RADIOGRAPHIC ENCHONDROMA SURVEILLANCE: ASSESSING CLINICAL OUTCOMES AND COSTS EFFECTIVENESS

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ABSTRACT

Background: Enchondromas are a common long bone benign tumor often discovered incidentally on imaging for adjacent pathology. These benign cartilaginous tumors can be difficult to differentiate from low-grade chondrosarcomas on imaging and histology. Multiple advanced imaging studies and clinic visits are required to confirm stability. Surveillance for these lesions can lead to significant patient costs without a clear oncologic or functional benefit. There is a lack of evidence-based consensus guidelines for the surveillance of enchondromas. The purposes of our study are: 1) to determine the number and proportion of low-grade cartilaginous tumors that demonstrate growth or require treatment and 2) to optimize the efficacy and cost-effectiveness of surveillance strategies for detecting biologically active lesions.

Methods: A retrospective single-institution study was performed on 55 subjects, 18 years or older, with long bone enchondromas without concerning radiographic characteristics that were referred to our institution's orthopaedic oncology clinic from July 1, 2009 to November 30, 2016. All subjects had at least 12 months of radiographic follow-up. We performed a chart and imaging review to assess for growth of the lesion over time. The number of pre-referral imaging and the number of follow-up imaging studies were recorded. The costs of plain radiographs and advanced imaging were estimated using our institution's global charge list in 2016.

Results: For stable enchondromas, 35 out of 52 lesions (67.3%) presented in the lower extremities compared to three out of three (100%) growing cartilaginous tumors. Three out of 55 (5.45%) long bone cartilaginous lesions exhibited growth at a median of 23 (range 21-25 months) follow-up. There was no apparent difference in median presenting age for stable versus growing lesions (58.5 versus 55.0 years old, p =0.5673) or median lesion size at presentation (4.1 cm versus 3.6 cm, p = 0.2923). None of these lesions presented with pain attributable to the lesion. One out of seven biopsied cartilaginous lesions (four stable and three growing) had a histology diagnosis of grade 1 chondrosarcoma. There was no significant difference in the median number of total clinical visits for stable (four) and growing (five) enchondromas (p = 0.0807). The median pre-referral costs per patient were: plain radiographs ($383.00), CT scans ($0.00), and MRI imaging ($3,969.00). The median post-referral costs for plain radiographs and MRI per patient were $1,326.00 and $4,668.00, respectively. The annual median costs for plain radiographs and MRI were $609.23 and $2,240.64, respectively.

Discussion: In conclusion, enchondroma growth was a rare event and typically occurred at two years follow-up in our series. Given the low risk for malignant transformation, we propose surveillance with plain radiographic follow-up for stable enchondromas every 3-6 months for the first year and then annually for at least three years of total follow-up. The most significant costs savings can be made by limiting MRI imaging in the absence of clinical or radiographic concern. Additional studies are needed to determine the long-term risk of growth or declaration of chondrosarcoma.

Level of Evidence: IV

Keywords: enchondroma, cartilaginous tumor, surveillance, cost analysis

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INTRODUCTION

Enchondromas are a common subset of benign cartilaginous lesions found in long bones with an estimated incidence of 2.1-2.8%.[1,2] The aggressiveness of benign

tumors is described by Enneking by three stages (1=latent, 2=active, 3=aggressive).[3] Enchondromas are often discovered incidentally from imaging for adjacent painful pathology, leading to orthopaedic referral.[4,5] Up to 85% of patients undergo unnecessary MRI imaging prior to presenting to the orthopaedic surgeon.[4,6] Biopsies are rarely needed in the setting of a stable enchondroma lesion.[7-9] Given that enchondromas are difficult to differentiate from low-grade chondrosarcomas,[10-12] imaging surveillance is needed to rule out progression. Although clinical and radiographic follow-up are justified,[4] multiple advanced imaging and clinic visits can lead to a significant cost for patients[13] without a clear benefit in survival or function.[6] Advanced imaging is not without risks and can increase patient exposure to radiation, although in this scenario it is likely negligible.[14,15] Although there have been national recommendations published for long-term surveillance of malignant bone tumors by the National Comprehensive Cancer Network (NCCN) and European Sarcoma Network Working Group (ESMO),[16,17] there is a lack of evidence-based consensus guidelines for the surveillance of benign bone tumors. The purposes of our study are: 1) to determine the number and proportion of low-grade cartilage tumors that demonstrate growth or require treatment and 2) to optimize the efficacy and cost-effectiveness of surveillance strategies for detecting biologically active lesions.

