Focal Periphyseal Edema (FOPE) Zone on MRI of the Adolescent Knee: A Potentially Painful Manifestation of Physiologic Physeal Fusion?

Andrew M. Zbojniewicz[1]
Tal Laor

OBJECTIVE. We have termed an MRI finding in the knees of adolescents characterized by a focal bone marrow edema pattern centered about the closing physis a "FOPE"—that is, focal periphyseal edema—zone. The cause of this appearance is unknown. Therefore, the purpose of this article is to review the MRI appearance of the FOPE zone and to postulate a causative mechanism.

MATERIALS AND METHODS. FOPE zones were identified on knee MRI examinations performed for pain in 12 patients (seven girls, five boys; age range, 11 years 9 months–15 years 8 months); the examinations were collected over 5 years. Clinical history, skeletal maturity, size and location of FOPE zone, and concomitant ipsilateral knee abnormalities were recorded at presentation and on follow-up MRI examinations when available. Bone ages were estimated from knee radiographs using published standards.

RESULTS. Fifteen FOPE zones measuring 2–27 mm were identified: eight were femoral; six, tibial; and one, fibular. All were centrally located. All physes were patent, albeit narrowed. The radiographic appearance of the physes was similar for both sexes. All patients with estimated bone ages of 11 and 12 years were girls. Two other girls had bone ages closer to 14 years, whereas all boys had estimated bone ages of 13 or 14 years.

CONCLUSION. On knee MRI, a FOPE zone can be seen in adolescents and likely relates to the early stages of physiologic physeal closure. It may be associated with pain particularly when no other MRI abnormalities are present. When the characteristic appearance of a FOPE zone is observed on MRI, we suggest that it not be mistaken for an abnormality, requires no invasive diagnostic procedure, and does not need imaging follow-up.

Abnormalities of the physis, which include both chronic and acute injuries such as fracture, have been described as a cause of debility in children and adolescents [1–3]. We repeatedly have encountered a finding on MRI that is distinct from other previously described disorders and that relates to the physis in adolescents who have been referred for the evaluation of knee pain. This MRI finding is characterized by a focal bone marrow edema pattern centered at the physis of the distal femur, proximal tibia, or proximal fibula and extending into both the adjacent metaphysis and epiphysis. We have termed this finding of a focal periphyseal edema (FOPE) pattern a "FOPE zone" (Fig. 1). The cause of this finding is unknown. Therefore, the purpose of our study was to evaluate the MRI appearance of FOPE zones in adolescent knees, to correlate MR findings with radiographic bone age estimates, and to postulate a causative mechanism.

Materials and Methods

This retrospective study was HIPAA compliant and was approved by the institutional review board. The requirement for informed patient consent was waived.

FOPE zones were identified on routine MRI examinations of the knee performed for acute or chronic pain in 12 patients (seven girls and five boys; age range, 11 years 9 months–15 years 8 months); the MR examinations were collected over 5 years (March 2005–February 2010). Patient history was obtained from clinic notes, which were accessed through the hospital clinical information system. The side of interest and duration of symptoms before and after the MRI examinations were recorded if available.

All knees were scanned on a 1.5- or 3-T imaging system. Each study included a coronal fat-suppressed fast spin-echo (FSE) T2-weighted sequence (1.5 T: TR range/TE range, 2740–3360/69.6–80.3; echo-train length [ETL], 6–8; matrix, 256–320 × 192; slice thickness, 3 mm; 3 T: TR/TE, 3360/61; ETL, 7; matrix, 320 × 256; slice thickness, 3 mm), a coronal STIR sequence (1.5 T: TR/TE, 4116/43; in-

Keywords: children, knee, marrow edema, MRI, physis, sports medicine

DOI:10.2214/AJR.10.6243

Received December 3, 2010; accepted after revision March 20, 2011.

[1]Both authors: Department of Radiology, Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine, 3333 Burnet Ave, Cincinnati, OH 45229-3039. Address correspondence to A. M. Zbojniewicz (Andrew.Zbojniewicz@cchmc.org).

