

# Three-Dimensional Analysis of Quantitative MRI of the Secondary Ossification Center and Metaphysis in Children with Legg-Calvé-Perthes Disease

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**INTRODUCTION:** Legg-Calvé-Perthes disease (LCPD) is a pediatric hip disorder caused by avascular necrosis of the femoral head, potentially leading to long-term deformity if not detected and monitored early [1]. Gadolinium-based contrast-enhanced MRI (CE-MRI) is the current clinical standard for assessing ischemia [2], but non-contrast techniques may also be useful as complementary techniques to evaluate compositional changes in bone and marrow as a result of ischemic injury and disease progression. Quantitative MRI methods, including T2 relaxation time mapping, fat fraction (FF) mapping, and molecular diffusion (D) mapping, have shown promise for this purpose in both animal models [3–7] and studies of patients with LCPD [8,9]. Building upon a preliminary study of T2, FF, and D mapping of the femoral heads in children with LCPD [8], this study analyzed quantitative MRI values in the 3D secondary ossification center (SOC; i.e., the bone and bone marrow of the femoral epiphysis) and metaphysis in children with Waldenström stage I or II LCPD. We hypothesized that T2 and D would increase and FF decrease in the affected vs unaffected femoral heads in both the SOC and metaphysis.

**METHODS:** This study was approved by our local IRB and included 10 participants (6–9 years old, 8 males, 2 females) with unilateral LCPD in Waldenström stage I or II (Table 1). Bilateral hip images were acquired using a clinical 3T MRI scanner. Research sequences included: (i) T2 mapping: multi-slice multi-echo spin echo (TR/TE = 3500 / 10,20,30,40,50,60,70 ms, ETL = 24, spatial resolution = 0.7x0.7 mm<sup>2</sup>, slice thickness = 3.0 mm, GRAPPA=2, and fat sat); (ii) FF mapping: VIBE Dixon (TR/TE1/TE2 = 5.90/2.46/3.69 ms, spatial resolution = 0.8x0.8 mm<sup>2</sup>, slice thickness = 2.0 mm, CAIPIRINHA=2, flip angle = 20); and (iii) diffusion (D) mapping: RESOLVE (b-values = 0,20,30,40,50,60,70,80,90,100,300,500 s/mm<sup>2</sup>, TR/TE1/TE2 = 2800/70/121 ms, EPI factor = 120, readout segments = 5, spatial resolution = 1.5x1.5 mm<sup>2</sup>, slice thickness = 3.0 mm, GRAPPA=2, and fat sat). Prior to analysis, T-NORDIC [10] and MPPCA [11] denoising were applied to T2 and D maps, respectively. T2, FF, and D were calculated on a pixel-by-pixel basis using (i) a simple mono-exponential curve, (ii) two-point Dixon [12], and (iii) an Optimized Analytical Segmented approach (opAS) [13], respectively. Manual 3D segmentation of two regions of interest (ROIs), the SOC and metaphysis, was performed using anatomical references from Dixon water images, and subsequently, T2 and D maps were rigidly co-registered to the reference image and segmentation. Median T2, FF, and D values were extracted for each ROI and compared between affected and unaffected hips using Wilcoxon signed-rank tests (p<0.05).

**RESULTS:** Paired comparisons of T2, FF, and D values are shown in Figure 1. In the SOC, T2 values showed no consistent directional change between affected and unaffected femoral heads (p=0.719), whereas FF was significantly decreased (mean decrease 42±21%, p=0.005) and IVIM D was significantly increased (mean increase 0.67±0.35 × 10<sup>-3</sup> mm<sup>2</sup>/s, p=0.005) in the affected vs unaffected femoral heads. In the metaphysis, T2 and D were significantly increased in affected femoral heads (mean increase of 17±12 ms, p=0.009 and 0.41±0.47 × 10<sup>-3</sup> mm<sup>2</sup>/s, p=0.007, respectively), while FF showed little to no change (p=0.075). Figure 2 shows T2, FF, and D maps and histograms for a representative case (Participant #10). In this case, heterogeneous T2 and FF patterns are apparent in the SOC: regions with higher T2 in affected vs. unaffected hips correspond to areas of higher FF, while regions with lower T2 in affected vs. unaffected hips had lower FF. These heterogeneous T2 and FF patterns were observed in 6/10 participants. For the 3D maps of the metaphysis, T2 and D show increases, and FF shows little to no changes in the affected vs. unaffected femoral heads.