METHODS

A retrospective single-institution study was performed at our institution to identify the surveillance of enchondromas. Using ICD-9 codes (213.4, 213.7, 213.9) and ICD-10 codes (D16.0, D16.20, D16.21, D16.22, D16.9) we identified 498 subjects with benign bone tumors that were referred to our institution's orthopaedic oncology clinic from July 1, 2009 to November 30, 2016. Institutional Review Board approval was obtained prior to data collection.

Our radiographic inclusion criteria included subjects older than 18 years old with a long bone enchondroma without worrisome features. Our goal was to select "textbook" cases that were consistent with benign enchondromas without concerning findings for malignancy. Radiographically, we selected cases with well-defined tumor margins (e.g. a geographic border), the presence of stippled calcification without surrounding radiolucency, no extra-osseous soft tissue mass, no bone deformity or cortical remodeling, less than 66% endosteal scalloping, no cortical disruption, and no evidence of periosteal reaction. Exclusion criteria included patients with syndromic associations (ie Ollier's disease, Maffucci disease), axial lesions, radiographic findings (periosteal reaction, cortical breakage, soft tissue mass) suggestive of malignancy, recurrent tumors, immature patients, and patients with less than 12 months of radiographic follow-up. All radiograph reports of the low-grade cartilaginous tumors were initially made by members of musculoskeletal radiology department. The plain radiographs were reviewed by fellowship-trained musculoskeletal oncologist (B.J.M.), blinded to the clinical history of the subjects, to confirm inclusion.

Our primary outcome of this study was stability over time for long bone enchondromas. Radiographic size of the enchondroma was defined as the largest dimension on the AP or lateral plain radiograph view of the affected extremity in centimeters (cm). Subjects were followed radiographically for a minimum of one year (median 25 months, range 12 to 88 months). Changes in radiographic appearance of the enchondroma including growth, scalloping, demineralization, and fracture were recorded. Additionally, surgical intervention such as time to intralesional biopsy, curettage, and fixation was recorded.

The secondary outcome of this study was to compare the cost of tumor surveillance. For our cost analysis, we utilized our institution's global charge list in 2016. These charges include both physician and facility fees associated with both clinic fees and imaging fees. New office visit charges were: CPT 99202 ($370.00), CPT 99203 ($525.00), CPT 99204 ($671.00), and CPT 99205 ($770.00). Established patient clinic charges included: CPT 99211 ($235.00), CPT 99212 ($301.00), CPT 99213 ($376.00), CPT 99214 ($636.00), and CPT 99215 ($750.00). Plain radiograph charges included: shoulder ($451.00), humerus ($383.00). elbow ($343.00), femur ($440.00), forearm ($358.00), bilateral hip ($600.00), knee ($412.00), and tibia/fibula ($383.00). MRI imaging with contrast charges included: upper extremity joint ($3,942.00), upper extremity other than joint ($3,886.00), lower extremity joint ($3,969.00), and lower extremity other than joint ($4,038.00). The charge for a full body CT scan was $2397.00. Non-contrast CT imaging charges included: upper extremity ($2,144.00) and lower extremity ($2,147.00). We recorded the number of pre-referral images prior to presentation at our institution. We differentiated between pre-referral and post-referral imaging (plain radiographs, CT scan, MRI, and body scans). We compared costs of plain radiograph versus advanced imaging surveillance at final follow-up.

