Comparison of reliability of magnetic resonance imaging using cartilage and TI-weighted sequences in the assessment of the closure of the growth plates at the knee Acta Radiologica Open 9(9) 1–9 © The Foundation Acta Radiologica 2020 Article reuse guidelines: sagepub.com/journals-permissions DOI: 10.1177/2058460120962732 journals.sagepub.com/home/arr



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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 TIW 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 TIW was 82% ( $\kappa = 0.73$ ) and 77% ( $\kappa = 0.65$ ) for the femur and 90% ( $\kappa = 0.82$ ) and 87% ( $\kappa = 0.75$ ) for the tibia. The inter-observer agreement for general radiologists on TIW was 69% ( $\kappa = 0.56$ ) for the femur and 56% ( $\kappa = 0.34$ ) for the tibia. Cohen's kappa coefficient showed a higher inter- and intra-observer agreement for cartilage sequences than for TIW: 93% ( $\kappa = 0.86$ ) and 89% ( $\kappa = 0.79$ ) for the femur and 95% ( $\kappa = 0.90$ ) and 91% ( $\kappa = 0.81$ ) for the tibia.

**Conclusion:** Cartilage sequences are more reliable than TIW 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.<sup>1</sup> With age, the height of the growth plate gradually declines.<sup>2,3</sup> 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.<sup>4</sup>

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.<sup>5–7</sup> Forensic medicine has raised interest in the assessment of the growth plate to determine the age of athletes,<sup>8–12</sup> and more recently to assess the age of refugees lacking age documentation.<sup>13</sup> Different MRI sequences and rating scales have been used for grading the growth plate related to age,<sup>9,14–17</sup> 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)<sup>18</sup> and Tanner–Whitehouse (TW).<sup>19</sup> Less known methods include knee assessment by Pyle and Hoerr.<sup>20</sup> Semi-automated methods have been developed in the last decade.<sup>21</sup> 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  $160 \times 160$  mm field of view and a pixel resolution of  $256 \times 256$ . 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.<sup>16</sup> and Kellinghaus et al.<sup>15</sup> modified version of the developmental stages of Schmeling et al.<sup>14</sup>

- 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

| Manufacturer                              | GE               |                                  | Philips         |                                    | Siemens         |                                  |  |
|---|------------------|----------------------------------|-----------------|------------------------------------|-----------------|----------------------------------|--|
| Sequence                                  | TIW (FSE)        | Cartilage<br>sequence<br>(MERGE) | TIW (TSE)       | Cartilage<br>sequence<br>(3dWATSc) | TIW (TSE)       | Cartilage<br>sequence<br>(MEDIC) |  |
| Plane                                     | Sagittal         | Coronal                          | Sagittal        | Coronal                            | Sagittal        | Coronal                          |  |
| TR<br>TE<br>Flip and a                    | 406 ms<br>7.6 ms | 40 ms<br>18 ms                   | 458 ms<br>17 ms | 20 ms<br>7.64 ms                   | 600 ms<br>12 ms | 46 ms<br>14 ms                   |  |
| Slice thickness<br>Spacing between slices | 3 mm<br>4 mm     | 5 <sup>-</sup><br>3 mm<br>1.5 mm | 3 mm<br>3.3 mm  | 25 <sup>-</sup><br>3 mm<br>3 mm    | 3 mm<br>3.3 mm  | 3 mm                             |  |

Table 1. Technical specifications for each manufacturer and their different sequence settings.

3dWATSc: water selective cartilage scan; FSE: fast spin echo; GE: General Electric; MEDIC: multi-echo data image combination; MERGE: multiple echo recombined gradient echo; T1W: T1-weighted; TSE: turbo spin echo; TR: repetition time; TE: echo time.

**Fig. 1.** Stage 3 in both the distal femur and proximal tibia: (a) cartilage sequence, (b) TIVV.

**Fig. 2.** Stage 4a in both the distal femur and the proximal tibia on cartilage sequence (a) and TIW (b) with an epiphyseal-metaphyseal fusion (white arrows) that completes one-third or less of the growth plate.

the epiphysis, representing epiphyseal-metaphyseal fusion.

