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ORIGINAL ARTICLE

Definitions for the Sonographic Features of Joints in Healthy Children

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Objective. **Musculoskeletal ultrasonography (US) has potential in the assessment of disease activity and structural damage in childhood arthritides. In order to assess pathology, the US characteristics of joints in healthy children need to be defined first. The aim of this study was to develop definitions for the various components of the normal pediatric joint.**

Methods. **The definitions were developed by an expert group and applicability was assessed on a collection of standardized scans of the knee and ankle joints by scoring the scans on a Likert scale. The definitions were then modified and applicability was reassessed before sending the definitions for approval to a larger panel of experts. A final scoring on stored images of all relevant joints at different ages followed.**

Results. **Five definitions were developed addressing the articular bone, cartilage, joint capsule, epiphyseal ossification center, and synovial membrane. In total, 224 US images of knees and ankles were acquired, of which 172 were selected for scoring. An agreement of ≥80% was not met for any of the definitions, but after modifications, 81–97% agreement was reached. This version of the definitions was approved by 15 US experts. In the final validation exercise, all definitions reached an agreement of ≥80% for the shoulder, elbow, wrist, metacarpophalangeal hip, knee, ankle and metatarsophalangeal joint.**

Conclusion. **US definitions for the normal pediatric joint were successfully developed through a Delphi process and validated in a practical exercise. These results provide the basis to develop definitions for pathology and to support the standardized use of US in pediatric rheumatology.**

INTRODUCTION

Imaging can add important information to the clinical examination in rheumatology, and this is no different in pediatric rheumatology (1–6). With new treatments, the induction of sustained remission is possible for an increasing percentage of children but cannot always be reliably demonstrated on clinical examination alone (7–10). In addition, the exact determination of remission status is important for the decision to taper medication, thereby preventing side effects from long-term use.

Among the various imaging modalities, musculoskeletal ultrasonography (MSUS) has been shown to be a reliable, relatively inexpensive, and well-tolerated tool for the precise assessment of disease activity (1,2,4,5). This is also important for long-term outcomes because ongoing, often subclinical disease activity can result in joint damage and structural deterioration (5). While pediatric-specific studies on the sonographic prediction of structural deteri-

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Significance & Innovations

- Pediatric musculoskeletal ultrasonography requires a clear understanding of pediatric anatomy.
- In order to determine pathology, ultrasonographic findings of the joint in healthy children need to be defined first.
- For the first time, definitions for the ultrasonographic components of various joints in healthy children were developed and validated.
- These definitions will support the clinical and research use of musculoskeletal ultrasonography in pediatric rheumatology.

oration do not currently exist, it is expected that this topic will be especially important in the pediatric field, given the young age of these patients and therefore the long-term impact of any damage.

The biggest limitation for the pediatric use of MSUS at this point is that surprisingly little has been done in terms of standardization and validation for children (2). An abundant number of studies have emerged in the literature over the past 2 decades for adult rheumatology, which included validation of the US detection of synovitis with histology and magnetic resonance imaging (MRI), standardization of the scanning technique, normative data acquisition, as well as documenting the responsiveness to change (11–15). These aspects have nevertheless only been partially addressed for pediatric patients (2,10,16); very few publications have started to collect information (16,17).

Given the unique anatomy of the growing child and adolescent, the sonographer should avoid to simply use standards that have been established for adults. This applies especially to the bones forming the joints. Children differ significantly from adults in their bony anatomy as seen on US; depending on the age and stage of maturity, their bones will not be completely ossified yet. All of the long bones as well as most of the short bones develop through enchondral ossification (18,19). At birth, cortical bone is present in most of the long bone diaphyses representing the primary ossification center. Many ossification centers in short bones (e.g., in the wrist) are not present yet and hardly any epiphyseal bone is present. The secondary ossification centers in the epiphyses will only subsequently become apparent. Some bones will have several secondary ossification centers and the number might vary among children (20). The pediatric skeleton therefore displays a varying degree of unossified hyaline cartilage in the epiphysis in addition to the portion of hyaline cartilage that constitutes the articular cartilage (Figure 1). While the progress of ossification relative to age and maturity will differ across various joints, the basic pattern as shown in Figure 1 is always the same. An atlas demonstrating the sonographic appearance of various joints at various ages has been published (21).