Independent variables collected included age, laterality, location of the enchondroma, incidental finding, radiographic size of the tumor, and interval growth. Statistical analysis was performed for descriptive statistics. Wilcoxon rank sum test and Fisher exact test were used to make group comparisons in continuous variables, and categorical variables, respectively. These statistical analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC) and statistical significance was set

Table 1. Demographics

	Stable	Growing	p-value
n	52	3	
Median age (years)	58.5	49.0	0.5673
Gender (female)	(69.23%)	0 (0%)	0.0369
Laterality (left)	18 (34.62%)	3 (100%)	0.0507
Pain at presentation	44 (84.62%)	2 (66.67)	0.4214
Incidental finding	52 (100%)	3 (100%)	1.0000
Number of pre-referral images [mean, median (range)]	[2.02, 2 (1-5)]	[3, 2 (1-6)]	0.7070
Median size @ px (cm)	5.01	3.6	0.2923
Fracture at presentation	0 (0%)	0 (0%)	1.0000

at a p-value <0.05.

RESULTS

A total of 55 out of 80 subjects (68.8%) with at least 12 months follow-up were included in our study (Table 1). The overall median age of our cohort was 58.0 years old. There were 19 males (36.5%, median age 58.0) and 36 females (69.2%, median age 57.5), (p =0.7480). Fifty-two of the lesions were stable and three demonstrated growth over time. There was no statistical difference in the median presenting age for stable versus growing lesions, respectively (58.65 versus 55.0 years old, p =0.5673), median lesion size at presentation (4.1 cm versus 3.6 cm, p = 0.2923), or median final follow-up (25 versus 26 months, p = 0.6802). Overall, the most common enchondroma locations were the proximal humerus (15/55=27.3%) and distal femur (16/55=29.1%), femoral shaft (9/55=16.4%), proximal tibia (4/55=7.3%), and fibula (4/55=7.3%) (Figure 1). For stable enchondromas, 35 out of 52 lesions (67.31%) presented in the lower extremities compared to 3 out of 3 (100%) growing cartilaginous tumors. All stable and growing cartilaginous lesions were found incidentally on imaging. Stable enchondromas presented with pain from adjacent pathology 44 out of 52 (84.6%) of cases while 2 out of 3 (66.6%) of growing cartilaginous lesions presented with pain from adjacent pathology (p = 0.4214). No patient presented with a fracture related to the tumor.

Three out of 55 (5.45%) of long bone enchondromas exhibited growth at a median of 23 (range 21 to 25) months follow-up. The first growing lesion was discovered incidentally in a 48 year-old healthy male and was located in his distal femur. At 23 months follow-up, the lesion grew from 3.6 cm to 4 cm and subsequently underwent an open biopsy which was most consistent with the diagnosis of an enchondroma. The second case of an enlarging cartilaginous lesion occurred in a 49 year-old male with a painful femoral shaft lesion (Figure 2). At 25 months follow-up, the lesion size grew from 7 cm to 7.43 cm and showed endosteal scalloping with cortical erosion. The patient underwent open curettage and bone grafting and biopsy results confirmed an enchondroma. The growing cartilaginous lesion was found incidentally in the femoral shaft of a 68 year-old male during screening for prostate cancer. At 21 months follow-up, the lesion grew from 3.2 cm to 10 cm and exhibited radiographic demineralization and endosteal scalloping. This subject underwent open biopsy and internal fixation of their lesion, and histol-