- Stage 4b (Fig. 3). The cartilage is not continuous. A hazy area involving between one-third and twothirds 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.

The slice with the highest grade of closure of the growth plate was selected and graded except for stage 5 in which all the slices must be completely closed. The methodology of staging is the same independent of the sequence chosen. This is to say, it is based on the percentage of bone bridging in the growth plate.

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 **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 TIW 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.)

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 interand 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; agreement.<sup>22</sup> agreement; 0.9 - 1.0excellent

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.<sup>23</sup>

## 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 18 years for males and 17 years for females. The maximum

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

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, and 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 TIW 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).

Table 2. Demographic Information.

| Age (yo)  | 14  | 15                                | 16                                    | 17                                     | 18  | 19                                  | 20  | 21                                    | Total                                   |
|---|---|-----------------------------------|---------------------------------------|--|---|-------------------------------------|---|---------------------------------------|---|
| Male (N)<br>Length (cm)<br>Weight (kg)            | $\begin{array}{c} 22 \\ 171.0 \pm 9.0 \\ 60.2 \pm 10.8 \end{array}$ | 25<br>175.3 ± 7.2<br>63.5 ± 9.9   | 31<br>177.6±7.5<br>67.6±12.3          | 23<br>180.4 ± 5.2<br>68.8 ± 11.9       | 23<br>181.2±7.9<br>74.9±14.4                  | 25<br> 78.8 ± 6.9<br>7 .3 ±  0.     | $35$   8   .2 $\pm$ 6.0<br>76.9 $\pm$   2.7 | 33<br>181.8±6.3<br>76.5±14.7          | 217<br>178.7±7.6<br>70.6±13.4           |
| Female (N)<br>Length (cm)<br>Weight (kg)<br>Total | $22\\ 163.2 \pm 6.4\\ 61.7 \pm 13.4\\ 44$                           | 21<br>164.4±4.3<br>59.4±9.0<br>46 | $30\\166.9 \pm 6.5\\60.8 \pm 8.7\\61$ | $26\\ 167.5\pm 6.0\\ 65.8\pm 9.5\\ 49$ | 9<br> 68.0 $\pm$ 5.8<br>54.8 $\pm$  1.2<br>42 | <br> 67.5 ± 7.3<br>59.7 ± 9.8<br>36 | $24\\ 165.5\pm5.9\\ 60.6\pm8.0\\ 59$        | 25<br>168.6 ± 7.3<br>66.7 ± 7.5<br>58 | $178\\166.5 \pm 6.3\\62.6 \pm 9.8\\395$ |

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

| Gender | Age | Cartilage sequences |          |          |         |         | TIW-TSE |          |          |          |         |      |
|--------|-----|---------------------|----------|----------|---------|---------|---------|----------|----------|----------|---------|------|
|        |     | Stage 4a            | Stage 4b | Stage 4c | Stage 5 | Stage 2 | Stage 3 | Stage 4a | Stage 4b | Stage 4c | Stage 5 | Tota |
| Male   | 14  | 9                   | 10       | 3        | 0       | 3       | 18      | I        | 0        | 0        | 0       | 22   |
|        | 15  | 9                   | 10       | 6        | 0       | 2       | 5       | 15       | 2        | I        | 0       | 25   |
|        | 16  | 5                   | 5        | 15       | 6       | 0       | 3       | 7        | 7        | 12       | 2       | 31   |
|        | 17  | 0                   | 4        | 10       | 9       | 0       | I       | 8        | 2        | 10       | 2       | 23   |
|        | 18  | 0                   | I        | 3        | 19      | 0       | 0       | I        | 2        | 8        | 12      | 23   |
|        | 19  | 0                   | 0        | I.       | 24      | 0       | 0       | 0        | I        | 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       | I       | 8        | 0        | 10       | 2       | 21   |
|        | 16  | 0                   | I        | 6        | 23      | 0       | 0       | 0        | 4        | 19       | 7       | 30   |
|        | 17  | 0                   | I        | 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        | I        | 10      | П    |
|        | 20  | 0                   | 0        | 0        | 24      | 0       | 0       | 0        | 0        | 2        | 22      | 24   |
|        | 21  | 0                   | 0        | 0        | 25      | 0       | 0       | 0        | 0        | I        | 24      | 25   |

**Table 3.** Ossification stages of the distal femur per gender and age group (in years) of the volunteers on cartilage sequences and TIW-TSE.

