Growth of the Distal Femoral Physis, Epiphysis, and Cartilage Cap in the Skeletally Immature an MRI-Based Study

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Background: Anterior cruciate ligament (ACL) injury and reconstruction is becoming more common in the skeletally immature. This has led to the development of several physeal sparing and transphyseal reconstructions based on the current, limited, understanding of the distal femur in the skeletally immature. The purpose of this study was to describe the growth and development of the distal femoral physis, epiphysis, and cartilaginous cap in the skeletally immature.

Methods: Magnetic resonance images (MRIs) of two hundred fifty-four skeletally immature children (age range 1+0 to 15+11 years) were evaluated. Using a human supervised interactive segmentation program, KSlice, T1 coronal MRIs of the distal femur were used to generate three dimensional maps of the epiphysis, physis, metaphysis, and the cartilaginous cap. The maps then underwent measurement and shape analysis.

Results: Femoral epiphyseal volumes ranged from 0.58cm3 to 88.77cm3. Physeal volumes reached a maximum of 7.60cm3 in females and 8.73cm3 in males plateauing at 12-13 years of age in females and 14-15 years in males. Cartilage cap volumes ranged from 1.99cm3 to 30.61cm3 in females and from 0.94cm3 to 20.81cm3 in males, peaking at age 8.5 in males and 10 in females. Femoral epiphyseal width ranged from 1.19cm to 9.35cm and total femoral cartilage cap width ranged from 3.56cm to 9cm. Average measured epiphyseal, physeal, and cartilaginous cap volumes and widths were larger in males at all ages.

Conclusions

Distal femoral growth plate volume increases linearly before plateauing and decreasing at 12-13 in females and 14-15 in males. Physeal and epiphyseal growth rates are significantly faster in males than females, however, male and female distal femora undergo similar volumetric changes during maturation. Male and female cartilage caps undergo parabolic volumetric growth, peaking in females between 8 and 9 and in males at age 10.

Introduction

Diagnosis of anterior cruciate ligament (ACL ) injury in skeletally immature patients has become increasingly prevalent due to increased participation in cutting and pivoting sports, improved physical examination skills, and the increased use of MRI technology to aid in diagnosis ([Majewski, Susanne et al. 2006](#_ENREF_23)) ([Micheli 1995](#_ENREF_26)) ([Caine, Caine et al. 2006](#_ENREF_8)) ([Jones, Lyons et al. 2001](#_ENREF_17)). The diagnosis of ACL disruption without tibial spine avulsion has become more commonly diagnosed ([DeLee and Curtis 1983](#_ENREF_12); [Angel and Hall 1989](#_ENREF_4); [Sullivan 1990](#_ENREF_33)). While some physicians recommend conservative management consisting of activity modification, bracing, and strengthening until skeletal maturity, there is substantial evidence supporting a higher incidence of meniscal injury, cartilage damage, and osteoarthritis in skeletally immature patients with residual ligamentous instability ([Kannus and Jarvinen 1988](#_ENREF_18); [Sherman, Lieber et al. 1991](#_ENREF_32); [Graf, Lange et al. 1992](#_ENREF_14); [Andrews, Noyes et al. 1994](#_ENREF_3); [McCarroll, Shelbourne et al. 1995](#_ENREF_24); [Mizuta, Kubota et al. 1995](#_ENREF_28); [Pressman, Letts et al. 1997](#_ENREF_30); [Aichroth, Patel et al. 2002](#_ENREF_1); [Millett, Willis et al. 2002](#_ENREF_27); [Beasley and Chudik 2003](#_ENREF_6); [Dorizas and Stanitski 2003](#_ENREF_13); [Bales, Guettler et al. 2004](#_ENREF_5); [Woods and O'Connor 2004](#_ENREF_34); [Beynnon, Johnson et al. 2005](#_ENREF_7); [Moksnes, Engebretsen et al. 2008](#_ENREF_29)). As such there is an increasing trend towards early operative intervention in the treatment of ACL injuries in the skeletally immature ([Kannus and Jarvinen 1988](#_ENREF_18); [Sherman, Lieber et al. 1991](#_ENREF_32); [Graf, Lange et al. 1992](#_ENREF_14); [Andrews, Noyes et al. 1994](#_ENREF_3); [Aichroth, Patel et al. 2002](#_ENREF_1)) and a variety of surgical techniques including primary repair ([Sherman, Lieber et al. 1991](#_ENREF_32)), partial transphyseal ([Andrews, Noyes et al. 1994](#_ENREF_3); [Lo, Kirkley et al. 1997](#_ENREF_22)), physeal-sparing ([Kocher, Garg et al. 2005](#_ENREF_19); [Kocher, Garg et al. 2006](#_ENREF_20); [Xerogeanes, Hammond et al. 2012](#_ENREF_35)), and transepiphyseal reconstructions ([Anderson 2004](#_ENREF_2)) have been proposed and utilized. Each of these techniques attempts to address the unique challenges of recreating normal knee kinematics while avoiding growth arresting damage to the developing physes, however few studies have been able to provide a clear understanding of the anatomic growth and development of the physis.