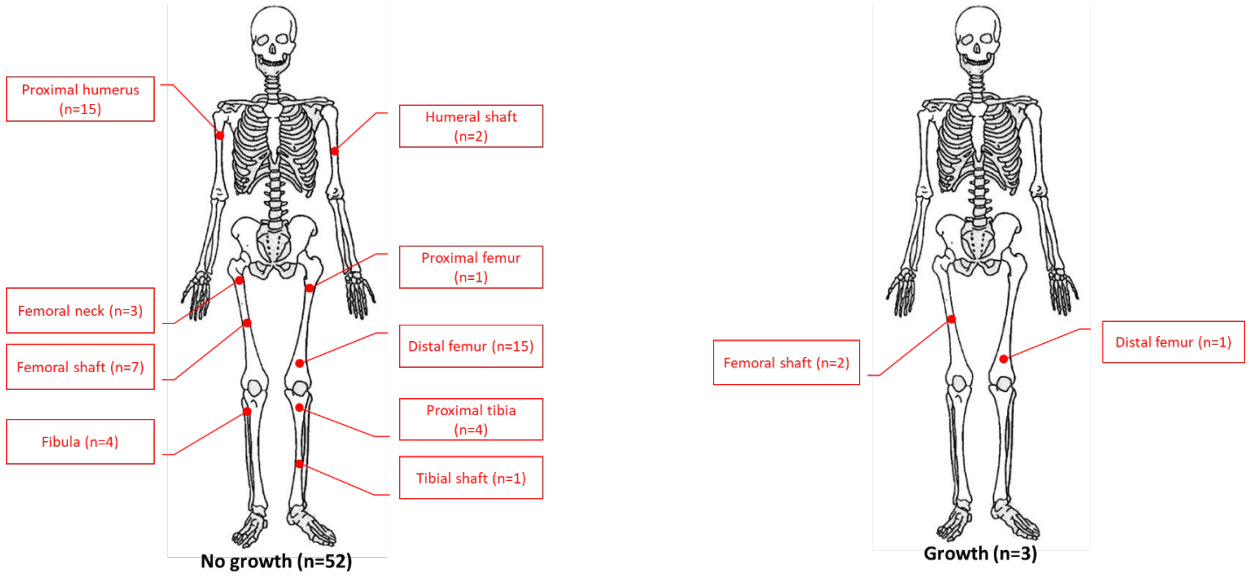

Figure 1. Location of enchondroma for stable (A) and growing (B) lesions.

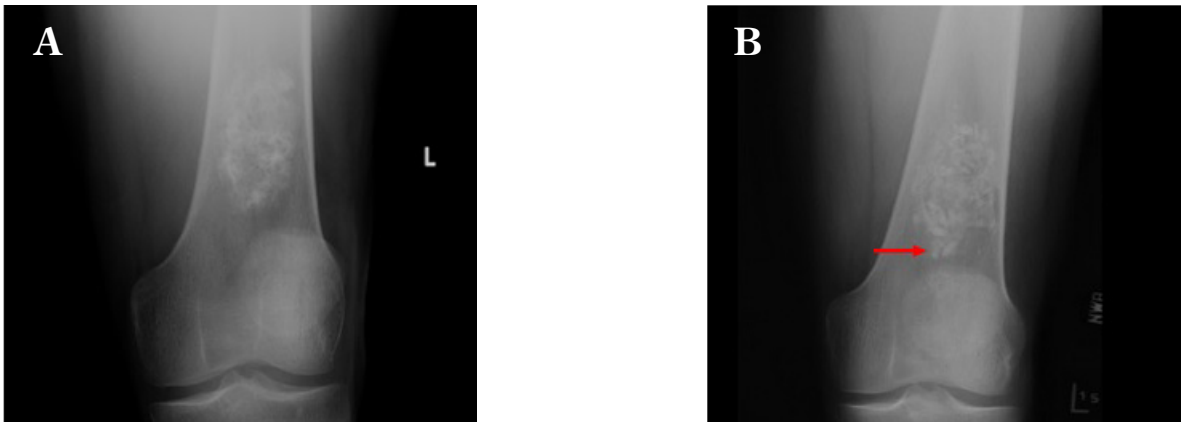

Figure 2. Growing enchondroma. Plain radiographs of the left femur of a 49 year-old male with a painful distal femoral shaft lesion. At 25 months follow-up, the lesion size grew from 7 cm (A) to 7.43 cm (B) inferiorly and showed endosteal scalloping with cortical erosion.

ogy revealed grade 1 chondrosarcoma. Incremental size increase at presentation for lower extremity [OR 1.282 CI (0.880-1.869)], metaphyseal [0.768 (0.208-2.835)], and diaphyseal [1.304 (0.724-2.3470] enchondromas lesions were not predictive of growth at final follow-up.