AJR 2011; 197:998–1004

0361–803X/11/1974–998

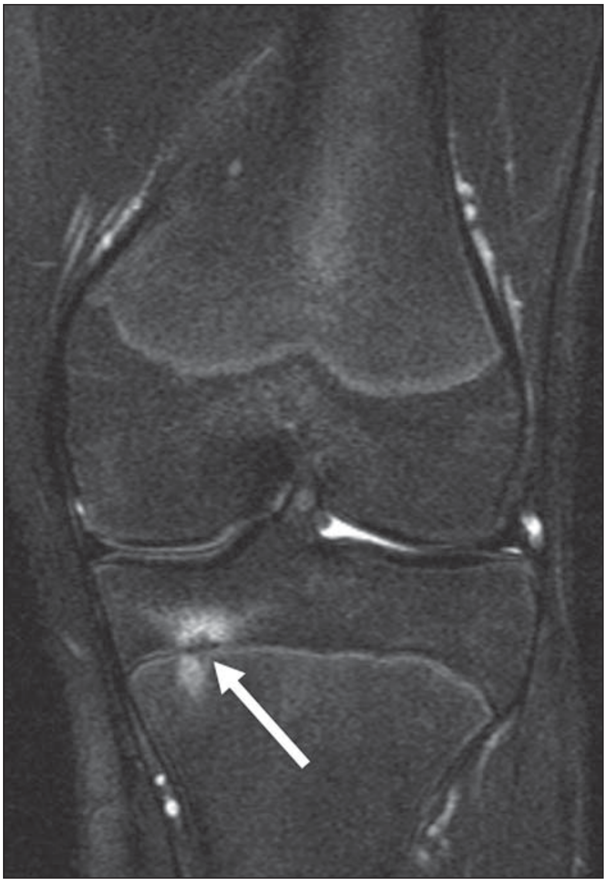


Fig. 1—14-year-old boy imaged for medial left knee pain of unknown duration. Patient is active in sports but recalled no specific traumatic event. Coronal fat-suppressed fast spin-echo T2-weighted image shows abnormal pattern of bone marrow edema within both epiphysis and metaphysis centered about anteromedial central tibia (*arrow*); we refer to this MR finding as "FOPE zone" (focal periphyseal edema zone). No additional abnormalities were identified at MRI evaluation.

version time, 150 ms; ETL, 10; matrix, 256 × 160; slice thickness, 5 mm), or a coronal fat-suppressed FSE intermediate-weighted sequence (1.5 T: TR range/TE range, 3000–3020/35–45; ETL, 7; matrix, 256–320 × 192; slice thickness, 3 mm). A sagittal fat-suppressed FSE T2-weighted sequence (1.5 T: TR range/TE range, 2000–3583/70.2–86.4; ETL, 7–8; matrix, 256–320 × 192–240; slice thickness, 3 mm; 3 T: TR/TE, 3000/61; ETL, 7; matrix, 320 × 256; slice thickness, 3 mm) or a sagittal fat-suppressed FSE intermediate-weighted sequence (1.5 T: TR/TE, 3020/45; ETL, 7; matrix, 320 × 240; slice thickness, 3 mm) was also available. In addition, all MRI examinations except one included a coronal spin-echo T1-weighted sequence (1.5 T: TR range/TE range, 350–900/10.58–22; matrix, 256–512 × 192–231; slice thickness, 3–5 mm; 3 T: TR range/TE range, 451–800/9.5–20; matrix, 384–400 × 288–332; slice thickness, 2.5–3.0 mm). Ten of 16 total examinations had a fat-suppressed 3D gradient-echo sequence that, depending on the vendor, consisted of TRs ranging from 20 to 50 ms, TEs ranging from 6 to 10 ms, flip angles ranging from 7° to 60°, and slice thicknesses ranging from 1.2 to 2.0 mm.

All MRI examinations were reviewed by a staff pediatric musculoskeletal radiologist (18 years' experience) and a staff fellowship-trained musculoskeletal radiologist (2 years' experience) by consensus. Skeletal maturation, the location and size of the FOPE zone, and concomitant ipsilateral knee abnormalities based on the MRI examination were recorded.

Skeletal maturation was reflected in the patency of the physes of the knee. The physes were defined as open or closed using a sagittal 3D gradient-echo sequence when available. Cartilage signal intensity across the entire physis was needed to define the physis as open. A fat-suppressed FSE T2-weighted sequence was used to determine physeal patency if no 3D gradient-echo sequence was available. The location of the FOPE zone was based on a cross-sectional map of the distal femoral, proximal tibial, or proximal fibular physis divided approximately into thirds using concentric rings and categorized as 1, peripheral; or 2, central. The inner two rings were considered central, whereas the outer ring was considered peripheral. These two locations were further subdivided into A, anterolateral; B, anteromedial; C, posterolateral; D, posteromedial; or E, bull's eye. The size of the FOPE zone was determined by the maximal transverse dimension measured at the level of the affected physis on either the sagittal or coronal sequence, whichever was greater. When a follow-up MRI examination was available, the marrow edema pattern was subjectively recorded as decreased, increased, or no change compared with the initial MR examination.

Evaluation for concomitant knee injuries included documentation of other sites of a bone marrow edema pattern and of injury to the cruciate ligaments, medial collateral ligament, lateral collateral ligament complex, patellofemoral joint, iliotibial band, articular cartilage, and menisci.

Conventional frontal and lateral radiographs of the knee obtained 0–21 days from the time of the MRI examination were available in 10 patients. The remaining two patients underwent radiography of the knee 4 months before and 5 months after MRI evaluation. Estimated bone ages were determined using the *Radiographic Atlas of Skeletal Development of the Knee* [4].

Results

The results are summarized in Table 1. Of the 12 patients included in this study, nine (75%) had symptoms that related to identifiable athletic activities and the remaining three did not reveal histories specifically associated with athletic activity. One patient had a chronic illness (i.e., juvenile idiopathic arthritis). Eight patients had left-sided symptoms and four had right-sided symptoms. The duration of symptoms, when known, ranged from 2 days to 1 year.