Improvements in magnetic resonance imaging (MRI) and the advent of three dimensional modeling has aided in the study of the anatomy of the distal femur and distal femoral physis in the skeletally immature. Several studies have attempted to characterize the development of the distal femur using standard two dimensional MR imaging ([Harcke, Synder et al. 1992](#_ENREF_15); [Sasaki, Ishibashi et al. 2002](#_ENREF_31); [McKissick, Gilley et al. 2008](#_ENREF_25)) These studies have identified a characteristic pattern of growth plate ossification with the presence of a spherical ossification center centrally which flattens as it expands, paralleling the metaphysis, and is gradually replaced with bone ([Harcke, Synder et al. 1992](#_ENREF_15)). In Stage 3 of physeal closure, as described by Harcke, the 'Drop-out' sign occurs where coronal and saggital images show discontinuity of the physeal cartilage in the center of the growth plate ([Sasaki, Ishibashi et al. 2002](#_ENREF_31); [McKissick, Gilley et al. 2008](#_ENREF_25)) This 'bone bridge' formation may indicate the end of vertical growth at the distal femoral physis and signify a time at which it may be safe to drill a transphyseal tunnel during Anterior Cruciate Ligament reconstruction without risking growth deformity ([Higuchi, Hara et al. 2009](#_ENREF_16)).

While several studies have described the distal femoral physis using standard MRI imaging, few studies have attempted to quantify distal femoral physis development and those that have involved small sample sizes ([Craig, Cramer et al. 1999](#_ENREF_11); [Craig, Cody et al. 2004](#_ENREF_10)). The purpose of our study was to describe the growth and development of the distal femoral physis, epiphysis, and cartilaginous cap in the skeletally immature using a three dimensional model.

Materials and Methods

After Institutional Review Board approval (#00009363), sequential radiology department records were reviewed to obtain a list of all patients who had received a lower extremity MRI since 2002. Out of greater than 3,000 MRIs, we selected 254 studies, 133 male and 121 female, which met our inclusion criteria of having open distal femoral physes, no evidence of bony pathology including fracture, tumor, or other osseous lesion, no history of prior surgery, and were from patients between the chronological ages of 1 and 15. Obtaining a sufficient number of MRIs for statistical analysis of children between the ages of 6 and 15 was relatively simple due to the large number of patients in this age range who received an MRI of the knee without pathology, however, the number of MRIs of younger patients, especially one year olds, was limited which accounts for the discrepancy between total number of males and females included in the study. The MRIs were all T1 weighted coronal views of the knee and included a mixture of 3 Tesla(T) and 1.5T studies. The Digital Imaging and Communications in Medicine (DICOM) image libraries were converted into a single meta image and all patient identifiers were removed from the image to preserve patient privacy.

Following image conversion a proprietary program developed in collaboration with researchers at The Georgia Institute of Technology (Atlanta, GA), KSlice, was used in conjunction with a Bamboo drawing pad produced by Wacom (Vancouver, WA) to perform user-assisted segmentation. The user indicates which slices of the MRI to map and the underlying automatic algorithm uses a variational active contour with a local-global segmentation to create an image volume the same size as the original image based on mean image intensity ([Chan and Vese 2001](#_ENREF_9); [Lankton and Tannenbaum 2008](#_ENREF_21)). This results in a contoured image volume based on voxel spacing, which is then used to compute physical quantities of bones and physes including volume and lengths (**REFERENCE**).