A total of seven open biopsies were performed on 4 out of 52 stable enchondromas and 3 out of 3 enlarging cartilaginous lesions at a median of 0.9 months (range 0.55 to 23) follow-up (Table 2). For the stable lesions undergoing biopsy, no patients had pain related to the lesion, one patient had endosteal scalloping without growth, and the remaining two had cystic regions within the cartilaginous matrix. All the stable lesions had a biopsy diagnosis of enchondroma while 1 out of 3 (33.3%) of the growing cartilaginous lesions ended up with a histologic diagnosis of grade 1 chondrosarcoma.

There was a total of 55 (45.1%) pre-referral plain radiographs, 5 (4.1%) CT scans, and 52 (42.6%) MRIs of the involved extremity (Table 3). There were also nine (7.4%) pre-referral full body bone scans. The median pre-referral costs per patient were plain radiographs ($383.00), CT scans ($0.00), and MRI imaging ($3,969.00) (Table 4A). The median follow-up time for stable and growing enchondromas was 25 and 26 months (p = 0.6802). The total median cost for post-referral follow-up was $8,982.00. The median post-referral costs for clinic fees, plain radiographs and MRI per patient were $1,799.00, $1,326.00, and $4,668.00, respectively. (Table 4B). The annual median costs for plain radiographs and MRI were $609.23 and $2,240.64, respectively.

DISCUSSION

There is much debate on the appropriate follow-up of long bone enchondromas without features of malignancy at presentation. Radiographically, it is often difficult to differentiate between enchondroma and low-grade chondrosarcomas.[10,11] Our exclusion criteria was similar to other studies that differentiated low and high-grade cartilaginous tumors.[12,18-20] In regards to radiographic diagnosis, Murphey et al. found that pain related to the cartilaginous lesion, endosteal scalloping greater than two-thirds the cortical thickness, periosteal reaction, and marked radionuclide uptake.[19] Geirnaerdt et al. did not find clinical pain to be associated with chondrosarcoma.[12] However, they found that radiographic size greater than 5 cm, axial skeleton location, and ill-defined margins were indicative of low-grade chondrosarcomas. The Skeletal Lesions Interobserver Correlation among Expert Diagnosticians (SLICED) study group reviewed 46 patients (mean age 47.7 years old) with low and high-grade cartilaginous tumors.[10] Despite analysis by nine expert bone tumor pathologists and eight expert bone tumor radiologists, there was low interobserver reliability for accurately differentiating between low and high-grade lesions on histology and radiographs. Clinically, our entire cohort presented incidentally on imaging for adjacent painful pathology such as mechanical knee pain or subacromial impingement. Levy et al. similarly found that 86% of enchondromas presented with pain from adjacent pathology.[21] Given the difficulty of differentiating enchondromas from low-grade chondrosarcomas at initial presentation, radiographic and clinical follow-up of cartilaginous lesions is warranted.

Our study is the first to our knowledge to assess the clinical follow-up and growth of isolated long bone enchondromas. Our overall median enchondroma size at presentation was 4.1 cm (mean 5.11 cm), and 3 out of 55 (5.45%) of long bone enchondromas exhibited growth at a median time of 23 months. Pain at presentation, location, and age did not appear to predict growth. The mean enchondroma size for Wilson's study was 4 cm.[6] Kumar et al. performed a retrospective study on 46 subjects (median lesion size 2.3 cm) with long bone cartilage lesions with a minimum of three years of MRI or CT follow-up.[22] They found that 11 out of 46 (23.9%) cartilaginous lesions ex-

Table 2. Open Biopsy Cohort

Stable	Age	Female	Laterality	Location	Size (cm)	Presentation	Radiographic features	Months to biopsy	Treatment	Final diagnosis
	53	M	R	proximal humerus	4.23	incidental	endosteal scalloping	2.5	open biopsy, curettage, grafting	enchondroma
	85	F	R	femoral neck	3.62	incidental, central hip arthritis	cystic cartilaginous lesion	0.57	open curettage, grafting, DHS	enchondroma
	48	F	R	distal femur	5.8	incidental, arthritis	central lucency	0.55	open biopsy, curettage, grafting	enchondroma
	68	F	L	distal femur	4.1	incidental	chondroid matrix	0.5	open biopsy and curettage	enchondroma
Growing										
	48	m	L	distal femur	3.6	incidental, knee osteoarthritis	cartilaginous matrix	1.16	open biopsy and curettage	enchondroma
	49	M	L	femoral shaft	7	pain from tumor	endosteal scalloping, cortical erosion	23	open biopsy, curettage, grafting	enchondroma
	68	M	L	femoral shaft	3.2	incidental, f/u prostate CA	scalloping, inferior area of demineralization	0.9	open biopsy, curettage, internal fixation	grade 1 chondrosarcoma