Fifteen FOPE zones were identified in the 12 patients. Eight FOPE zones were present in the femur; six, in the tibia; and one, in the fibula (Figs. 2 and 3). Two patients had two separate FOPE zones at presentation: One patient had one zone in the femur and one zone in the tibia, and the other patient had one zone in the femur and one zone in the fibula. One patient was shown to have developed a new FOPE zone on follow-up MRI evaluation. Ten FOPE zones were on the left side and five were on the right side.

FOPE zones were seen on all MRI sequences including non–fat-suppressed proton density and T1-weighted sequences but subjectively were most conspicuous when fat suppression was used with intermediate- or T2-weighting. All patients showed open, albeit relatively narrowed, physes (Fig. 4). FOPE zones measured at the level of the physis ranged in maximal diameter from 2 to 27 mm, but the extent of the adjacent bone marrow edema pattern was often larger. Within the central region, nine zones were central-lateral (2B or 2D), three were central-medial (2A or 2C), and three were bull's eye (2E).

In one patient, complete resolution of a FOPE zone in the tibia was seen on follow-up imaging 8 months later, but a new

TABLE 1: Clinical and Imaging Characteristics of Patients[a] With FOPE Zones

Patient				Location						
No.	Sex	Age	Side	Bone[b]	Distribution[c]	Size[d] (mm)	Bone Age (y)	Clinical History	Presenting Symptoms	Other Findings
1	F	11 y 11 mo	L	F	2A	10	11	Runner, dancer	Vague knee pain	Superolateral Hoffa fat edema, mild patellar chondral softening
2	M	15 y 6 mo	L	T	2A	2	13	Basketball	Basketball injury, vague knee pain	Partial discoid lateral meniscus
2[e]		15 y 8 mo	L	T	2A	2	13			At follow-up, FOPE zone had decreased in size but marrow edema pattern persisted
3	F	13 y 11 mo	R	F	2A	15	11	Remote history of patellar dislocation	No acute trauma, medial knee pain for 4 mo	Superolateral Hoffa fat edema, partial discoid meniscus
3[e]		14 y 9 mo	R	F	2A	15	11	Interval surgery for discoid meniscus and medial plica	Persistent pain	No change in FOPE zone; more prominent Hoffa edema, discoid meniscus treatment
4	M	14 y 6 mo	L	T	2B	7	14	Soccer, tennis	No acute trauma, persistent knee pain	None
5	F	14 y 4 mo	L	F	2A	13	14	Volleyball	Continued generalized pain despite physical therapy	Osgood-Schlatter disease changes
6	F	15 y 3 mo	R	T	2E	7	14	Juvenile idiopathic arthritis	Acute injury, pain for 2 wk	None
6[e]		15 y 4 mo	R	T	2E	7	14			At follow-up, FOPE zone had decreased in size but marrow edema pattern persisted
7	M	15 y 4 mo	L	T	2C	8	14	Football, track	No acute injury, medial knee pain for 1 y	Popliteal cyst
8	F	11 y 9 mo	L	F	2E	27	12		No known acute trauma, vague knee pain	None
9	M	15 y 0 mo	R	T	2E	19	14	Off-road bicycle racing, baseball, track, football	Acute football injury 2 d previously	Medial meniscal tear (nondisplaced)
9[e]		15 y 8 mo	R	F	2B	3	14		Reinjury	Tibial FOPE zone had resolved but there is a new femoral FOPE zone; medial meniscal tear (bucket-handle)
10	F	12 y 11 mo	R	F	2A	9	11	Competitive horseback rider	Chronic, 3–4 mo of knee pain	None
11	F	12 y 4 mo	L	F	2A	9	11	Volleyball	Acute patellar dislocation-relocation injury	Acute patellar dislocation-relocation injury
			L	T	2A	3	11			
12	M	13 y 8 mo	L	F	2B	12	14	Basketball, golf, baseball	Knee pain for 2 mo	None
			L	FB	2C	6				

Note—FOPE = focal periphyseal edema.
[a]All patients showed closing physes.
[b]Bone: F = femur, T = tibia, FB = fibula.
[c]Distribution: 1 = peripheral, 2 = central; A = anterolateral, B = anteromedial, C = posterolateral, D = posteromedial, E = bull's eye.
[d]Maximal dimension of FOPE zone.
[e]Follow-up MRI examination of patient listed in previous row.

Fig. 2—13-year-old male athlete who participates in several sports presented with 2-month history of left knee pain. Coronal fast spin-echo fat-suppressed T2-weighted image shows focal periphyseal edema (FOPE) zone, with bone marrow edema pattern centered about medial-central distal femoral physis (*arrow*). Similar zone was seen also in proximal fibula (not shown). No other abnormality of knee to account for patient's pain was identified at MRI evaluation.

