Comparison of reliability of magnetic resonance imaging using cartilage and T1-weighted sequences in the assessment of the closure of the growth plates at the knee

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Abstract

Background: Growth development is traditionally evaluated with plain radiographs of the hand and wrist to visualize bone structures using ionizing radiation. Meanwhile, MRI visualizes bone and cartilaginous tissue without radiation exposure.

Purpose: To determine the state of growth plate closure of the knee in healthy adolescents and young adults and compare the reliability of staging using cartilage sequences and T1-weighted (T1W) sequence between pediatric and general radiologists.

Material and Methods: A prospective, cross-sectional study of MRI of the knee with both cartilage and T1W sequences was performed in 395 male and female healthy subjects aged between 14.0 and 21.5 years old. The growth plate of the femur and the tibia were graded using a modified staging scale by two pediatric and two general radiologists. Femur and tibia were graded separately with both sequences.

Results: The intraclass correlation was overall excellent. The inter- and intra-observer agreement for pediatric radiologists on T1W was 82% (κ = 0.73) and 77% (κ = 0.65) for the femur and 90% (κ = 0.82) and 87% (κ = 0.75) for the tibia. The inter-observer agreement for general radiologists on T1W was 69% (κ = 0.56) for the femur and 56% (κ = 0.34) for the tibia. Cohen’s kappa coefficient showed a higher inter- and intra-observer agreement for cartilage sequences than for T1W: 93% (κ = 0.86) and 89% (κ = 0.79) for the femur and 95% (κ = 0.90) and 91% (κ = 0.81) for the tibia.

Conclusion: Cartilage sequences are more reliable than T1W sequence in the assessment of the growth plate in adolescents and young adults. Pediatric radiology experience is preferable.

Keywords

Growth plate, cartilage, MRI of the knee, growth failure, growth development

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Introduction

Bone formation occurs directly from the mesenchyme (cartilage) at the growth plate. The growth plate is a cartilaginous structure which often is subdivided into three layers: the resting, the proliferative, the hypertrophic zones. The zone of provisional calcification is the mineralized part of the hypertrophic zone, located closest to the metaphysis.\(^1\) With age, the height of the growth plate gradually declines.\(^2,3\) MRI takes advantage of the water content in cartilage (70% by volume) and depicts it with intermediate signal on T1-weighted (T1W) and high signal on T2-weighted (T2W) sequences. Gradient-Echo and water selective cartilage sequences have been developed to enhance the signal of cartilage.\(^4\)

The cartilage of the growth plate is of interest in any process that may affect its development and result in short stature, such as fractures (Salter–Harris), osteomyelitis, osteonecrosis, and dysplasia.\(^5–7\) Forensic medicine has raised interest in the assessment of the growth plate to determine the age of athletes,\(^8–12\) and more recently to assess the age of refugees lacking age documentation.\(^13\) Different MRI sequences and rating scales have been used for grading the growth plate related to age,\(^9,14–17\) but there is yet no consensus as to the most reliable approach.

Traditionally, the developing skeleton have been assessed with hand and wrist radiographs using different atlases: Greulich–Pyle (GP)\(^18\) and Tanner–Whitehouse (TW).\(^19\) Less known methods include knee assessment by Pyle and Hoerr.\(^20\) Semi-automated methods have been developed in the last decade.\(^21\) Radiographs are limited not only by ionizing radiation, but also in that they visualize the bone rather than the cartilage of the growth plate.

The purpose of this study is to determine the state of closure of the growth plate of the knee in healthy adolescents and young adults and to compare the reliability of staging using cartilage and T1W sequences between general and pediatric radiologists.

Material and Methods

Subjects

This prospective, cross-sectional, multi-center study was approved by the ethics committee of Stockholm, Sweden, and performed according to the Declaration of Helsinki. Written informed consent/assent was collected from all adult participants and from the parents/legal guardians of minor individuals. Between October 2017 and April 2018, a total of 395 healthy volunteers randomly selected (217 males and 178 females) between 14.0 and 21.5 years old were examined with MR technique of the knee at two different sites. Inclusion criteria were (1) birth in the country in which this study was conducted; (2) age verified by birth certificate issued by national authorities. Exclusion criteria were (1) history of bilateral fractures/trauma to the knee; (2) medical history of chronic disease or long-term medication of the participant; (3) noncompliance during MRI examination; (4) history of residency outside the country in which this study was conducted for more than six consecutive months; (5) past or current pregnancy (all female subjects tested). Prior examination measurements were taken to calculate BMI, and every participant filled out a questionnaire regarding physical activity and inactivity as well.