hibited at least 6 mm of growth at three years follow-up. One patient (2.2%) in Kumar's series exhibited 11 mm of growth at one year follow-up and was confirmed to have an atypical enchondroma at the time of surgery. Unlike our study, Kumar et al. did not exclude chondrosarcomas or atypical radiographic features in their cohort as 10% of their cohort had endosteal scalloping on plain radiographs at the time of presentation. They also found that growing cartilaginous lesions had greater than 50% demineralization compared to stable lesions. One of the subjects in our study exhibited significant growth from 3.2 to 10 mm and demineralization at 21 months follow-up. Upon open biopsy, this subject had grade 1 chondrosarcoma. This case confirms that growth of seemingly benign cartilaginous lesions warrants longer follow-up and surgical biopsy for a definitive diagnosis.

Most clinicians utilize radiographic findings to differentiate enchondromas from low-grade chondrosarcomas. However, atypical radiographic features or subsequent growth may require biopsy to confirm the diagnosis and surgical intervention. One growing cartilaginous lesion had a biopsy-confirmed diagnosis of a grade 1 chondrosarcoma at 21 months follow-up. Surgical intervention for low-grade cartilaginous lesions includes intralesional versus wide resection. Given the low occurrence of recurrence and metastasis for low-grade cartilaginous tumors, the treatment of choice is open biopsy and curettage.[23-25] Intralesional curettage allows for the preservation of the affected limb without significant morbidity. Leerapun et al. retrospectively compared 70 patients with grade 1 long bone chondrosarcomas that underwent wide resection or intralesional curratage.[26] At a mean of 8.5 years follow-up, one patient in each group had local recurrence and metastasis without any difference in overall outcomes. At 5.1 years follow-up, Hanna et al. reported a 5% recurrence rate in their retrospective cohort of low-grade long bone chondrosarcomas treated with intralesional curettage and cementation.[23] Verdegaal et al. retrospectively studied 85 patients that underwent intralesional curettage with phenol and ethanol adjuvant treatment.[24] At an average follow-up of 6.8 years, biopsy-confirmed recurrence occurred in 5.9% of cases, all of which were grade 1 chondrosarcomas. Dierselhuis et al. retrospectively reported on 108 patients with grade 1 chondrosarcomas treated with intralesional curettage, adjuvant phenol, and defect filling (polymethylmethacrylate, bone graft, or bone substitute).[25] Complications included residual tumor (4.6%), recurrence (0%), and fracture (10.2%) at a mean follow-up of 4.1 years. They recommended that intralesional curettage is safe for tumors less than 100 cm^2. One previous retrospective study by Schwab et al. of 164 patients with surgically treated grade 1 chondrosarcomas did show a high rate of local recurrence (13%), metastasis (4.3%), and death (3.7%).[27] More importantly, decreased survival was not seen until five years after surgical treatment. The occurrence of one biopsy-confirmed grade 1 chondrosarcoma in our cohort highlights the importance of follow-up longer than six months.

Table 3. Clinical Follow-up

	Stable (n=52)					Growing (N=3)					
	Min	Max	Median	Mean	SD	Min	Max	Median	Mean	SD	p-value
Age	34	85	58.5	58.65	12.65	48	68	49	55.00	11.27	0.5673
Presenting size	1.2	18.6	4.105	5.01	3.09	3.6	10	7	6.87	3.20	0.2923
Follow-up months	12	88	25	30.23	14.84	6	36	26	22.67	15.28	0.6802
Number of visits	2	11	4	4.37	1.79	5	10	5	6.67	2.89	0.0807
# Pre Clinical Imaging	0	5	2	2.02	1.02	1	6	2	3.00	2.65	0.7070
# Pre Clinical X-ray	0	2	1	0.90	0.57	1	5	1	2.33	2.31	0.1402
# Pre Clinical CT	0	1	0	0.10	0.30	0	0	0	0.00	0.00	1.0000
# Pre Clinical MRI	0	2	1	0.88	0.58	0	1	1	0.67	0.58	0.6208
# Final X-ray	0	9	3	3.33	2.06	2	9	3	4.67	3.79	0.6975

