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ORIGINAL STUDY

The safety of direct primary excision of low-grade chondral lesions based on radiological diagnosis alone

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The safety of treating low-grade chondral tumours by primary surgery without a pre- operative diagnostic needle biopsy was assessed by looking at the concordance between radiological and histological diagnoses. A retrospective review of the departmental histopathology registry from 2005 to 2009 was performed to identify cases of intramedullary chondral lesions in the appendicular skeleton. Cases with a pre-operative needle biopsy and with recurrence were excluded. Correlation between radiological and histological diagnosis was investigated with kappa analysis. Of 53 patients, bone expansion was seen in 18.4%, endosteal scalloping in 42.9% and extra-osseous extension in 14.3%. Concordance was 100% between the radiological and histological diagnoses (Kappa score = 1.0). If a radiological diagnosis of an enchondroma or low-grade chondrosarcoma is made, then direct surgical treatment without needle biopsy is safe. A biopsy should be considered if any atypical radiological features suggesting a high-grade chondrosarcoma exist. This increases the certainty of diagnosis and allows planning of surgical treatment.

Keywords : low-grade chondral tumours ; radiological diagnosis ; primary excision.

INTRODUCTION

The management of intramedullary chondral tumours of the appendicular skeleton is dependent on the type and grade of the lesion. An enchondroma is typically managed either by careful follow-up (*2,25*) or intra-lesional curettage, depending on symptoms (*5,11*). The treatment of a chondrosarcoma is primarily surgical as these tumours do not respond well to radiotherapy and/or chemotherapy (*8,19*). High-grade tumours of long bones are primarily treated by wide surgical excision. The treatment of low-grade lesions remains controversial. Recent evidence has demonstrated that low-grade lesions (grade ≤ 1 chondrosarcoma) may be treated by curettage and cementation alone (*13,20*), or supplemented by other local adjuvant therapy such as cryosurgery (*24,29,35*).

The difference in management between low and high-grade tumour types clearly depends on an accurate differentiation between these tumour types. An accurate diagnosis is reached by a combination of clinical, radiological and histological assessment. The differentiation of low-grade chondrosarcoma from an enchondroma is the most

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challenging aspect and is complicated by the radiological and histological similarities between the lesions (*31*). Grade 2 and 3 chondrosarcoma can be differentiated by standard histological examination more reliably (*22*). Many studies have attempted to define radiological parameters useful for discriminating between low and high-grade chondral tumours. The presence of endosteal scalloping greater than two-thirds of cortical thickness, cortical destruction, and soft tissue extension on cross-sectional imaging strongly favour a diagnosis of a malignant tumour (*27*). The size of the tumour is another important factor and it has been suggested that lesions greater than 5 cm in length are more likely to represent a chondrosarcoma (*11,27*). Other studies have suggested that on magnetic resonance imaging (MRI), abnormal marrow or soft-tissue signal change around a chondral tumour is specific for a chondrosarcoma, especially on STIR sequences (*16*). An accurate radiological diagnosis is useful to overcome the need for pre- operative biopsy, as the latter can be associated with considerable morbidity and delay in treatment. Furthermore, sampling errors can lead to incorrectly diagnosing the tumour grade and misdirecting treatment (*9*).

The study aim was to determine the safety of diagnosing and treating low-grade chondral tumours on radiological appearance alone without the need for biopsy, at a National bone tumour unit.

PATIENTS AND METHODS

A retrospective review of all chondral tumours between 2005 and 2009 was performed. All cases of intramedullary enchondroma and chondrosarcoma of the appendicular skeleton were analysed. In total 126 consecutive patients were identified fitting this criterion. This included 38 cases of enchondroma and 88 cases of chondrosarcoma. All cases that underwent a pre- operative needle biopsy assessment were excluded from the study. Furthermore, two cases within the chondrosarcoma sub-group that presented with a pathological fracture were excluded. These patients underwent resection and prosthetic replacement without a pre- operative needle biopsy as the presentation was suggestive of a high-grade lesion. This provided 28 cases of enchondroma and 25 cases of chondrosarcoma for further evaluation. A correlation between the pre-operative radiological diagnosis and the histological diagnosis of the lesions undergoing primary excision was then investigated.

In this unit all suspected bone tumour cases are discussed in a multi-disciplinary meeting with specialist musculoskeletal oncological radiologists, bone tumour surgeons and specialist musculoskeletal oncological histopathologists present. Decision making is specialist led via a combined review. Primary surgical excision was carried out on tumours felt to display the characteristics of a low-grade lesion. This decision was based on clinical findings and preoperative radiological imaging comprising of plain radiographs, magnetic resonance imaging and computed tomography scans where available.