MRI technique

The examinations were performed on a 1.5-T whole body MR scanner with dedicated knee coils. The knee on the non-dominant side was imaged. If there was a history of fracture to the non-dominant knee, the knee on the dominant side was examined instead. Site 1 used Magnetom Avanto Fit (Siemens Healthcare GmbH, Erlangen, Germany) and Achieva (Philips Healthcare, Amsterdam, The Netherlands) and site 2 used Signa (GE Healthcare, Milwaukee, Wisconsin). The technical specifications can be seen in Table 1. All MRI employed 160 × 160 mm field of view and a pixel resolution of 256 × 256. Time for each acquisition was approximately 4–5 min.

Image analysis

We used a staging system with minor modifications of older staging systems. Our staging scale was based on the five MRI developmental stages by Dedouit et al.\(^16\) and Kellinghaus et al.\(^15\) modified version of the developmental stages of Schmeling et al.\(^14\)

- Stage 1. Continuous, stripe-like, cartilage signal intensity is present between the metaphysis and the epiphysis with a thickness greater than 1.5 mm with a multilaminar appearance.
- Stage 2. Continuous cartilage signal intensity is present between the metaphysis and the epiphysis with a thickness greater than 1.5 mm with increased signal intensity but without a multilaminar appearance.
- Stage 3 (Fig. 1). Continuous cartilage signal intensity is present between the metaphysis and the epiphysis with a thickness less than 1.5 mm with increased signal intensity.
- Stage 4a (Fig. 2). The cartilage is not continuous. A hazy area involving one-third or less of the growth plate is present between the metaphysis and
the epiphysis, representing epiphyseal–metaphyseal fusion.

- Stage 4b (Fig. 3). The cartilage is not continuous. A hazy area involving between one-third and two-thirds of the growth plate is present between the metaphysis and the epiphysis, representing epiphyseal–metaphyseal fusion.

- Stage 4c (Figs 3 and 4). The cartilage is not continuous. A hazy area involving more than two-thirds of the growth plate is present between the metaphysis and the epiphysis, representing epiphyseal–metaphyseal fusion.

- Stage 5 (Fig. 5). The epiphyseal cartilage has fused completely, with or without an epiphyseal scar.

On T1W images one can clearly see the sclerotic dark rim on the edges of the metaphysis and epiphysis towards the growth plate and the slightly decreased signal intensity (low signal = dark/grey) of the growth plate cartilage. The first step of senescence is when the growth plate narrows, the sclerotic edges of the epiphysis/metaphysis become blurred and the cartilage becomes brighter which is considered as bone bridging.

On cartilage sequences the signal of the cartilage (high signal = white) enhances. Thus, black columns of bone invade the growth plate and it is easier to the eye to detect the bone bridging especially in the early stages.

The staging system was introduced to the observers for assessment of the growth plate. Two general radiologists, each with 2 years of experience in general MRI including pediatric patients and two pediatric radiologists with 3 and 13 years of experience blinded to the age and gender of the participants as well as to
the results of the other observers, graded separately the growth plate of the femur and tibia in each sequence. In case of disagreement between the observers, a third pediatric radiologist with 13 years of experience in pediatric radiology assessed the images.

After 4 weeks, a pediatric radiologist with 3 years of experience re-evaluated all the images in both sequences (T1W and cartilage sequences).

**Statistical analysis**

Statistical analysis was performed using SPSS version 25.0 for Windows (IBM Corp., Armonk, NY, USA). An intraclass correlation coefficient (ICC) (95% confidence interval) was used to measure the inter- and intra-observer reliability. A two-way random effects model was chosen to account for the random selection of the study population and to generalize the reliability of the results to raters with the same experience. A mean value of two raters was used to assess the population, hence a “mean of k- raters” of two. Absolute agreement of the ratings between the two observers was selected since it is more stringent than degree of consistency. A P-value <0.05 was considered significant. The ICC values were interpreted as follows:

- <0.5 poor agreement
- 0.5–0.75 moderate agreement
- 0.75–0.9 good agreement
- 0.9–1.0 excellent agreement

**Fig. 3.** Stage 4b in the proximal tibia and in the distal femur on cartilage sequence (a) with an epiphyseal–metaphyseal fusion (white arrows) that completes between one-third and two-thirds of the growth plate. Stage 4b in the proximal tibia (b) and in the distal femur (c) with an epiphyseal–metaphyseal fusion (white arrows). On image (c) there is Stage 4c in the proximal tibia and the white arrows indicate the area where the growth plate is still unfused.