Figure 2 gives an example of a metacarpophalangeal

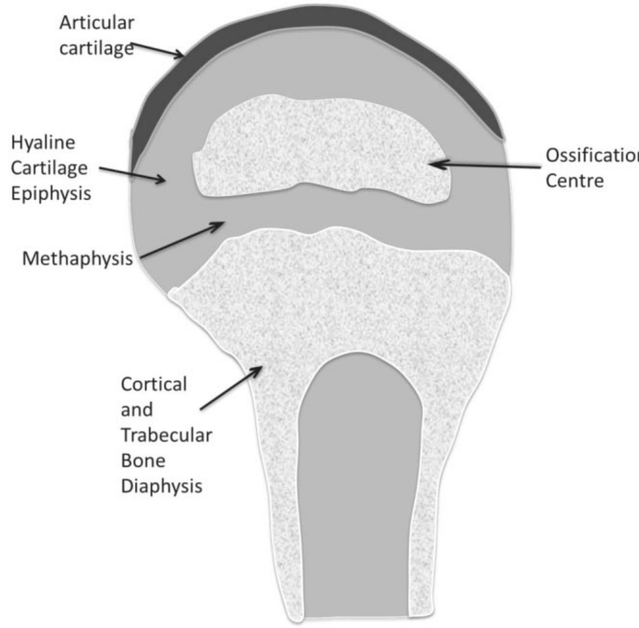

Figure 1. Schematic outline of the various structures within a bone forming a joint.

(MCP) joint in a 10-year-old with incomplete ossification (Figure 2A) compared to a 15-year-old with complete ossification in this joint (Figure 2B). In general, the hyaline cartilage appears anechoic or slightly hypoechoic on MSUS, with the secondary epiphyseal ossification center present depending on the age of the subject. The growth plate can also be seen as a hypoechoic line separating the

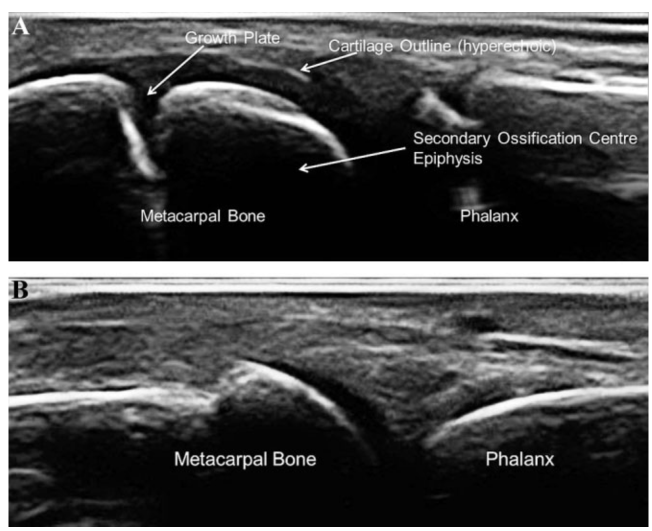

Figure 2. A, Ultrasonographic image of a metacarpophalangeal (MCP) joint in longitudinal view of a 10-year-old. This gray-scale image is showing the hyperechoic outline of the meta-epiphyseal regions of the bones forming the MCP joint with an incompletely ossified epiphysis. Between the diaphysis and the epiphysis, the metaphysis with the growth plate can be seen. Within the hyaline cartilage of the epiphysis, the secondary ossification center is shown. **B,** Ultrasonographic image of an MCP joint in the longitudinal view of a 15-year-old. This gray-scale image is showing the outline of the meta-epiphyseal regions of the bones forming the MCP joint with a completely ossified epiphysis. Only the articular portion of the hyaline cartilage remains.

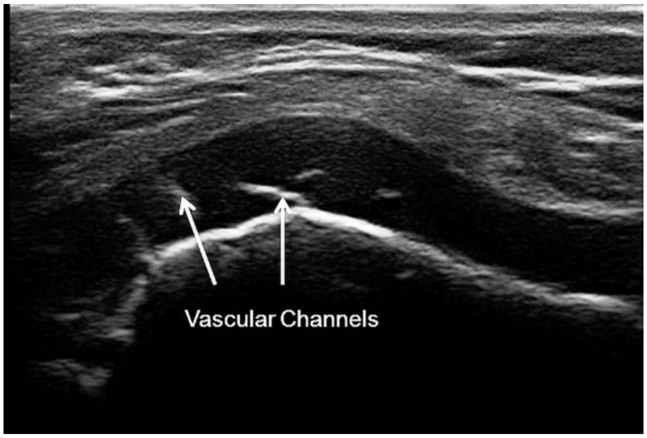

Figure 3. Ultrasonographic image of the medial femoral condyle. This ultrasonographic image of the femur condyle in a 3-year-old child shows hyperechoic spots within the cartilage that correspond to vascular channels.