The physis of the distal femur was easily segmented due to its low signal intensity surrounded by the high signal intensity of the epiphysis and metaphysis. The cartilaginous cap of the distal femur was more difficult to segment than any other component of this study because the low signal intensity of the cartilaginous cap was difficult to distinguish between surrounding soft tissue, muscle, and tendinous attachments. Due to the lack of sharply contrasting signal intensities, the segmentation program, KSlice, had difficulty determining the cartilaginous boundaries. As such, the cartilaginous caps frequently required manual segmentation. The ability to manually direct segmentation was built into KSlice to allow users to directly observe and dictate segmentation patterns thereby allowing for immediate correction of misidentification errors. Furthermore, the KSlice program actively learns from the user's input which enhances the ease and accuracy of analysis for future segmentation (Kolesov et al. 2011, Karasev et al. 2011).

The distal femoral physis, metaphysis, epiphysis, and cartilaginous cap from each coronal plane image was mapped using KSlice from anterior to posterior. During mapping the width of the epiphysis in the current slice was used as the lateral border for each image in order to help differentiate the physis from the cartilage cap in younger patients. The maps generated by KSlice then underwent measurement and shape analysis. During analysis the maps were split into medial and lateral components, width, depth, and length of all segments were taken individually and the measurements were differentiated by sex, plotted as growth versus age. In order to control for differences in child size and developmental stage an Analysis of Variance (ANOVA) was then performed to compare volume and length measurements between males and females.

**Need to further describe statistical evaluation and need to add a sentence stating that p value less than 0.05 was used to determine statistical significance.**

Results

Of the 254 MRIs reviewed: 133 were male and 121 were female with chronological age ranging from 1+0 to 15+11. Our results are summarized in figure XX

Female total femoral epiphysis volume ranged from 0.58cm3 to 78.19cm3 with medial and lateral volumes ranging from 0.29cm3 to 40.06cm3 and 0.28cm3 to 38.13cm3 respectively. Male total femoral epiphysis volume ranged from 1.15cm3 to 88.77cm3 with medial and lateral volumes ranging from 0.54cm3 to 46.46cm3 and 0.62cm3 to 42.31cm3 respectively. Males had faster medial, lateral, and total femoral epiphyseal growth rates than females (need to locate p-values or re-calculate to confirm) (Table \_\_\_\_ ). Physeal volumes increased linearly with age to a maximum volume of 7.60cm3 in females and 8.73cm3 in males before plateauing and decreasing at 12-13 years of age in females and 14-15 years in males. Female and male femoral cartilaginous cap volumes exhibited parabolic growth with male volumes ranging from 1.99cm3 to 30.61cm3 and peaking at 10 years of age and female volumes ranging from 0.94cm3 to 20.81cm3 peaking at 8.5 years of age. Femoral epiphyseal width ranged from 1.46cm to 9.35cm in males and 1.19cm to 8.95cm in females, increasing linearly with age at a faster rate (Need to locate p-values or re-calculate them) of 3.80mm/year in males compared to 3.07mm/year in females. Total femoral cartilage cap width ranged from 3.56cm to 8.00cm in females and from 3.74cm to 9.00cm in males.

In order to identify development trends as children aged ratios between the femoral physis and epiphysis volumes, medial and lateral epiphysis volumes, cartilage cap width and epiphysis volume, and cartilage cap to epiphysis volumes were calculated and differences between genders were assessed. Males had significantly larger ratios of femoral physis to epiphysis volumes, femoral cartilage cap to epiphysis volumes, and cartilage cap width to epiphysis volumes compared to females. There were no significant differences between males and females when comparing medial and lateral epiphysis volumes as both ratios began at 1 and approached 1.1 at age 15 Table XX.

**need tables with individual age group results for both males and females, ranges/SD/p-values/etc**

Discussion:

The distal femur represents the largest growth percentage for the maturing lower extremity. The proximal and distal ends of long bones contain a horizontal growth plate, commonly referred to as the physis, and a spherical growth plate, also known as the perichondral ring of LaCroix, in the epiphysis which allows epiphyseal growth. Both the physis and perichondral ring undergo three-dimensional growth at varying rates until skeletal maturity. Each of these growth centers is composed of three histologic zones: reserve, proliferative, and hypertrophic (Review of Orthopaedics 5th edition, Miller) **need to find a basic science chapter or review article rather than referencing Miller**. Although these zones cannot be differentiated on MRI the gross anatomy of the distal femoral physis can be evaluated. Craig et al. described the distal femoral growth plate as being concave when viewed superiorly, convex when viewed inferiorly, and having medial and lateral aspects which are contoured similar to the femoral condyles ([Craig, Cody et al. 2004](#_ENREF_10)). This morphology was observed in the MRIs reviewed in our study, however, over time, the shape of the physis changed as children developed.