**Fig. 4.** Stage 4c in the proximal tibia and in the distal femur on cartilage sequence (a) and in the proximal tibia (b) and in the distal femur (c) on T1W with an epiphyseal–metaphyseal fusion that completes more than two-thirds of the growth plate. (The arrows indicate areas where there is still unfused growth plate.)
Cohen’s kappa coefficient $\kappa$ was used to evaluate the intra- and the inter-observer agreement for T1W and cartilage sequences separately between the observers. The values for the femur and the tibia were calculated separately. The Kappa values were interpreted as follows: poor agreement $< 0.20$; fair agreement $0.20–0.40$; moderate agreement $0.40–0.60$; good agreement $0.60–0.80$; very good agreement $0.80–1.00$.23

Results
Demographic information of the 395 healthy volunteers examined is shown in Table 2.

Femur: On T1W the minimum age for stage 5 was 16 years for males and 15 years for females (Table 3). The maximum age assessed in stage 4b was 19 years for males and 16 years for females. The minimum age assessed in stage 4c was 15 years for males. Stage 4c was observed in every age group among females in this study. In cartilage sequences the minimum age for stage 5 for males was 16 years, while stage 5 was observed in every age group among females in this study. The maximum age for stage 4b was 17 years for males and 15 years for females. The maximum age for stage 4c was 19 years for males and 17 years for females.

Tibia: On T1W the minimum age for stage 5 was 16 years for males and stage 5 was observed in every age group among females in this study (Table 4). The maximum age for stage 4b was 17 years for males and 15 years for females. The minimum age for stage 4c was 15 years for males and stage 4c was observed in every age group among females in this study, excepting 19- and 20-year-old females. On cartilage sequences the minimum age for stage 5 was 15 years for males, while stage 5 was observed in every age group among females in this study. The maximum age for stage 4b was 17 years for males and 15 years for females. The maximum age for stage 4c was 19 years for males and 17 years for females.

The inter-observer agreement of the femur on T1W was 82% ($\kappa = 0.73$), ICC $= 0.96$ (95% confident interval of 0.94–0.98) for pediatric radiologists and 69% ($\kappa = 0.56$), ICC $= 0.95$ (95% confident interval of 0.94–0.96) for the general radiologists (Table 5). The inter-observer agreement of the tibia was 90% ($\kappa = 0.82$), ICC $= 0.97$ (95% confident interval of 0.96–0.98) for the pediatric radiologists and 56% ($\kappa = 0.34$), ICC $= 0.90$ (95% confident interval of 0.87–0.93) for the general radiologists.

The inter-observer agreement for the femur on cartilage sequences was 93% ($\kappa = 0.86$), ICC $= 0.96$ (95% confident interval of 0.95–0.97) and for the tibia was 95% ($\kappa = 0.90$), ICC $= 0.96$ (95% confident interval of 0.95–0.97) for pediatric radiologists.

The intra-observer agreement (pediatric radiologist with 3 years of experience) of the femur on T1W was 77% ($\kappa = 0.65$), ICC $= 0.95$ (95% confident interval of 0.93–0.96) and for the tibia 87% ($\kappa = 0.75$), ICC $= 0.95$ (95% confident interval of 0.94–0.96). For the cartilage sequences, the intra-observer agreement for the femur was 89% ($\kappa = 0.79$), ICC $= 0.96$ (95% confident interval of 0.95–0.97) and for the tibia 91% ($\kappa = 0.81$), ICC $= 0.96$ (95% confident interval of 0.95–0.97).

Fig. 5. Stage 5 in both the distal femur and proximal tibia: (a) cartilage sequence, (b) T1W.