In this study, the important radiographic parameters evaluated were tumour size, determined by measuring the maximal lesion length, the presence of bone expansion, endosteal scalloping and extra-osseous extension. These parameters were assessed on MR imaging. Furthermore, the patient age, gender and lesion site were recorded.

The histological assessment of excised lesions was performed by specialist musculoskeletal oncological histopathologists. The histological grading system used is modified from Jaffe (1958) (*15*). A grade was assigned after evaluation for various cytological and histological features. Histologically, enchondromas are defined as lesions with cellularity that exceeds resting articular cartilage and the presence of cells with small uniform nuclei and abundant cytoplasm (*15*). A diagnosis of an enchondroma is further facilitated by two distinctive histological findings including nodules of cartilage separated by fat – "benign islands of cartilage pattern", and nodules of cartilage encased by plates of lamellar bone – "enchondroma encasement pattern" (*3*). Clinical findings are also considered to reach an accurate diagnosis. A primary chondrosarcoma tends to be a single mass of malignant hyaline cartilage with a variable degree of calcification. A grade 1 lesion demonstrates increased cellularity, mild nuclear atypia and binucleate cells (*15*). Furthermore, the permeation of marrow fat by cartilage with trapping of host lamellar bone is also seen (*22,23*). Cytological changes become more obvious in grades 2 and 3 with the presence of mitoses. More aggressive marrow infiltration is seen in high-grade chondrosarcoma with tumour cells infiltrating and replacing marrow fat. Invasion of Haversian canals leads to reactive periosteal reactions. Eventually, there is erosion through the cortex to form a soft tissue mass.

Statistical analysis was carried out in the form of a two-sample *t*-test for continuous variables (including age

Table I. — Skeletal distribution of the 53 low-grade chondral lesions

	Skeletal distribution (%)
Clavicle	2 (3.8)
Humerus	19 (35.8)
Radius	2 (3.8)
Ulna	1 (1.9)
Femur	16 (32.1)
Tibia	7 (13.2)
Fibula	6 (11.3)

and lesion size). The agreement between the radiological and histological diagnoses was measured using kappa statistical analysis (*4,18*). A score of 1.0 indicates 100% concordance between tests whilst a score of 0 implies no correlation. A kappa value of greater than 0.75 implies excellent agreement (*28*). Ethical approval was not sought, as this was a retrospective review of the current practice in our unit.

RESULTS

In total 53 patients (25 male ; 28 female) were included in this study. The average age was 46.0 years (range : 9-77 years). In the enchondroma sub-group, the average age of presentation was 41.2 years (range : 9-71) ; this was not significantly different from the chondrosarcoma group (average age : 49.3 years ; range : 28-71 ; $p > 0.05$).

The most common tumour locations were the proximal humerus (19 cases ; 35.8%) and femur (16 cases ; 30.2%) (Table I). The femoral lesions were located proximally in 1 case (1.9%), diaphyseal in 1 case (1.9%) and distally in 14 cases (26.4%). The clavicle was affected at the medial end (2 cases ; 3.8%), the radius and ulna were both affected distally. The fibular lesions were located around the fibular neck (6 cases ; 11.3%), whilst 6 tibial lesions were located proximally and 1 at the distal end. Three patients (5.7%) presented with a pathological fracture, 2 were located in the humerus (Fig. 1) and one in the distal radius.

Image analysis

All patients received a radiological diagnosis by analysis of plain radiographs and MRI. Patients often also had other imaging modalities available (e.g. CT and radionucleotide imaging), however, the radiological parameters assessed in this study were derived from MRI. The average maximum tumour length was 5.1 cm (Range : 1.6-16 cm). Bone expansion was seen in 18.4% of cases, endosteal scalloping in 42.9% and extra-osseous extension in 14.3% of cases (Fig. 1 & 2).

Histological analysis

The histological assessment of the specimens revealed 28 cases of enchondroma of which 15 (28.3%) were cellular enchondromata. There was one case of multiple enchondromata (Ollier's disease). There were 25 cases of low-grade chondrosarcoma (47.2% ; grade ≤ 1).

Concordance analysis

Radiologically, all 53 lesions were diagnosed as low-grade chondral tumours, either enchondroma or low-grade chondrosarcoma. This correlated directly with the histological assessment of the specimens. This demonstrated a 100% concordance between the radiological and histological diagnosis (Kappa score = 1.0).