Using Wilcoxon Rank-sum test

Our study also aimed to determine the appropriate time and costs of clinical and radiographic follow-up for isolated, non-syndromic long bone enchondromas. The median follow-up for stable and growing enchondroma in our cohort was 25 and 26 months, respectively. Enchondromas rarely undergo malignant transformation into chondrosarcomas, except in the setting of Ollier disease (25% occurrence) or Maffucci syndrome (100% occurrence).[28] Additionally, when malignant transformation occurs, it is often low-grade chondrosarcoma and metastasis is rare.[29] Clinical surveillance for low grade bone sarcomas have been previously published.[16,17] Both the National Comprehensive Cancer Network (NCCN)[17] and the European Sarcoma Network Working Group (ESMO)[16] recommend follow-up imaging for low-grade bone sarcomas every six months for two years, and then annually. For cartilaginous lesions, Kumar et al. concluded in their retrospective study that MRI surveillance should be performed at one year and then at three year follow-up. They also suggested that surgical intervention should be performed if growth greater than 6 mm is seen.[22] Most recently, the Musculoskeletal Tumor Society (MSTS) published new guidelines for surveillance of newly identified bone lesions.[30] For asymptomatic stable lesions, they recommended serial radiographs and review by a fellowship-trained musculoskeletal radiologist every three to six months for two years. Observed growth or aggressive radiographic findings warrants immediate referral to an orthopaedic oncologist. Given the time to growth seen in our study, our proposed surveillance would include radiographic follow-up every 6 months for the first year, and then annually for a total of at least three years.

Our goal with this investigation was to investigate if there was a means to identify a low-grade cartilaginous lesion with no potential for growth after short-term radiographic surveillance. While we did find the majority of lesions remained stable and painless, the identification of a grade 1 chondrosarcoma in an asymptomatic patient at nearly 2 years of radiographic follow-up is concerning and gives pause to a global recommendation of limiting follow-up to 6 months in stable "textbook" lesions.

One way to view this issue is that the vast majority of patients (48 out of 55 in our cohort) in retrospect did not require any intervention. Even for the biopsied lesions that exhibited growth (n=3) or atypical features (n=4), only one lesion was diagnosed as a grade 1 chondrosarcoma and no lesions were limb-threatening. One should remember that the goal of radiographic surveillance is not to identify growing enchondromas, but to accurately diagnose chondrosarcomas. In addition, the patient with a grade 1 chondrosarcoma was referred to us after identification of growth in a radiograph performed nearly two years after the initial presentation without intervening surveillance, so it is not clear whether this progression would have been recognized earlier. Given the substantial growth between studies, it is likely that the progression would have been apparent at shorter surveillance. These observations would suggest that shorter follow-up is likely sufficient to identify a potential malignancy.

Alternatively, none of the patients with growth over time, in particular the patient with chondrosarcoma, exhibited pain. This is concerning as often clinicians will advise individuals with apparently non-aggressive pathology to return if symptoms arise. Because we cannot depend on discomfort to prompt return evaluation, radiographic surveillance is the only option to determine tumor biology over time. In addition, growth was not clear until two years after the initial study in our cases, arising concern that perhaps more lesions will demonstrate growth with a longer period of follow-up.

Table 4. Cost Analysis for Pre-Referral (A) and Post-Referral (B) Costs

A.

Pre-referral imaging	X-ray	MRI	CT	Full body scan	Total pre-referral imaging	Total pre-referral Cost
Mean costs	$405.47	$3,456.53	$233.69	$305.07	2.07	$4,406.51
Median costs	$383.00	$3,969.00	$0	$0.00	2	$4,411.00
Range	$0 to $880.00	$0 to $8076.00	$0 to $2850.00	$0 to $2397.00	0 to 4	$383.00 to $11,300.00
Standard deviation	$335.92	$2,301.03	$749.03	$806.23	1.14	$2,712.25

B.