Table 2. Demographic Information.

| Age (yo) | 14  | 15  | 16  | 17  | 18  | 19  | 20  | 21  | Total |
|---------|-----|-----|-----|-----|-----|-----|-----|-----|-------|
| Male (N) | 22  | 25  | 31  | 23  | 23  | 25  | 35  | 33  | 217   |
| Length (cm) | 171.0 ± 9.0 | 175.3 ± 7.2 | 177.6 ± 7.5 | 180.4 ± 5.2 | 181.2 ± 7.9 | 178.8 ± 6.9 | 181.2 ± 6.0 | 181.8 ± 6.3 | 178.7 ± 7.6 |
| Weight (kg) | 60.2 ± 10.8 | 63.5 ± 9.9 | 67.6 ± 12.3 | 68.8 ± 11.9 | 74.9 ± 14.4 | 71.3 ± 10.1 | 76.9 ± 12.7 | 76.5 ± 14.7 | 70.6 ± 13.4 |
| Female (N) | 22  | 21  | 30  | 26  | 19  | 11  | 24  | 25  | 178   |
| Length (cm) | 163.2 ± 6.4 | 164.4 ± 4.3 | 166.9 ± 6.5 | 167.5 ± 6.0 | 168.0 ± 5.8 | 167.5 ± 7.3 | 165.5 ± 5.9 | 168.6 ± 7.3 | 166.5 ± 6.3 |
| Weight (kg) | 61.7 ± 13.4 | 59.4 ± 9.0 | 60.8 ± 8.7 | 65.8 ± 9.5 | 54.8 ± 11.2 | 59.7 ± 9.8 | 60.6 ± 8.0 | 66.7 ± 7.5 | 62.6 ± 9.8 |
| Total | 44  | 46  | 61  | 49  | 42  | 36  | 59  | 58  | 395   |

Mean weight and length ± standard deviation is presented in each age group for males and females.
N: number of participants; yo: years old.
Discussion

Different methods to assess the chronological age of adolescents have an interest in clinical, as well as in medico-legal terms. There have always been discrepancies and a degree of uncertainty when comparing different methods such as the atlases of GP and TW. These differences are more substantial when it comes to clinical evaluation of age, regarding individuals who come from different strata than the GP\textsuperscript{18} and TW\textsuperscript{19} cohorts. Also, even in the best of tests, chronological age is not equivalent to biological age in the medical world. This cross-sectional study was performed in order to evaluate the growth plates of the knee (femur and tibia) in a descriptive manner from a clinical standpoint. It was not designed to assess

| Table 3. Ossification stages of the distal femur per gender and age group (in years) of the volunteers on cartilage sequences and T1W-TSE. |
| --- |
| Gender | Age | Stage 4a | Stage 4b | Stage 4c | Stage 5 | Stage 2 | Stage 3 | Stage 4a | Stage 4b | Stage 4c | Stage 5 | Total |
| Male | 14 | 9 | 10 | 3 | 0 | 3 | 18 | 1 | 0 | 0 | 0 | 22 |
| 15 | 9 | 10 | 6 | 0 | 2 | 5 | 15 | 2 | 1 | 0 | 25 |
| 16 | 5 | 5 | 15 | 6 | 0 | 3 | 7 | 7 | 12 | 2 | 31 |
| 17 | 0 | 4 | 10 | 9 | 0 | 1 | 8 | 2 | 10 | 2 | 23 |
| 18 | 0 | 1 | 3 | 19 | 0 | 0 | 1 | 2 | 8 | 12 | 23 |
| 19 | 0 | 0 | 1 | 24 | 0 | 0 | 0 | 1 | 3 | 21 | 25 |
| 20 | 0 | 0 | 0 | 35 | 0 | 0 | 0 | 0 | 3 | 32 | 35 |
| 21 | 0 | 0 | 0 | 33 | 0 | 0 | 0 | 0 | 2 | 31 | 33 |
| Female | 14 | 9 | 4 | 6 | 3 | 0 | 3 | 12 | 4 | 3 | 0 | 22 |
| 15 | 1 | 4 | 9 | 7 | 0 | 1 | 8 | 0 | 10 | 2 | 21 |
| 16 | 0 | 1 | 6 | 23 | 0 | 0 | 0 | 4 | 19 | 7 | 30 |
| 17 | 0 | 1 | 4 | 21 | 0 | 0 | 1 | 0 | 12 | 13 | 26 |
| 18 | 0 | 0 | 0 | 19 | 0 | 0 | 0 | 0 | 4 | 15 | 19 |
| 19 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 1 | 10 | 11 |
| 20 | 0 | 0 | 0 | 24 | 0 | 0 | 0 | 0 | 2 | 22 | 24 |
| 21 | 0 | 0 | 0 | 25 | 0 | 0 | 0 | 0 | 1 | 24 | 25 |

T1W: T1-weighted; TSE: turbo spin echo sequence.