,epiphyseal from the metaphyseal/diaphyseal part of the bone. The outline of the epiphyseal cartilage can be shown and might appear hyperechoic depending on the angle of insonation (Figure 2A). It is important to note that the cartilage might exhibit small scattered hyperechoic echoes that likely represent vascular channels and that are not pathologic (22) (Figure 3). These vascular channels differ from the secondary ossification center in that they are multiple in number, rather small, and diffusely distributed. Other structures relevant to the joint include the synovial membrane, which cannot be detected by US unless hypertrophied/hyperplastic in a pathologic condition, as well as the joint capsule, which is detectable to a varying degree and depending on the joint (Figure 4).

US is an excellent technique to differentiate these various components of joints, including cartilage, but the sonographer will need to take into account the specific aspects of pediatric anatomy when acquiring and interpreting the images. Given the lack of definitions for normal sonoanatomy as well as synovitis in children (2), a task force for pediatric US was established within the Outcome Measures in Rheumatology (OMERACT) Ultrasound Group to start the essential process of standardization of US assessment in children. Standardization, including precise definitions for US findings, has been shown in adults to be essential for good interrater reliability (14). In order to reflect the variability of relevant anatomy according to age and maturity in children, a decision was taken to start with definitions of the components of the healthy joint first. The aim of this study was to develop definitions for the various components of the pediatric joint that can be evaluated by gray-scale MSUS through a consensus process and to verify the applicability at various ages and in various anatomic locations.

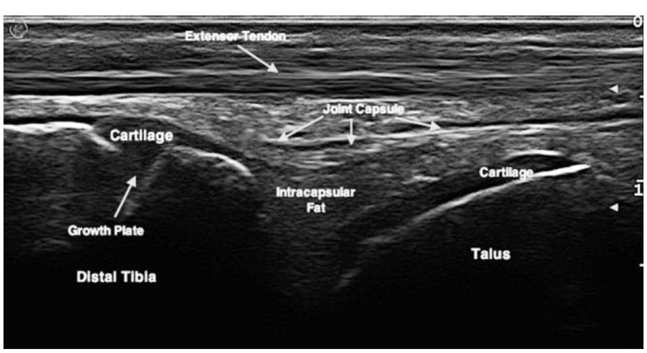

Figure 4. The joint capsule in the tibiotalar joint. This longitudinal view of the tibiotalar joint shows the joint capsule as a fibrillar structure along the joint. In addition, the metaphyseal growth area of the distal tibia is shown.

MATERIALS AND METHODS

The definitions as well as their validation were developed in a multistep consensus process involving a panel of international experts on MSUS in children (Figure 5).

Step 1. A group of 14 experts were invited to join a web-based consensus process to develop definitions for the various components of the normal pediatric joint. All of these experts had extensive experience (5–15 years) in MSUS, including in children, with the majority being pediatric rheumatologists. All have been part of the scientific validation of MSUS previously, including participation in the work of OMERACT. In order to agree on a definition, ≥80% of participants needed to reach ≥80% agreement on a 5-point Likert scale, where 1 = strongly disagree, 2 = disagree, 3 = neutral, 4 = agree, and 5 = strongly agree. In practical terms, this means that ≥80% of participants needed to score the respective definition/component as either 4 or 5 on the Likert scale.

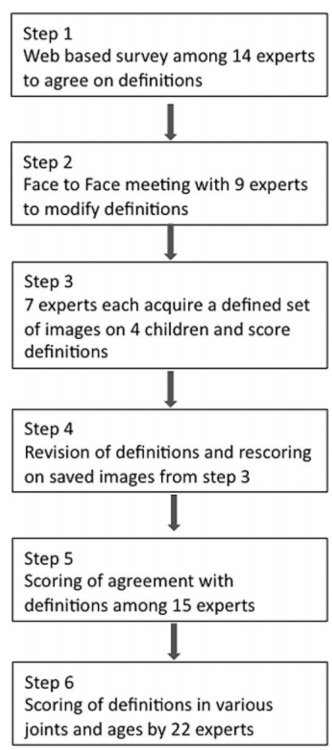

Figure 5. The definitions of the various components of the pediatric joint as well as their validation were developed in a multistep consensus process involving a panel of international experts on musculoskeletal ultrasound in children.

