2) whether the Doppler image corresponded to the selected area in B-mode and displayed all detectable blood flow at that specific scanning position. The coordinator collected the most representative images that fulfilled the above criteria and used them to create an atlas of reference images.

Researchers at 1 of the participating centers (JCN, EN) examined the 4 joints twice in 7 children at different ages, to evaluate the effect of machine quality in assessing healthy joint vascularization. Interequipment response was evaluated for 2 different machines, General Electric Logiq E9 and General Electric Logiq e. As the sensitivity of both CD and PD is particularly affected both by PRF adjustments and Doppler gain, the lowest possible PRF and gain were recommended. Each image was identified by an equipment identification number to analyze the differences between the 2 US machines.

Statistical analysis. Most data included in this study were categorical and were analyzed only descriptively. The interequipment agreement was evaluated using the Cohen's kappa agreement index (unweighted for dichotomous scoring of the presence or absence of blood flow). The level of kappa agreement was defined as follows: $\kappa \leq 20$ indicates poor agreement, 21–40 fair, 41–60 moderate, 61–80 good, and 81–100 indicates high or almost

perfect. The analysis was separately performed for each of the 4 joints.

RESULTS

Standard scanning positions. Sixty-four healthy children were enrolled in the study: 18 in group 1 (ages 2–4 years), 16 in group 2 (ages 5–8 years), 16 in group 3 (ages 9–12 years), and 14 in group 4 (ages 13–16 years). A total of 240 joints were evaluated. Table 1 shows the standard scanning positions and landmarks that were found to be reproducible among all investigators in this study.

The US evaluation showed a high homogeneity in the quality of the images provided by the sonographers, particularly in B-mode. Most of the images were acquired using a scanning frequency of 12 MHz for the examination of the knee, the ankle, and the wrist joints, except the images from Logiq 9, which were collected at 13 MHz. The B-mode frequency was increased for the MCP joint by all sonographers as follows: 15 MHz in Logiq E9 and Logiq S8, 14 MHz in Logiq 9, 13 MHz in Logiq e, and 12 MHz in Philips iU22.

For US examination of the joints, the longitudinal axis was the first axis used in nearly all approaches (with the parapatellar recess being the exception) to identify each structure and image orientation. In the knee, the transverse view of the parapatellar recess allowed detection of a minimum amount of fluid, which was not detected by sweeping the transducer from the medial to lateral side of the knee joint, using only the longitudinal suprapatellar approach (Figure 1).

Image atlas and age-specific findings. B-mode and Doppler images representative of the normal sonoanatomy structures of the 4 joints were collected for creating an MSUS reference image atlas (Figures 2 and 3). Depending on the degree of ossification of the epiphyseal cartilage, 2



Figure 2. Standardized longitudinal ultrasound examination of the ankle joint. The ankle is dorsally extended $\sim 120^{\circ}$ with the sole resting on the examination table. The transducer is placed at the sagittal position of the ankle, with the distal end of the transducer positioned on the dome of the talus. The right upper image shows the medial dorsal approach of the tibiotalar joint. The lower images show the midline (left) and lateral (right) dorsal approaches of the tibiotalar joint.

main sonographic patterns were observed in B-mode. In groups 1, 2, and 3, the epiphyseal cartilage appeared as an anechoic or hypoechoic structure, with its thickness decreasing with increasing age of the children. In fact, in the oldest group (group 4) the secondary ossification center appeared entirely formed with a hypoechoic gap or interruption in the cortical surface. This finding represents the growth plate cartilage (or the physis) and is a common finding resulting from the incomplete fusion between the secondary and primary ossification centers (Figure 4). On the contrary, the secondary center was often not visible in group 1, whereas children of groups 2 and 3 showed signs of ossification. Finally, B-mode images displayed soft tissue structures, such as tendons and ligaments, of which the appearance did not vary according to the age of the children. Presence of a Doppler signal, indicating blood flow, was seen mostly within the epiphyseal cartilage. Table 2 describes specific vascularization findings in each joint, evaluated in different age groups. As

shown in Table 2, the blood flow was easier to detect in younger children than preteens and teenagers.