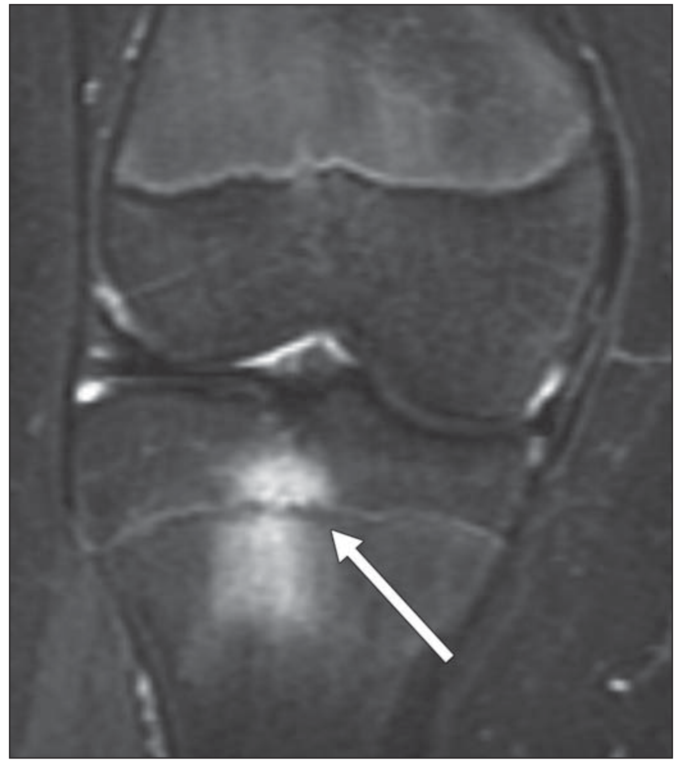


Fig. 3—15-year-old girl with juvenile idiopathic arthritis and right lateral knee pain after injury 2 weeks earlier. Coronal fat-suppressed fast spin-echo T2-weighted image shows FOPE (focal periphyseal edema pattern) zone (*arrow*) with typical bone marrow edema pattern involving both central tibial metaphysis and epiphysis.

FOPE zone was shown to have developed in a different location within the femur (Fig. 5). For the three other patients with follow-up MRI, MR examinations performed at 2 weeks, 7 weeks, and 10 months after the initial MR examination showed no change in the size of the FOPE zone at the level of the physis. The surrounding marrow edema pattern, although still present, was slightly decreased in two patients (at 2 weeks and 7 weeks) and was unchanged in one patient (at 10 months). One patient, in whom the possibility of infection was raised but no antibiotic treatment was initiated, showed a slight decrease in the size of the FOPE zone on follow-up imaging 2 weeks later. Seven patients had other MRI abnormalities identified in the knee, which are listed in Table 1. Eight patients had no known acute injury; of these patients, four had additional findings on MRI evaluation.

One patient had resolution of clinical symptoms after bearing no weight for 4 weeks, treatment similar to that for a stress fracture. One patient had resolution of symptoms after 6 weeks of physical therapy. One patient had incomplete relief despite two separate surgeries for a partial discoid meniscus and a mediopatellar plica. Nine patients did not return for orthopedic or other clinical follow-up related to the initial symptoms.