**DISCUSSION:** This study demonstrates that 3D analysis of quantitative MRI can detect and localize compositional alterations in the femoral head and metaphysis due to LCPD in children. The observed FF decrease and D increase in the SOC are consistent with prior reports of marrow fat loss and increased extracellular water due to ischemic injury [3,6]. The heterogeneity for T2 and FF observed in Figure 2 and in 6/10 participants may reflect localized differences in marrow composition and water content associated with disease evolution. Regions of increased T2 with higher FF may correspond to areas of fatty marrow infiltration or less severe or earlier ischemic injury, whereas regions with decreased T2 and lower FF may indicate persistent ischemia with reduced lipid content. These findings suggest that the combined use of T2 and FF may provide unique insights into the localized severity of disease and its evolution. The metaphyseal increases in T2 and D suggest that the effects of ischemic injury may extend beyond the epiphysis, an MRI finding that has been reported in animal models using T2 [7] and in children with LCPD using D [9].

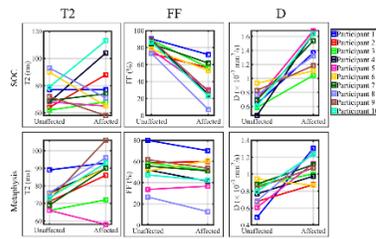
**SIGNIFICANCE/CLINICAL RELEVANCE:** Quantitative MRI provides a feasible, non-contrast-enhanced approach for assessing tissue composition in the SOC and metaphysis of children with LCPD. FF and D may provide a robust sensitivity to ischemic injury, while spatial T2–FF patterns may provide additional insight into disease heterogeneity and progression. These methods may complement CE-MRI for staging and monitoring of LCPD, with potential utility in evaluating treatment response.

**REFERENCES:** [1] Kim HK. JBJS Am 2012; 94:659–669. [2] Laine JC, et al. J Am Acad Orthop Surg 2018; 26:526–536. [3] Menezes NM, et al. Radiology 2007; 242:129–136. [4] Johnson CP, et al. Radiology 2018; 289:386–395. [5] Johnson CP, et al. JOR 2022; 40:484–494. [6] Buko EO, et al. JOR 2024; 42:855–863. [7] Buko EO, et al. JOR 2024; 42:2277–2286. [8] Buko EO, et al. Proc ORS 2025; Abstract No. 139. [9] Yoo WJ, et al. Radiology 2016; 279:567–570. [10] Moeller S, et al. bioRxiv 2023; 2023.11.21.568193. [11] Veraart J, et al. MRM 2016; 76:1582–1593. [12] Coombs BD, et al. MRM 1993; 38:884–889. [13] Buko EO, et al. MRM 2025; doi.org/10.1002/mrm.30636.

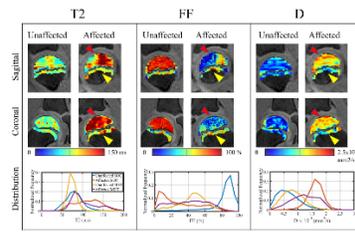
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Participant #	Gender	Age (Years)	Affected Hip	Waldenström LCPD stage
1	Female	7	Left	Ib
2	Male	8	Right	Ib
3	Female	8	Right	Ib
4	Male	8	Right	Ib
5	Male	9	Left	Ib/IIa
6	Male	7	Right	Ib
7	Male	9	Left	Ib
8	Male	6	Right	IIa/b
9	Male	6	Right	IIb
10	Male	9	Right	IIb

**Table 1.** Demographic information of the study participants.



**Figure 1.** The median values of the estimated T2, fat fraction (FF), and molecular diffusion (D) within the SOC and metaphysis of the affected and unaffected femoral heads. Overall, within the SOC, T2 showed no specific changes, FF decreased, and D increased in the affected vs. unaffected femoral heads. Within the metaphysis, T2 and D increased in the affected vs. the unaffected femoral heads, while FF showed little to no change.



**Figure 2.** T2, fat fraction (FF), and molecular diffusion (D) maps of the SOC and metaphysis of the unaffected and affected femoral heads of a representative case (Participant #10) and the corresponding histograms of values in the entire SOC and metaphysis. In the SOC, T2 increased, FF decreased, and D increased in the affected vs. unaffected femoral heads (red arrows). T2 and FF had a heterogeneous response in the affected femoral head, with regions of increased T2 compared to the unaffected femoral head marked with higher FF. In the metaphysis, T2 and D increased, and FF had little to no change in the affected vs. unaffected femoral head (yellow arrows).