Post-referral Costs	Clinic	X-ray	MRI	Total	Annual X-ray	Annual MRI	Annual X-ray + MRI
Mean	$1,914.93	$1,506.98	$6,501.95	$10,344.11	$700.96	$2,584.20	$3,285.16
Median	$1,799.00	$1,326.00	$4,668.00	$8,982.00	$609.23	$2,240.64	$2,628.68
Range	$ 901.00 to $4656.00	$0 to $4059.00	$0 to $29,220.00	$2117.00 to $37,284.00	$0 to $2,250.75	$0 to $9,740.00	$338.25 to $10,876.00
Standard deviation	$787.98	$943.63	$7,771.81	$8,029.40	$469.57	$2,921.96	$2,764.99

We suggest a common-sense approach that minimizes cost, maximizes efficiency, and accurately identifies clearly biologically active cartilage tumors. An initial period of close follow-up every 3-6 months as recommended by the MSTS, is reasonable to identify growing lesions in the short- or medium-term.[30] If there is no growth for one year, lengthening the period of time to annual surveillance is acceptable. Unless there is a clinical concern, such as pain that cannot be attributed to another source or growth on plain radiographs, advanced imaging is unnecessary. Because we saw growth at an average of two years, we would recommend a full three years of follow-up, and would suggest future studies investigate if a longer period of surveillance is beneficial. Additional cost-saving measures could include local surveillance with repeat specialty referral only if there is radiographic growth or unexplained pain, remote appointments with telemedicine, or surveillance performed by specialized advanced practice providers.

Our results indicate that there is a significant cost associated with pre-referral imaging, with 42% of costs coming from MRI. Wilson et al. retrospectively reviewed 121 patients (105 enchondromas and 19 chondrosarcomas) and utilized decision analysis to determine the number of unnecessary images.[6] They found that 85% of enchondromas had at least one unnecessary advanced image and 58% had two unnecessary images. They also found that the average unnecessary cost per enchondroma was $1346.18. Donthineni et al. also found that 85% of patients presented with MRI imaging and 15% of patients with pre-referral MRI imaging did not have plain radiographs.[4] Our study similarly found that 54.8% of pre-referral and 29.2% of post-referral imaging were advanced images. In clinical practice, it is common for orthopaedic surgeons to practice defensive medicine by obtaining excessive imaging to prevent litigation.[31] Pre-referral costs can be reduced by properly educating non-oncology physicians when to obtain advanced imaging. Intraarticular lesions and lesions with evidence of aggressive features warrants advanced imaging. If the benefits of advanced imaging are in question, then the patient should be referred to an oncology center for proper management. Once referred to an oncology physician, extended follow-up and appropriate imaging may reduce the risk of missing a malignant tumor. A proposed cost-savings protocol would include plain radiograph imaging for three years for stable lesions. This would amount to an annual savings per patient of $2,240.64 per year.

There are several limitations of this study. This was a retrospective study with a significant amount of the cohort lacking adequate imaging follow-up. These excluded patients may have altered the results obtained. Although we intentionally excluded patients without long bone enchondromas, our study may have been underpowered as a result and thus not able to detect a statistical significance for size of the lesion and growth. We followed tumor growth with plain radiographs, which may not be as accurate at following growth as advanced imaging modalities. Additionally, we did not follow-up patients after biopsy and surgical intervention to determine the

rate of recurrence and metastasis. Given our limited follow-up after surgical treatment, future studies should address continued long-term surveillance of low-grade cartilaginous lesions and risk for subsequent malignant identification.

In conclusion, enchondroma growth was a rare event and typically occurred at two years follow-up in our series. We propose plain radiographic follow-up for stable enchondromas every six months for the first year and then annually for at least three years of total follow-up. Significant costs savings can be made by limiting MRI imaging for stable lesions. Additional studies are needed to determine the risk of recurrence and malignant transformation for lesions exhibiting growth.

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