Management and Follow-up

The majority of patients in this study underwent intralesional curettage and adjuvant treatment with polymethylmethacrylate bone cement. In total 49.1% of patients (26 cases) had this form of treatment. Two enchondroma cases were treated by excision of an exostosis type lesion. Two further cases were treated by a resection and prosthetic replacement (Fig. 1 & 2). The first case was an enchondroma which developed at the site of a humeral neck fracture and was complicated by extra-osseous extension (Fig. 1). This patient was treated with a proximal humeral replacement. In the second, the presence of symptomatic osteoarthritis with an associated proximal tibial lesion was treated with a long stemmed total knee replacement (Fig. 2). A proximal fibulectomy was performed for two chondrosarcoma cases. The treatment

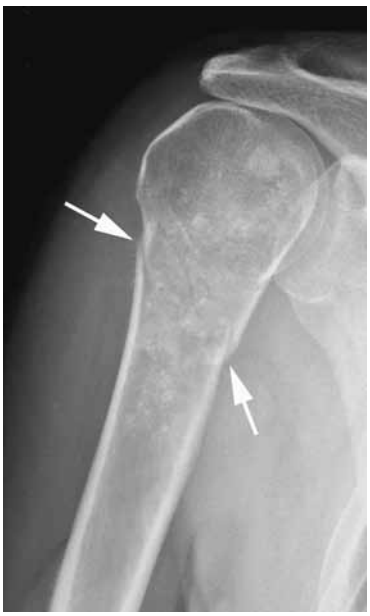

Fig. 1a. — Anteroposterior radiograph of the right shoulder in a 50-year-old male demonstrates an extensive proximal humeral low-grade chondral tumour associated with a minimally displaced pathological fracture (arrows).

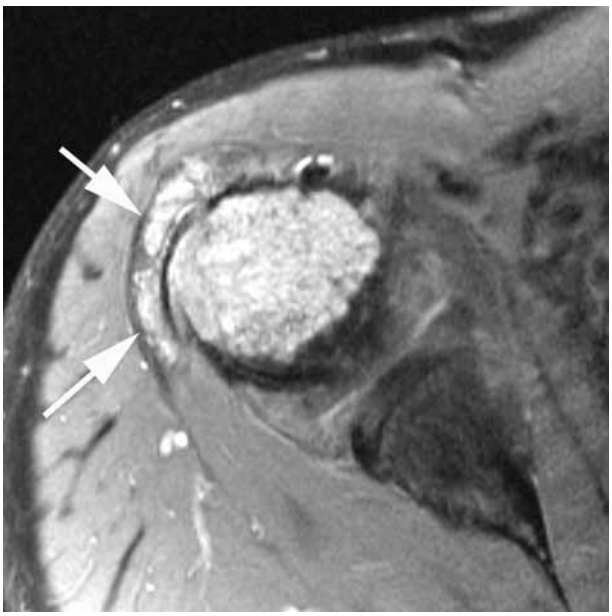

Fig. 1c. — Axial fat suppressed T2W FSE magnetic resonance image showing minor extraosseous extension of tumour due to the fracture (arrows).

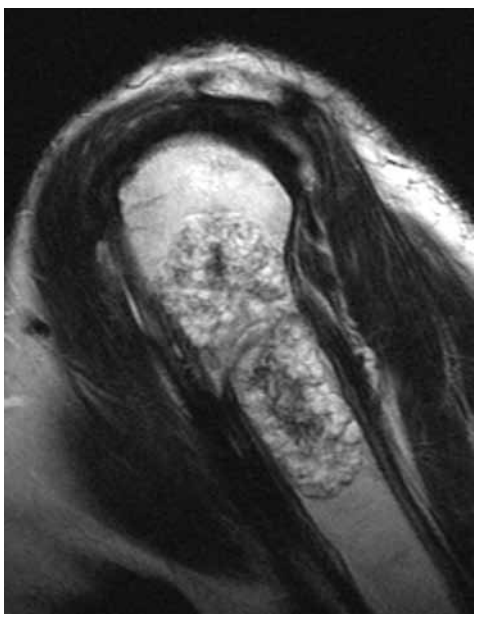

Fig. 1b. — Sagittal T2W FSE magnetic resonance image showing the classical appearance of a low-grade chondrosarcoma measuring 7.3 cm in length.

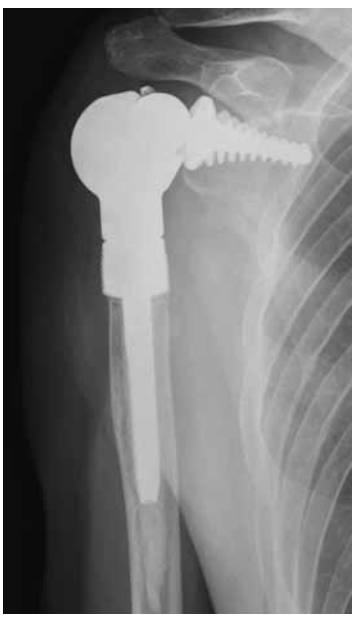

Fig. 1d. — The lesion has been treated with a massive proximal humeral replacement.