Influence of equipment used on detection of vascularization. Seven children were scanned twice to investigate whether or not vascularization was detectable based on the type of US equipment used. This study subgroup included 2 children age 3 years (group 1), 4 children age 6 years (group 2), and 1 child age 14 years (group 4). A total of 168 images (24 images per child) were captured. The images were evaluated for the presence of blood flow, namely the detection of the same Doppler findings in each joint scanned by both machines. The Doppler settings used in the General Electric Logic E9 were frequency 8 MHz, gain 9, and PRF 0.5 Hz, and in the General Electric Logic e were frequency 8 MHz, gain 10, and PRF 0.9 Hz. The results were given in absolute frequencies of images that displayed similar findings. A high level of agreement was found between the 2 US machines for the evaluation



Figure 3. Standardized longitudinal ultrasound examination of the second metacarpophalangeal (MCP) joint. The finger is examined with the palm facing downwards, laterally, or upwards. The transducer is longitudinally placed at the sagittal midline of the MCP joint, showing dorsal (upper), lateral (middle), and volar (lower) approaches. The proximal end of the transducer is positioned at the head of the metacarpal (MC) bone, and the distal end at the proximal phalanx bone. Color figure can be viewed in the online issue, which is available at http://onlinelibrary. wiley.com/journal/doi/10.1002/acr.22670/abstract.

in the knee and ankle joints ($\kappa = 81$ and 89, respectively), good for the MCP joint ($\kappa = 79$), and moderate for the wrist joint ($\kappa = 53$).

DISCUSSION

In addition to limited knowledge of sonographic anatomy in healthy children, operator knowledge of how to conduct an MSUS examination has affected the validity of this imaging technique. Consequently, it is crucial to set up a standardized US examination method, particularly in the pediatric population. This study is the first step, among several necessary and challenging steps that have to be undertaken to develop an examination protocol and standardize a scanning method to obtain US images in children. Although for US examinations, the transducer was first placed in the sagittal plane, the parasagittal planes were revealed to be important for a more comprehensive evaluation of the joint. In order to improve examination feasibility, we deliberately limited our investigation to those scanning planes that produce a relatively faster procedure and better child compliance during the examination (6,13). Moreover, to overcome the operator dependency, we defined visible reference points for each scanning approach, to make the method reproducible and easy to learn. Since the results of the study showed a high quality of images obtained by all investigators, the method used in the study seemed feasible and the US standard scans proposed were appropriate and reproducible in



Figure 4. Standardized longitudinal ultrasound examination of the knee joint, showing a longitudinal scan on B-mode for the suprapatellar recess, with $30^{\circ}-40^{\circ}$ flexion of the knee in children at different ages. The transducer is placed at the sagittal midline of the leg, with the distal end of the transducer positioned just cranial to the superior edge of the patella. The image provides anatomic information on the following structures: suprapatellar recess, superior edge of the patella (p), distal insertion of quadriceps tendon, and distal end of the femur. The image also depicts the patella as an unossified structure located anterior to the distal epiphysis of the femoral condyle (fc). Epiphyseal cartilage (white asterisks) of the femoral condyle and the patella decrease during the growth of the child. A minimum fluid may be detected as a normal US finding (arrow).

children, regardless of their age. The predefined scanning approaches provided essential information about blood flow (feeding vessels), as well as anatomic bone reference points within the joints explored (knee, ankle, wrist, and second MCP), showing that the theoretically agreed MSUS definitions on normal joint structures in children are consistent when applied in practice for acquiring images (5). The standardized US examination and the agreed US definitions enable us to clearly identify the age-related changes of the growing skeleton in each joint. Ossification of the secondary center was variable, depending on the bones of the joint evaluated, but overall it was usually not visible in the toddlers and infants, particularly in the hand joints. Since sex variation was not evaluated in the present study, no assumption can be drawn about sex or comparison made with other observations (14).

The combination of B-mode with Doppler images has proven that synovial recesses of the 4 joints explored do not show any Doppler signal under normal circumstances. This finding is in agreement with previously reported findings by Collado et al (15). In addition, we demonstrated that intraarticular blood flow, particularly within the epiphyseal cartilage, is present in younger children. So far, there are few publications focused on MSUS discussing this issue. Grechenig et al (16) reported US agerelated variations and normal blood flow in the apophyseal cartilage of the calcaneus. Similarly, the presence of blood flow has been described in the normal epiphyseal cartilage of the distal femur, using magnetic resonance imaging (17). Since that study was conducted only in healthy children, there is no available evidence to show that this flow seen in healthy children could change in pathologic circumstances. This aspect should be further explored in children with JIA. Nevertheless, US detection of enhanced vascularity in the epiphyseal cartilage of the MCP joints, along with effusion or synovial hypertrophy, has been reported by Karmazyn et al in children with JIA (18). Given that this matter has not really been studied, we think it should be a second necessary step as soon as the US definition of synovitis for pediatric patients has fully been defined and validated.