| Table 4. Ossification stages of the proximal tibia per gender and age group (in years) of the volunteers on cartilage sequences and T1W-TSE. |
| --- |
| Gender | Age | Stage 4a | Stage 4b | Stage 4c | Stage 5 | Stage 2 | Stage 3 | Stage 4a | Stage 4b | Stage 4c | Stage 5 | Total |
| Male | 14 | 7 | 11 | 4 | 0 | 0 | 13 | 8 | 1 | 0 | 0 | 22 |
| 15 | 6 | 4 | 13 | 2 | 1 | 4 | 9 | 3 | 8 | 0 | 25 |
| 16 | 2 | 1 | 21 | 7 | 0 | 0 | 6 | 2 | 17 | 6 | 31 |
| 17 | 0 | 1 | 9 | 13 | 0 | 0 | 2 | 1 | 12 | 8 | 23 |
| 18 | 0 | 0 | 2 | 23 | 0 | 0 | 0 | 0 | 4 | 19 | 23 |
| 19 | 0 | 0 | 2 | 24 | 0 | 0 | 0 | 0 | 3 | 22 | 25 |
| 20 | 0 | 0 | 0 | 35 | 0 | 0 | 0 | 0 | 2 | 33 | 35 |
| 21 | 0 | 0 | 0 | 33 | 0 | 0 | 0 | 0 | 1 | 32 | 33 |
| Female | 14 | 3 | 2 | 11 | 6 | 0 | 1 | 7 | 1 | 10 | 3 | 22 |
| 15 | 1 | 1 | 10 | 9 | 0 | 0 | 3 | 1 | 10 | 7 | 21 |
| 16 | 0 | 0 | 3 | 27 | 0 | 0 | 0 | 0 | 10 | 20 | 30 |
| 17 | 0 | 0 | 1 | 25 | 0 | 0 | 0 | 0 | 7 | 19 | 26 |
| 18 | 0 | 0 | 0 | 19 | 0 | 0 | 0 | 0 | 1 | 18 | 19 |
| 19 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 | 11 | 11 |
| 20 | 0 | 0 | 0 | 24 | 0 | 0 | 0 | 0 | 0 | 24 | 24 |
| 21 | 0 | 0 | 0 | 25 | 0 | 0 | 0 | 0 | 1 | 24 | 25 |

TSE: turbo spin echo sequence.
chronological estimations of age. Therefore, this study cannot draw any such conclusions nor does it aspire to.

The growth plate has not been thoroughly studied with MRI as the articular cartilage. We created our own staging scale with fewer subgrades and then decided to compare the traditional sequence (T1W) with a cartilage/water based sequence which we thought would be more efficient (even though T1W sequence remains as reference standard in skeletal assessment).

We found that the inter- and intra-observer agreements among the pediatric radiologists were in favor of using cartilage sequences. This result meant that it was easier to identify bone bridging and grade it when the background was black and the growth plate was white, thus the bone bridging was black, as was with the cartilage sequence. Conversely in T1W sequence the degree of uncertainty was comparatively higher due to that the eye has more difficulty in identifying almost off white over a grey/black background in the growth plate.

In this study a higher number of participants were graded as stage 4c rather than stage 5 on T1W in comparison to the cartilage sequences. This result meant that it was easier to identify bone bridging and grade it when the background was black and the growth plate was white, thus the bone bridging was black, as was with the cartilage sequence. Conversely in T1W sequence the degree of uncertainty was comparatively higher due to that the eye has more difficulty in identifying almost off white over a grey/black background in the growth plate.

In this study a higher number of participants were graded as stage 4c rather than stage 5 on T1W in comparison to the cartilage sequences. These cases had a mostly ossified growth plate minimally open at the edges on the T1W. Dvorak et al.9 termed this “residual physis,” stage 5 in their six-stage system. Vieth et al.24 described this finding as a centrally thin-lined “fusion’s scar” with a discontinuous intermediate line at the edges on T1W. Radiological studies have also shown visible remnants of the growth plate (physeal scar) on radiographs both in the knee25 and upper extremity.26,27 Faisant et al.25 showed a physeal scar in at least one of the bones of the knee joint in 96% of females and 98% of the males in a population aged between 15 and 40 years. A residual physis can be seen on T1W in the femur (both males and females) and in the tibia (in males) in all the older age groups, 18–21-year-olds. Among the 21-year-old females, there was one outlier graded as stage 4c on T1W (Table 4). On a second assessment of the images graded stage 4c and 5, we observed that the dorso-lateral aspect of the physis was thick and blury on T1W in line with a residual physis, but on the cartilage sequences there was no residual cartilage detectable nor was there a visible hyperintense line, indicating that the growth plate was completely fused and only the epiphyseal bone plate remains. A residual physis could be a potential confounder leading to individuals being under-graded as stage 4c instead of 5 on T1W. Observers’ feedback claimed that T1W was more difficult and time-consuming to evaluate than cartilage sequences. As time was not a measured factor in our study, this information is subjective and not objective. The main difficulty with T1W is that it depicts bone rather than cartilage, making it difficult to detect tiny bone bridging in such a narrow structure as the growth plate. We hypothesize that the water signal of the growth plate on a black background in the cartilage sequences makes easier to identify discrete bone bridging which is hard to detect on T1W.