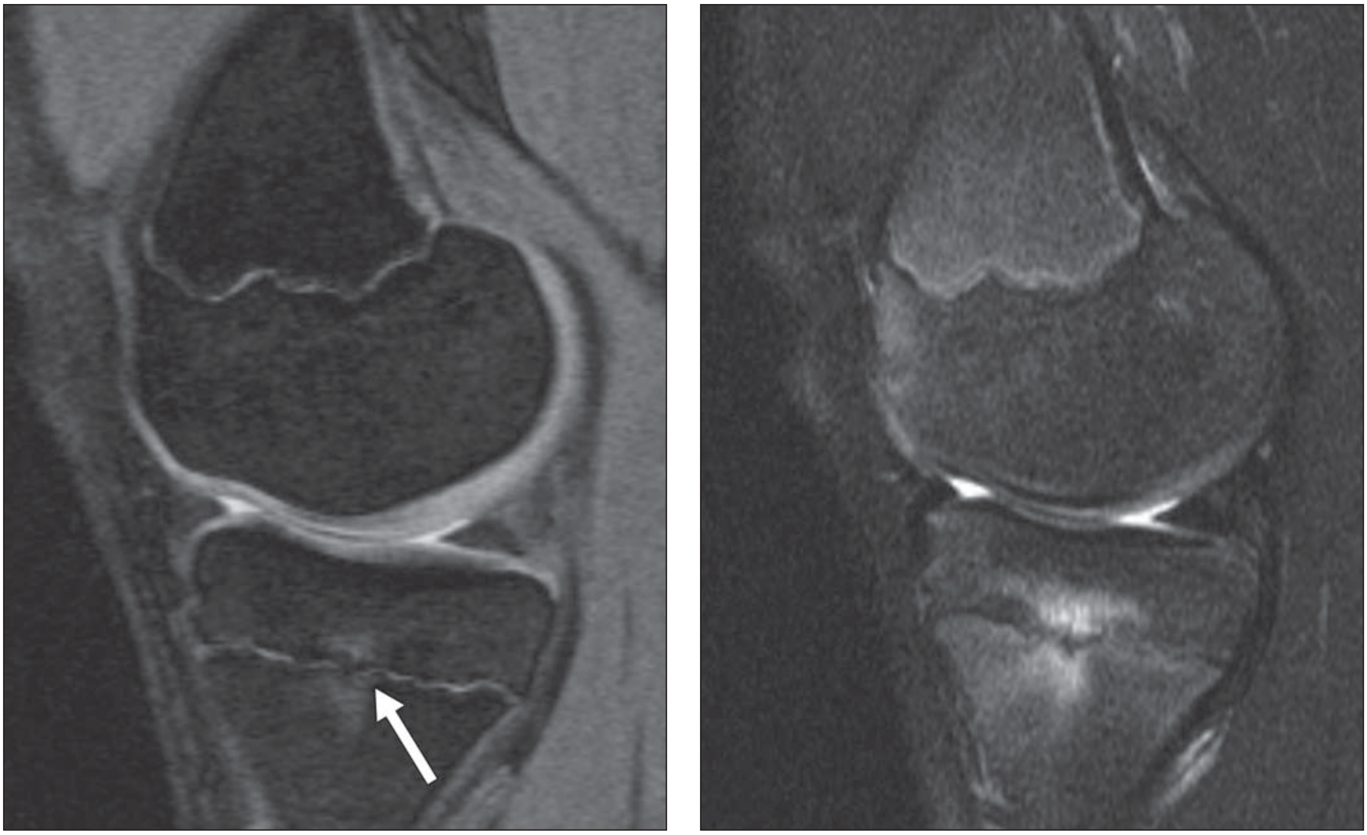
Estimated bone age based on the conventional radiographs ranged from 11 years to 14 years. All patients with bone ages of 11 and 12 years were girls. Two other girls had a bone age of 14 years, whereas all boys had estimated bone ages of 13 or 14 years. The conventional radiographic degree of skeletal maturation was similar for all 12 patients regardless of sex (Fig. 6).

Discussion

Given the remarkably consistent degree of skeletal maturation between subjects and the location within each affected bone, we postulate that the MRI appearance of a FOPE zone may be a manifestation of normal skeletal maturation—namely, physiologic physeal fusion.

Physeal fusion is a normal physiologic process of skeletal maturation. It begins with the first mineralized bridge between the diaphysis and epiphysis and ends with complete replacement of the cartilaginous physis by bone and marrow [5]. The process of physeal closure occurs through different types of union. This process ranges from an initial single narrow perforation of cartilage by bone to multiple initial perforations followed by spread to involve the entire physis [5]. Perforations can be peripheral, eccentric and central, or central within the physis. Each physis may have a different pattern of closure [6]. However, most frequently, the process of physeal fusion starts centrally and proceeds centrifugally with small remnants of cartilaginous physis remaining peripherally [6]. Previous MRI studies of the knee indicate that physeal closure is initiated centrally within the distal femur and proximal tibia [7, 8].

During the process of skeletal maturation, new cartilage is added to the epiphyseal border of the physis that subsequently is mineralized as a form of metaplastic bone, forming the first union between the epiphysis and diaphysis [5]. The formation of these metaplastic bone–neofibrocartilage perforations of the physis may act as tethers to



A B

Fig. 4—14-year-old male athlete (same patient as in Fig. 1) who presented with medial knee pain but no known injury.
A, Sagittal 3D gradient-echo sequence shows focal periphyseal edema (FOPE) pattern (*arrow*). FOPE zone is much less conspicuous on 3D gradient-echo sequence than on fat-suppressed T2 fast spin-echo sequence. This sequence was used, when available, to determine physeal patency. Distal femoral and proximal tibial physes are thinned but are still open.
B, Sagittal fat-suppressed fast spin-echo T2-weighted image shows same FOPE zone seen in **A** to better advantage.

the surrounding bone and may alter localized mechanics. The diminution in relative bone flexibility at these areas during stress may be accentuated in athletic teens, causing localized microtrauma with possible vascular damage and bleeding. This mechanism may account for the increased signal seen on fluid-sensitive MRI sequences. Consequently, these alterations may also result in pain similar to the tethering mechanism and resultant symptoms attributed to coalitions in the foot [9].

Although the cause of a tarsal coalition (thought to be a segmentation abnormality) and the cause of the early stage of physeal fusion (a normal physiologic process) are different, the end result of diminished localized bone compliance might be similar. Histopathologic analysis of patients with coalitions of the foot shows no inflammatory debris, but the MRI appearance in symptomatic coalitions reveals increased T2 signal intensity and enhancement consistent with a bone marrow edema pattern on either side of the site of coalition (Fig. 7). This edema pattern is thought to reflect the prominent neovascularity and bleeding seen related to microfractures in nonosseous coalitions [9] and is also a plausible mechanism for the increased fluid signal seen on MRI of patients with a FOPE zone.