When studying the sonoanatomy of children, US machines provided with CD and PD modules (low-speed flows) must be used to assess the normal feeding vessels and to obtain good-quality images. For the present study, we found a high Doppler sensitivity to low-velocity flow, namely low PRF and low gain. The comparative part of the study showed that even when using different

US examination	Vascularization findings
Longitudinal anterior suprapatellar recess	Vessels within or surrounding the suprapatellar recess (when the recess was visualized) were not found in any age groups. There was only a vessel located inside the suprapatellar fat pad.
	Vascularization detectable at 3 different levels:
	1) Extraarticular vessel parallel to the periosteum of the diaphysis and metaphysis in the age groups 2–4, 5–8, and 9–12 years.
	 Vessels in the epiphyseal cartilage of the secondary ossification center of the femur, mainly in the age group 2–4 years.
	3) Vessels in the physis of femur in the age groups 2–4 years (commonly) and 5–8 years (usually). Here, the transducer was located in longitudinal plane but more laterally (not in midline of knee).
Transverse lateral	Vessels within or surrounding the parapatellar recess (when the recess was visualized) were no
parapatellar recess	found in any age groups. Vascularization was visualized in or close to the epiphyseal cartilag of the femoral condyles and the patella.
Longitudinal wrist dorsal lateral	Vessels within or surrounding the synovial recess (when the recess was visualized) were not found in any age groups. There were 1 or 2 vessels located in the intraarticular connective tissue on some carpal bones.
	Vascularization detectable at 3 different levels of the joint:
	1) Vessels in the epiphyseal cartilage of the radius. However, they were not detected in image from the oldest age group.
	2) Vessel in the epiphyseal cartilage of the scaphoid, mainly in group 1.
Longitudinal wrist dorsal midline	Vessels surrounding the synovial recess (when it was visualized) were not found in any age groups. There were 1 or 2 vessels located within the intraarticular connective tissue on some carnal hones (deep dorsal carni branches of the radial artery)
	Vascularization was infrequently detected in the epiphyseal cartilage of the lunate.
Longitudinal wrist	Vascularization was rare in this area of the joint. It was found mainly in the intraarticular
dorsal medial	connective tissue on the epiphyseal cartilage of the triquetrum.
	Vascularization was infrequently detected in the epiphyseal cartilage of the ulna.
Longitudinal MCP	Vascularization findings were highly similar across the 3 different approaches.
dorsal, MCP volar, MCP lateral	Vessels within or surrounding the synovial recesses were not found in any of the age groups. Vascularization detectable at 2 different levels of the joint:
	 Vessels in the physis/epiphyseal cartilage of the metacarpal head and phalanx bone. It was not detected in images from the oldest age group (≥13 years).
	 Extraarticular vessels detected on/close to the diaphysis of metacarpal bone (the palmar digital artery).
dorsal medial	Vessels in the synovial recess were not found in any age groups. There were vessels located in the intraarticular connective tissue (branches of the dorsalis pedis artery).
I an aite din al an bla	vascularization detectable in the epiphyseal cartilage of the tibial malleolus, mainly in younger children (2-4 and 5-8 years).
dorsal midline	There were vessels located in the intraarticular connective tissue on the tarsal bones (branches of the dorsalis pedis artery)
	Vascularization detectable in the epiphyseal cartilage of the distal end of tibia, mainly in younger children (2–4 and 5–8 years).
	The anterior tibial artery was detected as an extraarticular vessel over the diaphysis of tibia and or joint capsule.
Longitudinal ankle	Vessels in the synovial recess were not found in any age groups.
dorsal lateral	Vessel detected on the talus locating into the intraarticular connective tissue (the lateral tarsal artery).

machines, the same examiner obtained similar results (presence versus absence of blood flow in the same location) following the standard scans and adjusting the machine to the best settings. Additional factors (i.e., room temperature or child movement) can cause artefact signals (19), and therefore should be considered during any examination. In conclusion, our study has provided for the first time a detailed description of scanning approaches that can be used for sonographic evaluation of children, regardless of age. Additionally, a baseline collection of images showing blood vessels in the joints examined was developed. The present study could provide a framework for ongoing MSUS studies as well as for clinical practice in pediatric rheumatology. The next steps, already ongoing, are focused on the standardization of synovitis findings in JIA, especially on the detection of abnormal vascularization by Doppler.

ACKNOWLEDGMENTS

The authors thank Ms Laura Gonzalez Collado for her expert image assistance as well as the children who participated in this study. We also thank María Jesús García de Yébenes (InMusc), who provided statistic analysis support, and the Outcome Measures in Rheumatology Ultrasound Pediatric Group: Sandrine Jousse-Joulin, Nikolay Tzaribachev, Ana Rodriguez, Madeleine Roone, Johannes Roth, Marina Backhaus, Peter Balint, Alessandra Bruns, Fulvia Ceccarelli, Severine Guillaume, Petra Hanova, Cristina Hernandez, Carsten Heuck, Kei Ikeda, Stefano Lanni, Suzanne Li, Clara Malattia, Bethany Marston, Rina Mina, Kenta Misaki, Consuelo Modesto, Sarah Ohmdorf, Nano Swen, Viviana Ravagnani, and Linda Rossi.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Collado had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. **Study conception and design.** Collado, Vojinovic, Naredo. **Acquisition of data.** Collado, Nieto, Windschall, Magni-Manzoni. **Analysis and interpretation of data.** Collado, Vojinovic, Bruyn, Iagnocco, D'Agostino, Naredo.