We tried to overcome the complexity of classification in our stage system by removing the sub-classification of stage 4. A re-grading of the images improved the inter-observer agreement for the pediatric radiologists on both T1W (femur: \( \kappa = 0.81 \); tibia \( \kappa = 0.87 \)) and the cartilage sequences (femur: \( \kappa = 0.95 \); tibia: \( \kappa = 0.97 \)). However, it remained the same for general radiologists (femur: \( \kappa = 0.56 \); tibia: \( \kappa = 0.34 \)). At this point, due to the low performance of the general radiologists, we make the decision to evaluate cartilage sequences only by pediatric radiologists with different years of experience.

We found a higher intra- and inter-observer agreement for cartilage sequences at both the femur and the

| Table 5. Summary of the inter-observer agreement in Kappa value with percentage agreement in parentheses as well as the intra-class correlation coefficients with 95% confidence intervals in parentheses. |
|---|---|---|---|---|---|---|---|---|---|---|
| | Femur | | | | Tibia | | | | | |
| | T1W-TSE | Cartilage sequences | T1W-TSE | Cartilage sequences | | | | | |
| Inter-observer agreement | | | | | | | | | |
| Pediatric radiologists | Kappa | 0.73 | 0.86 | 0.82 | 0.90 | 0.95 | 0.97 | 0.95 | 0.97 |
| | ICC | 0.96 | 0.96 | 0.97 | 0.96 | 0.97 | 0.96 | 0.96 | 0.96 |
| | (82%) | (93%) | (90%) | (95%) | (95%) | (95%) | (95%) | (95%) |
| General radiologists | Kappa | 0.56 | 0.34 | 0.75 | 0.81 | 0.79 | 0.95 | 0.95 | 0.96 |
| | ICC | 0.95 | 0.90 | 0.95 | 0.96 | 0.96 | 0.96 | 0.96 | 0.96 |
| | (69%) | (56%) | (87%) | (91%) | (89%) | (95%) | (97%) | (97%) |
| Intra-observer agreement | | | | | | | | | |
| Pediatric radiologist | Kappa | 0.65 | 0.75 | 0.75 | 0.81 | 0.79 | 0.95 | 0.95 | 0.96 |
| | ICC | 0.95 | 0.95 | 0.95 | 0.96 | 0.95 | 0.95 | 0.95 | 0.95 |
| | (77%) | (89%) | (87%) | (91%) | (89%) | (95%) | (97%) | (97%) |

95% CI: 95% confidence interval; ICC: intraclass correlation coefficient; TSE: turbo spin echo sequence.
tibia. The highest inter-observer agreement (95%) and intra-observer agreement (91%) was found in the tibia on the cartilage sequences. Looking to the technical aspects, we tried to determine whether the size of slice overlapping improved the results, and a re-calculation of the Kappa values for the cartilage sequences was performed. Unexpectedly, the GE scanner with a 1.5 mm spacing between slices showed a lower Kappa value (femur: \( \kappa = 0.85 \); tibia: \( \kappa = 0.88 \)) for the 297 individuals examined, in comparison to value (femur: \( \kappa = 0.91 \); tibia: \( \kappa = 0.96 \)) for the 98 individuals examined on Philips and Siemens with a 3-mm spacing between the slices. Thus, reduction of overlapping did not improve the grading system.