Harcke et al. described four stages of physeal development: in Stage I there was a spherical or elliptical ossification center with a mainly cartilaginous epiphysis, in Stage II the ossification center had flattened and contoured to parallel the metaphysis, in Stage III no new cartilage is formed and the physis is gradually replaced with bone, and in Stage IV there is no cartilage remaining ([Harcke, Synder et al. 1992](#_ENREF_15)). **Locate and include 3D recon images of each of Harcke's stages**. As children developed the distal femur epiphysis and physis underwent volumetric growth and Harcke's stages were visualized. Males had significantly faster growth rates with respect to epiphyseal volume and width (figure/table xx), however, when the ratios of medial to lateral epiphyseal volumes were compared there was no difference between males and females (table/figure xx). This indicates that during development male and female distal femora undergo similar volumetric changes despite the fact that males grow at a faster rate.

As shown in figures xx, the male and female distal femoral physes followed linear volumetric growth patterns before beginning to decrease at age 12-13 in females and 14-15 in males. This decrease in physeal volume is synonymous to Stage III of physeal development. During Stage III cartilage replacement with bone is first noted centrally and the 'drop-out' sign occurs when the central area of the plate is completely replaced by bone ([Harcke, Synder et al. 1992](#_ENREF_15)). At this point longitudinal growth of the distal femur is complete but skeletal maturity/Stage IV has not been reached. Harcke et al. noted that the drop out sign was seen at age 14 to 15. In a study of 320 Japanese patients Sasaki et al. reported that the drop out sign occurred at age 13 in females, age 15 in males, and was visible in 60% of patients at age 12, 80% at age 13, and 97% of patients at age 14 ([Sasaki, Ishibashi et al. 2002](#_ENREF_31)). While the drop out sign was observed on several MRIs during the analysis, the presence or absence of the drop-out sign was not specifically recorded. The ratio of the male distal femoral physis to epiphysis volumes was significantly larger when compared to females until age 15 when the ratio began to approach zero (figure/table xx). Given the more rapid rate of volumetric growth and the fact that males reach skeletal maturity later than females it is not surprising that the physis to epiphysis volume is greater than that of females. However, the physis to epiphysis ratio trend toward zero serves as an indicator of growth plate closure and skeletal maturity. Further software development would allow for more accurate identification of the drop-out sign, indicating radiographic evidence of longitudinal growth arrest, which would improve preoperative planning and will allow physicians to use a standard transphyseal femoral tunnel during ACL reconstruction with no risk for growth disturbance.

A review of the current literature returned no studies specifically evaluating the growth and development of the femoral cartilaginous cap. Once accurate segmentation was performed both males and females exhibited parabolic growth with males peaking in cartilage cap volume near age 10 and females peaking between ages 8 and 9 (figure xx). Furthermore, the width of the cartilage of both sexes exhibited linear growth until age 15 when ossification was complete, and males again exhibited a significantly larger ratio of cartilage cap to distal femoral epiphysis than females (figures/table xx). Although the clinical significance of these findings is not clearly understood, improved understanding of the growth of the cartilage cap will aid in surgical planning in the future, especially as it relates to skeletally immature ligamentous surgery.

Limitations:

There are limitations to this study. The measurements were based on chronological rather than physiological age, and there may be innate differences from child to child on the rate of skeletal maturation. The number of male and female subjects in each age group was unequal. Although there was no difference in measurement accuracy between the 3T and 1.5T studies, it would have been preferable to use a standard resolution for all measurements. There were a smaller number of satisfactory MRIs available for analysis in ages 1 through 3, thus more information is needed to draw broad conclusions about younger patients. Finally, our results are not comparable to cadaveric/gross anatomic measurements for obvious reasons, however, accurate dissection of a gross specimen to perform volumetric analysis would be difficult, as such these measurements may be more accurate than anatomic dissection.

Conclusions:

KSlice is a novel 3D modeling program that provides accurate measurements of volumetric analysis from MRI studies while utilizing user-assisted segmentation to improve measurement reliability. The results from this study add to the current knowledge of distal femoral physis development and expand it with data from a younger patient population. Furthermore, it is the first study to perform volumetric measurements of the cartilaginous cap in skeletally immature patients. **need to add a sentence or two re-stating the factual results that we found including: 1. growth rates, 2. plateauing/growth plate closure, 3. cartilage cap disappearance, 4. no difference between male and female growth ratios**

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