All subjects included in our study had a strikingly similar degree of skeletal maturation based on conventional radiographs. Girls mature at an earlier chronologic age compared with boys. Therefore, as we anticipated, the conventional radiographic bone ages were younger in the female subjects. The onset of physiologic physeal fusion in girls is thought to be due to the relative greater levels of estrogenic compounds, which accelerate cartilage replacement and osseous maturation [10].

All subjects showed either a bull's-eye or eccentric central location of the FOPE zone in the region of expected initiation of physiologic physeal fusion. Follow-up imaging of one patient 8 months later showed interval closure of the central physis with resolution of the periphyseal edema pattern. We found no bone predilection for FOPE zones within the knee in our small cohort; similarly, there was no substantial sex dominance. This finding is not surprising because all long bones in both sexes undergo physiologic physeal fusion.

Although all patients in this study were imaged for knee pain, it is unclear whether the bone marrow edema pattern that surrounds the FOPE zone is responsible for the presenting symptoms. Two thirds of the subjects in our study did not have an acute injury, suggesting that the FOPE zone could result also from chronic repetitive microtrauma at the site of focal tethering. Nearly half of the patients had no other finding on MRI evaluation to explain the knee pain.

Of the patients with additional MRI findings, one patient had an intact partial discoid lateral meniscus. This patient had resolution of

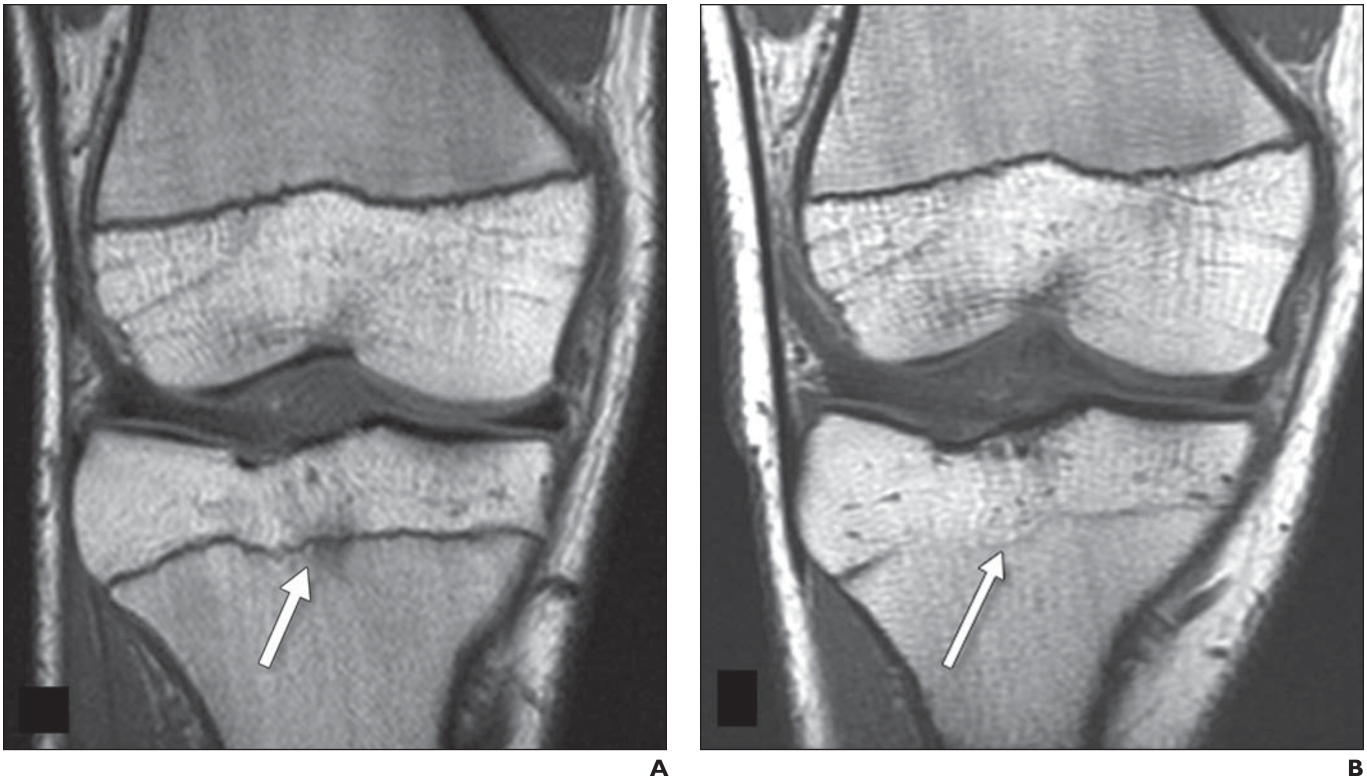


Fig. 5—15-year-old boy with right knee pain after football injury.
A, Coronal spin-echo T1-weighted image shows focal periphyseal edema (FOPE) pattern (*arrow*), or FOPE zone, with decreased signal relative to surrounding fatty marrow signal in both metaphysis and epiphysis centered about proximal tibial physis. This patient also had nondisplaced medial meniscal tear and posterolateral marrow edema pattern (not shown).
B, Coronal spin-echo T1-weighted image obtained 8 months after **A** when patient presented with medial knee pain after baseball injury. Bridging trabecular bone (*arrow*) is now seen across area of physis previously involved with FOPE zone. Meniscal tear, which had not been treated, had progressed to bucket-handle tear (not shown) and likely accounts for patient's pain.