We also assessed if the Kappa value varied over time by dividing the results from each age group and gender into three groups depending on the date of evaluation. On cartilage sequences, the Kappa value increased slightly over time, from \( \kappa = 0.83 \) to 0.90 for the femur, and from \( \kappa = 0.84 \) to 0.96 for the tibia. The same pattern was seen for the femur on T1W. The Kappa value for the femur increased from \( \kappa = 0.60 \) to \( \kappa = 0.81 \) for the pediatric radiologists and from \( \kappa = 0.40 \) to 0.69 for the general radiologists on T1W. Surprisingly, the Kappa value for the tibia had a peak in the middle portion, with \( \kappa = 0.36 \) for the general radiologists and \( \kappa = 0.90 \) for the pediatric radiologists. The Kappa value for the tibia increased from \( \kappa = 0.72 \) to 0.81 for the pediatric radiologists but decreased from \( \kappa = 0.34 \) to 0.32 for the general radiologists on T1W. We are uncertain why the lowest Kappa values for the tibia were seen in the last third for the general radiologists, but the experience of pediatric radiology seems to be favorable in terms of assessment of the cartilage in the growth plate and the ability to grade it according to our staging scale.

Our study has some limitations: Firstly, the entire population was examined post-puberty to avoid hormonal interference as much as possible. Secondly, from a technical point of view, we could have improved the spatial and the temporal resolution of the images by using a 3.0-T rather than a 1.5-T. A comparative study by Wong et al.\(^{28} \) showed that a 3-T system is superior in comparison to a 1.5-T system concerning the visualization of the knee anatomy as well as to detect and grade cartilage lesions. The choice of scanner was based on general availability in most tertiary care centers. Isovolumetric voxels and the option of multiplanar reconstructions might have improved the grading accuracy at the cost of time, regarding both the image acquisition and the grading. Thirdly, the slice orientation could have influenced the results. Partial volume effect, especially in the intercondylar area of the distal femur, could have been minimized if sagittal plane had been implemented in all sequences. Our slice orientation was based on prior studies. We reviewed four studies with only sagittal orientation of their T1W slices,\(^ {10,29-31} \) one study used both coronal and sagittal slices,\(^ {32} \) and three studies only coronal orientation but the chosen sequences were either T1W,\(^ {33} \) T2W,\(^ {34} \) or PDW.\(^ {16} \)

In conclusion, to our knowledge, this is the first study of a large healthy population dedicated to analyzing the growth plate, and the value of experience in pediatric radiology when assessing the maturing growth plate in adolescents and young adults. We have shown that cartilage sequences are superior to T1W when evaluating the growth plate and should be part of a standardized MRI protocol. Pediatric radiology experience is preferable in this assessment.

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**Authors’ contributions**

All authors listed in this article fulfill the ICMJE recommendations for authorship. OK performed the data collection, analysis, and primary write-up of the manuscript. OK, SD, and ON contributed parts of the manuscript. SD and CEF conceived the idea of the research project. All authors have had an input in reviewing and editing the final draft of this manuscript.

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**References**

1. Kronenberg HM. Developmental regulation of the growth plate. Nature 2003;423:332–336.

2. Nilsson O and Baron J. Fundamental limits on longitudinal bone growth: growth plate senescence and epiphyseal seal fusion. *Trends Endocrinol Metab* 2004;15:370–374.
3. Lui JC, Jee YH, Garrison P, et al. Differential aging of growth plate cartilage underlies differences in bone length and thus helps determine skeletal proportions. PLoS Biol 2018;16:e2005263.

4. Crema MD, Roemer FW, Marra MD, et al. Articular cartilage in the knee: current MR imaging techniques and applications in clinical practice and research. Radiographics 2011;31:37–61.

5. Jaimes C, Chauvin NA, Delgado J, et al. MR imaging of normal epiphyseal development and common epiphyseal disorders. Radiographics 2014;34:449–471.

6. Nguyen JC, Markhardt BK, Merrow AC, et al. Imaging of pediatric growth plate disturbances. Radiographics 2017;37:1791–1812.

7. Yun HH, Kim HJ, Jeong MS, et al. Changes of the growth plate in children: 3-dimensional magnetic resonance imaging analysis. Korean J Pediatr 2018;61:226–230.

8. Dvorak J, George J, Junge A, et al. Application of MRI of the wrist for age determination in international U-17 soccer competitions. Br J Sports Med 2007;41:497–500.

9. Dvorak J, George J, Junge A, et al. Age determination by magnetic resonance imaging of the wrist in adolescent male football players. Br J Sports Med 2007;41:45–52.

10. Schmidt S, Vieth V, Timme M, et al. Examination of ossification of the distal radial epiphysis using magnetic resonance imaging. New insights for age estimation in young footballers in FIFA tournaments. Sc J Sci 2015;55:139–144.