TIW: TI-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 TIW-TSE.

| Gender |     | Cartilage sequences |          |          |         |         | TIW-TSE |          |          |          |         |       |
|--------|-----|---------------------|----------|----------|---------|---------|---------|----------|----------|----------|---------|-------|
|        | 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        | I        | 0        | 0       | 22    |
|        | 15  | 6                   | 4        | 13       | 2       | I       | 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        | 1        | 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        | I        | 32      | 33    |
| Female | 14  | 3                   | 2        | 11       | 6       | 0       | I       | 7        | I        | 10       | 3       | 22    |
|        | 15  | I                   | I        | 10       | 9       | 0       | 0       | 3        | I.       | 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        | I        | 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        | I        | 24      | 25    |

TSE: turbo spin echo sequence.

# 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  $GP^{18}$  and  $TW^{19}$ 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

|                          | Femur   |             |                     |             | Tibia   |             |                     |                                       |  |
|--------------------------|---------|-------------|---------------------|-------------|---------|-------------|---------------------|---------------------------------------|--|
|                          | TIW-TSE |             | Cartilage sequences |             | TIW-TSE |             | Cartilage sequences |                                       |  |
|                          | Kappa   | ICC         | Kappa               | ICC         | Карра   | ICC         | Kappa               | ICC                                   |  |
| Inter-observer agreement |         |             |                     |             |         |             |                     |                                       |  |
| Pediatric radiologists   | 0.73    | 0.96        | 0.86                | 0.96        | 0.82    | 0.97        | 0.90                | 0.96                                  |  |
| _                        | (82%)   | (0.94–0.98) | (93%)               | (0.95–0.97) | (90%)   | (0.96–0.98) | (95%)               | (0.95–0.97)                           |  |
| General radiologists     | 0.56    | 0.95        | . ,                 | , ,         | 0.34    | 0.90        |                     | , , , , , , , , , , , , , , , , , , , |  |
| -                        | (69%)   | (0.94–0.96) |                     |             | (56%)   | (0.87–0.93) |                     |                                       |  |
| Intra-observer agreement |         |             |                     |             |         |             |                     |                                       |  |
| Pediatric radiologist    | 0.65    | 0.95        | 0.79                | 0.96        | 0.75    | 0.95        | 0.81                | 0.96                                  |  |
|                          | (77%)   | (0.93–0.96) | (89%)               | (0.95–0.97) | (87%)   | (0.94–0.96) | (91%)               | (0.95–0.97)                           |  |

**Table 5.** Summary of the inter-observer agreement in Kappa value with percentage agreement in parentheses as well as the intraclass correlation coefficients with 95% confidence intervals in parentheses.

95% CI: 95% confidence interval; ICC: intraclass correlation coefficient; 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 thoughT1W 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. These cases had a mostly ossified growth plate minimally open at the edges on the T1W. Dvorak et al.<sup>9</sup> termed this "residual physis," stage 5 in their six-stage system. Vieth et al.<sup>24</sup> 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 knee<sup>25</sup> and upper extremity.<sup>26,27</sup> Faisant et al.<sup>25</sup> 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 blurry 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 undergraded 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 subclassification 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 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.<sup>28</sup> 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 had 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,<sup>10,29–31</sup> one study used both coronal and sagittal slices,<sup>32</sup> and three studies only coronal orientation but the chosen sequences were either T1W,<sup>33</sup> T2W,<sup>34</sup> or PDW.<sup>16</sup>

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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