Step 2. During a face-to-face meeting in Madrid, Spain in March 2012, a subgroup of 9 of these experts revised the definitions developed in step 1 covering the following structures: hyaline cartilage, cartilage surface, joint capsule, synovial membrane, and bone surface.

Step 3. The applicability of the revised definitions was then tested in an exercise evaluating healthy children by 7 participants on the same day. Four children were evaluated: 1 female age 12 years, 1 female age 10 years, and 2 males ages 4 years. The knee and ankle were selected to be scanned because they contain all of the joint components covered by the definitions and because of their frequent involvement in juvenile idiopathic arthritis (23). Informed consent to the US assessments was obtained before scanning the children.

The assessments were done using 3 Logiq E9 and 1 Logiq S8 machines (General Electric) with standardized presets. The scans included a suprapatellar transverse and longitudinal scan, an infrapatellar knee longitudinal and transverse scan, a tibiotalar longitudinal and transverse scan, as well as an Achilles tendon longitudinal and transverse scan. The participants were given precise instructions on the probe positioning and anatomic landmarks where the images should be acquired. Only gray-scale images but no Doppler images were acquired. The 7 participants scanned and saved a representative image of the 8 areas in each child. Subsequently, all images were evaluated by all participants individually for quality parameters. These parameters were an image with appropriate magnification of the target structures and clearly displayed bone contours and an image corresponding to the selected area and correctly displaying all relevant structures. In order to qualify for scoring of the definitions, an image had to be scored as 4 or 5 on the previously described Likert scale by at least 80% of the participants for each of the quality parameters. The revised definitions were then scored on each of the selected images by all of the participants independently.

Step 4. The definitions were revised again, taking into account imprecisions that might have led to the failure to validate them initially. The 5 definitions were then scored again by the 7 participants on a reduced set of images taken from the knee and ankle that included the structures described in the definitions using the same Likert scale, with a scoring requirement of 4 or 5 by ≥80% of the participants.

Step 5. The 5 definitions were then sent out for approval by a larger group of 15 MSUS experts with the same qualifications as those in step 1, with the same scoring requirements on a Likert scale as described above.

Step 6. In order to validate this final version of the definitions for all joint regions and across various ages, a new set of images was sent to a group of 22 MSUS experts again with the same qualifications as in step 1 for scoring. The images had been acquired by a single examiner (PC) and consisted of 1 scan each of the posterior shoulder recess, the humeroradial joint in long view, a dorsal long view of the wrist joint at the level of the lunate and capitate bone, a dorsal long view of the MCP 2 joint, an anterior long view of the hip joint, a long view of the suprapatellar recess, a long view of the tibiotalar joint, and a dorsal long view of the metatarsophalangeal (MTP) 1 joint. All scans were taken from children ages 2, 5, 10, and 15 years.

Definition 1

The hyaline cartilage will present as a well-defined anechoic structure (with/without bright echoes/dots) that is non-compressible. The cartilage surface can (but does not have to) be detected as a hyperechoic line.

Definition 2

With advancing maturity, the epiphyseal secondary ossification center will appear as a hyperechoic structure, with a smooth or irregular surface within the cartilage.

Definition 3

Normal Joint Capsule - A hyperechoic structure which can (but does not have to) be seen over bone, cartilage and other intraarticular tissue of the joint.

Definition 4

Normal synovial membrane - Under normal circumstances, the thin synovial membrane is undetectable.

Definition 5

The ossified portion of articular bone is detected as a hyperechoic line. Interruptions of this hyperechoic line may be detected at the growth plate and at the junction of two or more ossification centers.

Figure 6. The final versions of the definitions.