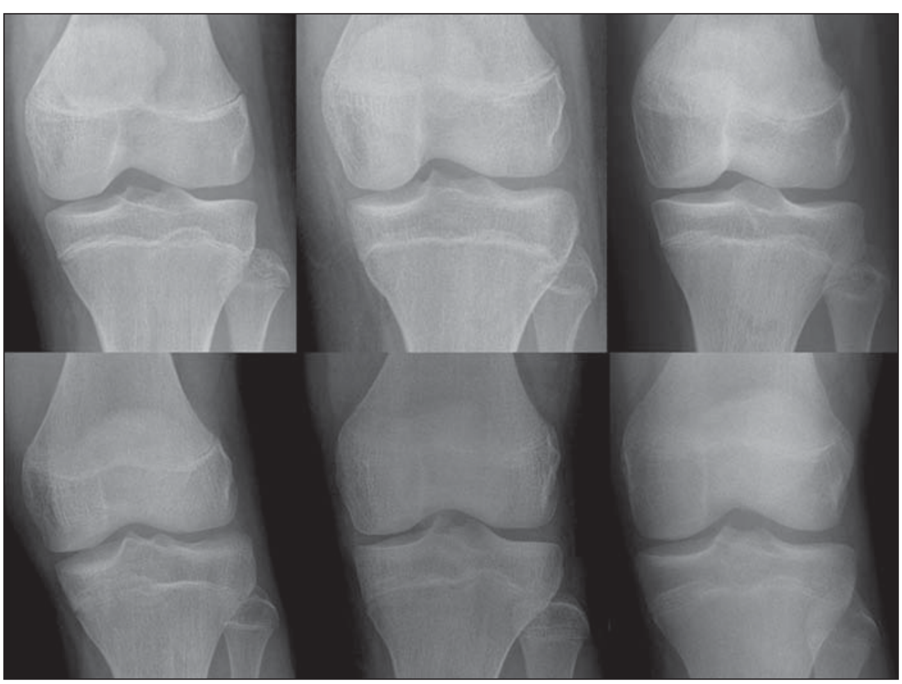


Fig. 6—Frontal knee radiographs (uniformly projected to allow comparison) of three girls (top row) ranging in age from 11 years 11 months to 14 years 4 months and three boys (bottom row) ranging in age from 13 years 8 months to 15 years 4 months. All had FOPE (focal periphyseal edema pattern) zones identified on knee MRI examinations. There is striking similarity in degree of skeletal maturation and extent of physeal closure in all patients both within and between sexes.

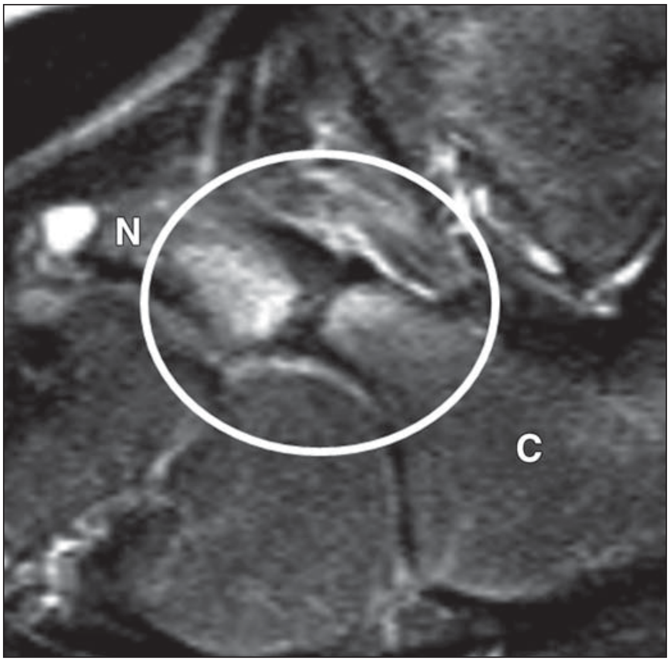


Fig. 7—9-year-old male athlete with right subtalar foot pain. Sagittal fat-suppressed fast spin-echo T2-weighted images of foot show nonosseous calcaneonavicular coalition with bone marrow edema pattern (*circle*) on either side of joint, similar to MRI appearance of FOPE (focal periphyseal edema) zone. N = navicular bone, C = calcaneus.