REFERENCES

- Bellah R. Ultrasound in pediatric musculoskeletal disease: techniques and applications. Radiol Clin N Am 2001;39: 597–618.
- Lanni S, Wood M, Ravelli A, Magni-Manzoni S, Emery P, Wakefield R. Towards a role of ultrasound in children with juvenile idiopathic arthritis. Rheumatology (Oxford) 2013; 52:413–20.
- 3. Collado P, Jousse-Joulin S, Alcalde M, Naredo E, D'Agostino MA. Is ultrasound a validated imaging tool for the diagnosis and management of synovitis in juvenile idiopathic arth-

ritis? A systematic literature review. Arthritis Care Res (Hoboken) 2012;64:1011–9.

- Naredo E, Wakefield RJ, Iagnocco A, Terslev L, Filippucci E, Gandjbakhch F, et al. The OMERACT Ultrasound Task Force: status and perspectives. J Rheumatol 2011;38;2063–7.
- Roth J, Jousse-Joulin S, Magni-Manzoni S, Rodriguez A, Tzaribachev N, Iagnocco A, et al. Definitions for the sonographic features of joints in healthy children. Arthritis Care Res (Hoboken) 2015;67:136–42.
- Collado P, Naredo E, Calvo C, Gamir ML, Calvo I, Garcia ML, et al. Reduced joint assessment versus comprehensive assessment for ultrasound detection of synovitis in Juvenile Idiopathic Arthritis. Rheumatology (Oxford) 2013;52:1477–84.
- Laurell L, Hochbergs P, Rydholm, Wingstrand H. Capsular distance in the hip of the healthy child: normal values with sonography and MR imaging. Acta Radiologica 2002;4:213–6.
 Robben SG, Lequin MH, Diepstraten AF, Hollander JC,
- Robben SG, Lequin MH, Diepstraten AF, Hollander JC, Entius CA, Meradji M. Anterior joint capsule of the normal hip and in children with transient synovitis: US study with anatomic and histologic correlation. Radiology 1999;210: 499–507.
- 9. Ogden JA. Radiology of postnatal skeletal development IX: proximal tibia and fibula. Skeletal Radiol 1984;11:169–77.
- 10. Ogden JA. Radiology of postnatal skeletal development X: patella and tibial tuberosity. Skeletal Radiol 1984;11:246–57.
- Ogden JA, McCarthy SM. Radiology of postnatal skeletal development VIII: distal tibia and fibula. Skeletal Radiol 1983;10:209–20.
- Ozonoff MB. The upper extremity. In: Pediatric orthopedia radiology, 2nd edition. Philadelphia: WB Saunders; 1992. pp. 117–63.
- Collado P, Naredo E. Sonographic images of children's joints. Badalona (Spain): EUROMEDICE, Ediciones Medicas SL; 2007.
- 14. Spannow AH, Stenboeg E, Pfeiffer-Jensen M, Herlin T. Ultrasound measurement of joint cartilage thickness in large and small joints in healthy children: a clinical pilot study assessing observer variability. Pediatr Rheum 2007;5:3.
- Collado P, Naredo E, Calvo C, Crespo M. Assessment of the joint recesses and tendon sheaths in healthy children by high-resolution B-mode and power Doppler sonography. Clin Exp Rheumatol 2007;25:915-21.
- Grechenig W, Mayr J, Peicha G, Randolf Hammerl R, Schatz B, Grechenig S. Sonoanatomy of the Achilles tendon insertion in children. Clin Ultrasound 2004;32:33–43.
- Daldrup-Link HE, Steinbach L. MR imaging of pediatric arthritis. Magn Reson Imaging Clin N Am 2009;17:451–67.
 Karmazyn B, Bowyer SL, Schmidt KM, Ballinger SH,
- Karmazyn B, Bowyer SL, Schmidt KM, Ballinger SH, Buckwalter K, Beam TT, et al. US findings of metacarpophalangeal joints in children with idiopathic juvenile ar thritis. Pediatr Radiol 2007;37:475–82.
- Torp-Pedersen ST, Terslev L. Settings and artefacts relevant in colour/power Doppler ultrasound in rheumatology. Ann Rheum Dis 2008;67:143–9.