RESULTS

In the first step, no agreement was reached for any definition in the web-based process. In step 2, an agreement was reached on the following definitions: 1) the normal hyaline cartilage appears as a well-defined homogeneous hypoechoic/anechoic structure (with/without bright echoes/dots) that is noncompressible, and the cartilage surface can be detected as a hyperechoic line; 2) with advancing maturity, the epiphyseal secondary ossification center appears as a hyperechoic structure, with smooth surface or irregular surface within the cartilage; 3) the normal joint capsule can be seen as a hyperechoic band over bones and cartilage of the joint; 4) under normal circumstances, the thin synovial membrane is undetectable, but in case of hypertrophy, it can be detected as a hypoechoic structure (relative to adjacent hypoechoic tissues); and 5) the articular bone surface appears as a sharp hyperechoic line (relative to adjacent hypoechoic tissues).

In step 3, a total of 224 images were acquired; 172 of these images were approved and selected for analysis during the first round of scoring that addressed the quality parameters only. On each of the images, the new definitions were then rated by all 7 participants. Summarizing all scores for all scans for a given definition, the minimum of ≥80% agreement was not met for any definition. Looking at the results for individual scans, ≥80% agreement was reached for definition 1 in the suprapatellar longitudinal, infrapatellar knee longitudinal, and tibiotalar transverse scans (3 of 8 scans) and for definition 5 in the tibiotalar longitudinal and transverse scan (2 of 8 scans). None of the other scans reached ≥80% agreement for any of the definitions. The validation of the definitions on these images was therefore not achieved.

In step 4, the wide age range and the range of joints in which the definitions would need to apply were identified as the main reasons why the initial definitions did not achieve approval. The challenge therefore was to ensure the general applicability. This was especially relevant for the definition of the joint capsule, which is very prominent in some joints, such as the hip or ankle, but not necessarily as prominent in other joints. The challenge also applied to the epiphyseal cartilage and the ossification center, which undergo significant changes throughout the maturation of the child. Therefore, the main changes in the definitions included a more cautious wording in definition 3 from "the joint capsule can be seen" to "the joint capsule can but does not have to be seen," as well as the addition of further details (e.g., including the description of the growth plate in definition 5 to accommodate the appearance at various ages). The final version of the new definitions are shown in Figure 6 (for practical examples, see Figures 2–4). It is important to emphasize that some features of these definitions, for example, the description of the secondary epiphyseal ossification center in definition 2, do apply to the immature skeleton of a growing child but will not be detectable in the fully ossified bone of an older adolescent. Upon rescoring, a Likert scale score of 4 or 5 was achieved in 95% for definition 1, 81% for definition 2, 86% for definition 3, 97% for definition 4, and 91% for definition 5. The subsequent approval rates for the 5 definitions by a larger group of experts in step 5 were 93.3% for definition 1, 100% for definition 2, 86.7% for definition 3, 100% for definition 4, and 100% for definition 5. The results of the scoring of these definitions by a larger panel of experts on all relevant joints in step 6 are shown in Table 1. The cumulative results were an agreement of ≥80% for all joint regions and at all ages, except in the

Table 1. Agreement for definitions at different ages in various joints*

Age	Definition 1	Definition 2	Definition 3	Definition 4	Definition 5
Shoulder					
2 years	91	80	86	95	86
5 years	100	100	95	100	95
10 years	100	100	95	100	100
15 years	90	75	95	100	91
Elbow					
2 years	91	80	86	95	81
5 years	100	100	91	100	100
10 years	100	100	100	100	100
15 years	91	90	100	100	95
Wrist					
2 years	82	80	91	95	86
5 years	100	100	91	100	100
10 years	91	100	100	100	100
15 years	90	84	100	90	100
MCP 2					
2 years	95	85	95	100	91
5 years	100	100	100	100	100
10 years	91	100	100	100	100
15 years	86	85	100	100	100
Hip					
2 years	95	85	82	100	91
5 years	100	100	95	100	100
10 years	100	100	95	100	100
15 years	86	90	95	95	100
Knee					
2 years	95	85	82	100	91
5 years	100	100	95	100	100
10 years	90	90	95	100	100
15 years	86	91	95	100	100
Ankle					
2 years	91	80	86	100	91
5 years	100	100	100	100	100
10 years	90	100	100	100	100
15 years	86	90	95	100	100
MTP 1					
2 years	90	86	95	95	86
5 years	100	100	95	95	100
10 years	100	100	100	95	100
15 years	99	75	55	95	100

* Values are the percentage of raters who scored the definition as grade 4 or 5 for each of the scans on a Likert scale (range 1–5). MCP = metacarpophalangeal; MTP = metatarsophalangeal.

case of the 15-year-old in the shoulder and MTP 1 joint for definition 2 and in the MTP 1 joint for definition 3.