11. Tscholl PM, Junge A, Dvorak J, et al. MRI of the wrist is not recommended for age determination in female football players of U-16/U-17 competitions. Scand J Med Sci Sports 2016;26:324–328.

12. Timme M, Steinacker JM, Schmeling A. Age estimation in competitive sports. Int J Legal Med 2017;131:225–233.

13. EASO. EASO Age Assessment Practice in Europe. 2013. https://www.easo.europa.eu/sites/default/files/easo-practical-guide-on-age-assessment-v3-2018.pdf

14. Schmeling A, Schulz R, Reisinger W, et al. Studies on the time frame for ossification of the medial clavicular epiphyseal cartilage in conventional radiography. Int J Legal Med 2004;118:5–8.

15. Kellinghaus M, Schulz R, Vieth Y, et al. Enhanced possibilities to make statements on the ossification status of the medial clavicular epiphysis using an amplified staging scheme in evaluating thin-slice CT scans. Int J Legal Med 2010;124:321–325.

16. Dedouit F, Auriol J, Rousseau H, et al. Age assessment by magnetic resonance imaging of the knee: a preliminary study. Forensic Sc Int 2012;217:232.e1–232.e7.

17. Saint-Martin P, Rerolle C, Dedouit F, et al. Age estimation by magnetic resonance imaging of the distal tibial epiphysis and the calcaneum. Int J Legal Med 2013;127:1023–1030.

18. Greulich W, Pyle S. Radiograph atlas of skeletal development of the hand and wrist. 2nd ed. Stanford: Stanford University Press, 1959.

19. Tanner J, Whitehouse R, Cameron N, et al. Assessment of skeletal maturity and prediction of adult height (TW2 method). London: Academic Press, 1983.

20. Pyle S, Hoerr N. Radiographic atlas of skeletal development of the knee. Springfield: Charles C Thomas, 1955.

21. Thodberg HH, van Rijn RR, Jenni OG, et al. Automated determination of bone age from hand X-rays at the end of puberty and its applicability for age estimation. Int J Legal Med 2017;131:771–780.

22. Koo TK, Li MY. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. J Chiropr Med 2016;15:155–163.

23. McHugh ML. Interrater reliability: the kappa statistic. Biochem Med (Zagreb) 2012;22:276–282.

24. Vieth V, Schulz R, Heindel W, et al. Forensic age assessment by 3.0T MRI of the knee: proposal of a new MRI classification of ossification stages. Eur Radiol 2018;28:3255–3262.

25. Faisant M, Rerolle C, Faber C, et al. Is the persistence of an epiphyseal scar of the knee a reliable marker of biological age? Int J Legal Med 2015;129:603–608.

26. Davies C, Hackman L, Black S. The epiphyseal scar: changing perceptions in relation to skeletal age estimation. Ann Hum Biol 2015;42:348–357.

27. Davies C, Hackman L, Black S. The persistence of epiphyseal scars in the distal radius in adult individuals. Int J Legal Med 2016;130:199–206.

28. Wong S, Steinbach L, Zhao J, et al. Comparative study of imaging at 3.0 T versus 1.5 T of the knee. Skeletal Radiol 2009;38:761–769.

29. Kramer JA, Schmidt S, Jurgens KU, et al. Forensic age estimation in living individuals using 3.0 T MRI of the distal femur. Int J Legal Med 2014;128:509–514.

30. Kramer JA, Schmidt S, Jurgens KU, et al. The use of magnetic resonance imaging to examine ossification of the proximal tibial epiphysis for forensic age estimation in living individuals. Forensic Sci Med Pat 2014;10:306–313.

31. Fan F, Zhang K, Peng Z, et al. Forensic age estimation of living persons from the knee: comparison of MRI with radiographs. Forensic Sci Int 2016;268:145–150.

32. Pennoek AT, Bomar JD, Manning JD. The creation and validation of a knee bone age atlas utilizing MRI. J Bone Joint Surg Am 2018;100:e20.

33. Ottow C, Schulz R, Pfeiffer H, et al. Forensic age estimation by magnetic resonance imaging of the knee: the definite relevance in bony fusion of the distal femoral and the proximal tibial epiphyses using closest-to-bone T1 TSE sequence. Eur Radiol 2017;27:5041–5048.

34. Ekizoglu O, Hocaoglu E, Inci E, et al. Forensic age estimation via 3-T magnetic resonance imaging of ossification of the proximal tibial and distal femoral epiphyses: use of a T2-weighted fast spin-echo technique. Forensic Sci Int 2016;260:102e1–102e7.