pain at 6 weeks after physical therapy; however, follow-up MRI examination at 7 weeks showed persistence of the FOPE zone, although the marrow edema pattern was slightly less conspicuous. An additional patient with edema in Hoffa fat-pad and a partial discoid lateral meniscus continued to have pain after surgical treatment of the meniscus and resection of a mediopatellar plica. Follow-up MRI examination of this patient at 10 months showed no substantial change in the appearance of the distal femoral FOPE zone. Five other patients had abnormal findings within the affected knee, and whether identification of a FOPE zone was incidental is unknown. Because three quarters of the subjects in our study were involved in competitive athletic activities, we suggest that the additional stresses placed on the knee during high-level play might accentuate the tethering of early physeal fusion more than in less active adolescents.

The limitations of our study include its small size and retrospective nature. We collected the subjects from patients who presented with knee pain and had been referred for MRI evaluation. A FOPE zone may also be present in asymptomatic maturing adolescents who have no indication for MRI evaluation. No nerve endings are found at the site of tarsal coalitions, and the pain from this entity is presumed to be secondary to stimulation of the nearby articular capsule and periosteum [9]. Similarly, it is possible that some FOPE zones in maturing adolescents are so localized and central that they do not ultimately result in irritation of nerve endings in the joint capsule or adjacent periosteum.

No histology results were available in any subject to confirm that physiologic physeal fusion is the process responsible for the MRI finding of a FOPE zone. Additionally, because these patients were near skeletal maturity, the physes were inherently thin and, therefore, focal physeal signal intensity abnormalities that might be associated with a FOPE zone were not delineated. One subject did show resolution of the FOPE zone at 8 months' follow-up and the other three patients with follow-up MRI examinations showed no decrease in zone diameter at the level of the physis, but the degree of marrow edema pattern was subjectively decreased in two of those three patients. It is possible that these FOPE zones were imaged early during the course of physeal closure.

The temporal course of physeal closure is not well understood. Serial conventional radiography of the phalanges in the hand showed a mean of 13 months between cessation of longitudinal growth and radiographically complete closure [10]. This time gap may account for the relatively little change seen in the FOPE zones of the knee at follow-up imaging in patients who might have presented early in the process of physeal closure and were not reimaged at a time interval long enough to see change. We expect the FOPE zone to be a transient finding until full skeletal maturation; however, we do not have follow-up MRI to resolution in all subjects. In addition, we did not have long-term clinical follow-up on all patients.

Whether a FOPE zone is found in the physes of all other bones that undergo endochondral ossification is unknown. However, we have anecdotally seen a similar FOPE zone in the proximal femur of an adolescent. Lastly, bone age determination from radiographs inherently is subjective.

In summary, we suggest that the FOPE zone identified in the knee of adolescents around the time of expected skeletal age of maturation likely relates to the early stages of physiologic physeal fusion. This MRI appearance also may be responsible for the patient's clinical symptom of pain, particularly when no other imaging findings are present. When the characteristic appearance of a bone marrow edema pattern centered about the central portion of a closing physis at the knee in an adolescent is observed, we suggest that this finding should not be mistaken for an abnormality, requires no invasive diagnostic procedure, and does not need imaging follow-up.

References

1. Salter R, Harris W. Injuries involving the epiphyseal plate. *J Bone Joint Surg Am* 1963; 45:587–622
2. Laor T, Wall EJ, Vu LP. Physeal widening in the knee due to stress injury in child athletes. *AJR* 2006; 186:1260–1264
3. Shih C, Chang CY, Penn IW, Tiu CM, Chang T, Wu JJ. Chronically stressed wrists in adolescent gymnasts: MR imaging appearance. *Radiology* 1995; 195:855–859
4. Pyle S, Hoerr N. *Radiographic atlas of skeletal development of the knee: a standard of reference*, 1st ed. Springfield, IL: Charles C Thomas, 1955
5. Haines RW. The histology of epiphyseal union in mammals. *J Anat* 1975; 120:1–25
6. Ogden J. *Anatomy and physiology of skeletal development: skeletal injury in the child*. New York, NY: Springer-Verlag, 2000:17–18
7. Harcke HT, Snyder M, Caro PA, Bowen JR. Growth plate of the normal knee: evaluation with MR imaging. *Radiology* 1992; 183:119–123
8. Sasaki T, Ishibashi I, Okamura Y, Toh S, Sasaki K. MRI evaluation of growth plate closure rate and pattern in the normal knee joint. *J Knee Surg* 2002; 15:72–76
9. Kumai T, Takakura Y, Akiyama K, Higashiyama I, Tamai S. Histopathological study of nonosseous tarsal coalition. *Foot Ankle Int* 1998; 19:525–531
10. Uhtoff H, Wiley J. Defining the growth plate. In: Uhthoff HK, Wiley JJ, eds. *Behavior of the growth plate*. New York, NY: Raven Press, 1985:12–13