DISCUSSION

Definitions for the US appearance of joints in healthy children were successfully developed through a consensus process and validated in several practical exercises. The present study represents an essential first step toward a more reliable use of MSUS in children and will serve as the basis to standardize scanning of other relevant structures, such as the enthesis, and to develop definitions for pathology. The need for many steps in the development of these definitions emphasizes the lack of validation in the US assessment of pediatric joints, which are subject to great variability (2).

Previous work done in adults by the OMERACT Ultrasound Group has shown that even assessments of single types of joints can be challenging and might need a relatively lengthy development process of precise definitions in order to achieve good intra- and interrater reliability of this method (14). Our study focused on the structures of the healthy joint but was restricted to the main structures of the diarthrodial joint. We neither addressed the enthesis nor the findings on Doppler US in healthy children. The enthesis by itself is a relatively complex anatomic structure (2) and the interpretation of Doppler findings in children is very complex (1,24,25). Additional studies are needed to address this.

The final definitions were validated on all joints and at all locations, except for 3 scans of the 15-year-old. This might be explained by the fact that these pediatric definitions do not entirely apply to the relatively mature skeleton of a 15-year-old. In fact, the images of the shoulder and MTP 1 joint of the 15-year-old were the only images where the growth plate had already fused completely and thus a separate epiphyseal ossification center could not be distinguished. Because definition 2 explicitly comments on the epiphyseal ossification center, some of the experts might therefore have believed that this definition was not applicable in these 2 scans of the 15-year-old. We believe that this does not disqualify the definition itself, which is clearly aiming at characterizing the sonographic appearance of the immature skeleton and not the mature bone that is partially already present in a 15-year-old; it will simply be important to emphasize this latter point. The failure of definition 3 to reach agreement for the MTP 1 joint of the 15-year-old is more difficult to explain because this definition clearly states that the joint capsule may or may not be seen. There is no difference in this aspect of the MTP 1 joint of the 15-year-old from any other age or joint, and we therefore believe that approval not being met for this single joint and age does not preclude us from concluding that the definition was validated. Overall, we have covered an appropriate age range in the validation parts of our study. While females and males will differ in the timing of their ossification, the process itself is not different and thus the definitions will apply to both sexes as well.

No validation of our definitions using a comparison method, such as MRI, was done for 2 reasons: the aim of this study was to define components of the healthy joint as seen on US, and there are limited data available from other methods, including MRI, that will need further validation themselves (3).

US will likely be an important imaging technique for the pediatric joint. It is relatively cheap, fast, and virtually free of side effects and does not require sedation, and all peripheral joints can be examined as many times as required at the time of consultation, improving the accuracy of clinical evaluation (6–10).

The definitions in this study are reliable and feasible to apply; they will hopefully support MSUS in the routine clinical assessment and as an outcome measure in research and serve as a basis for the future development of US definitions for pediatric pathology. The definitions also align well with the work currently planned for the pediatric subgroup of the OMERACT Ultrasound Group that will now extend to the Doppler characteristics of the healthy joint and then proceed with standardization and definitions of pathology for the synovial recess, the tendons, as well as the enthesis. In doing so, it will use the same techniques and principles already established during previous work in adults. During the regular OMERACT meetings, the specific role of MSUS in relation to other outcome measures, including other imaging techniques, will also be defined.

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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. Roth 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. Roth, Jousse-Joulin, Magni-Manzoni, Naredo, D'Agostino, Collado.

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Analysis and interpretation of data. Roth, Jousse-Joulin, Magni-Manzoni, Rodriguez, Tzaribachev, Iagnocco, Naredo, D'Agostino, Collado.

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APPENDIX A: MEMBERS OF THE OUTCOME MEASURES IN RHEUMATOLOGY ULTRASOUND GROUP

Members of the Outcome Measures in Rheumatology Ultrasound Group are as follows: Marina Backhaus, Peter Balint, Fulvia Ceccarelli, Severine Guillaume, Petra Hanova, Cristina Hernandez, Kei Ikeda, Suzanne Li, Rina Mina, Consuelo Modesto, Sarah Ohmdorf, Nano Swen, Viviana Ravagnani, Linda Rossi, Jelena Vojinovic, and Daniel Windschall.