modalities for all cases are summarised in Table II. Follow-up was available for 51 patients ; the remaining 3 patients were lost to follow-up. Cases were followed up clinically and radiographically till the end of 2010. The average follow-up period was 24.2 months (range : 6-65 months). Chondro-

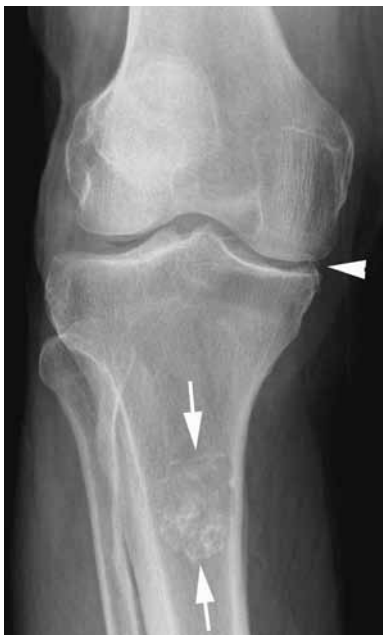

Fig. 2a. — Anteroposterior radiograph demonstrates end-stage medial compartment knee osteoarthritis in a 71 year old male (arrowhead) with an associated small low-grade chondral tumour in the proximal tibia (arrows).

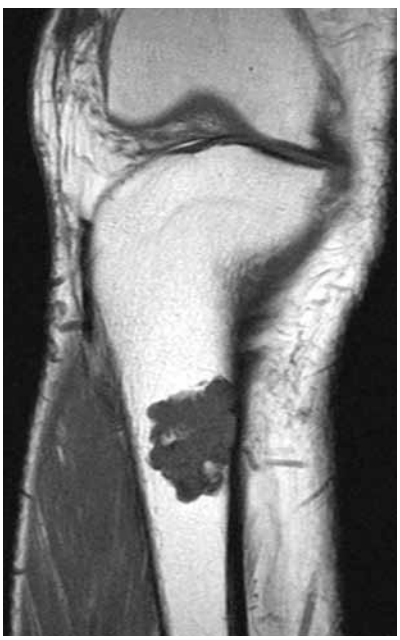

Fig. 2b. — Coronal T1W SE magnetic resonance image showing the classical appearances of a small enchondroma measuring 3.3 cm in length.

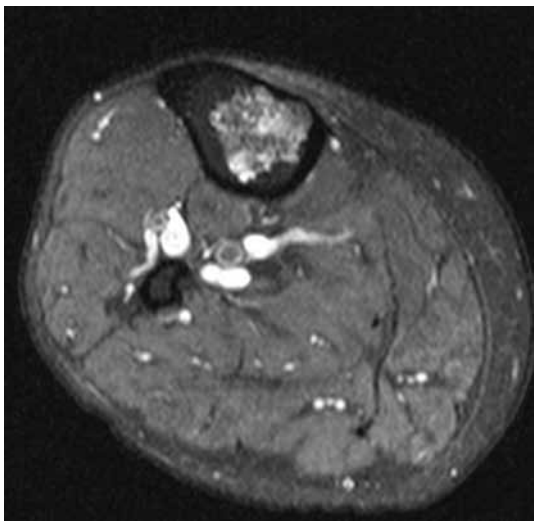

Fig. 2c. — Axial fat suppressed T2W FSE magnetic resonance image showing minor endosteal scalloping.

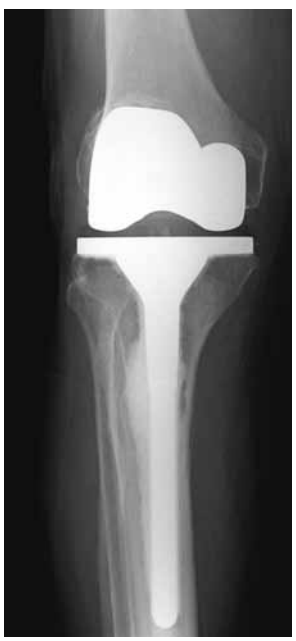

Fig. 2d. — The lesion has been treated with curettage and TKR.

sarcoma cases were typically monitored for longer durations unlike enchondromata. In this period, three cases were found to have residual tumour after curettage and bone cementation procedures. The first case was a proximal humeral chondrosar-

Table II. — Table summarising the surgical treatment of the 53 cases

	Enchondroma	Chondrosarcoma
Curettage	6 (11.3)	6 (11.3)
Curettage and bone cement	15 (28.3)	11 (20.8)
Curettage and bone graft	2 (3.8)	–
Curettage, cement and internal fixation	1 (1.9)	3 (5.7)
Curettage, bone graft and internal fixation	–	1 (1.9)
Excision	2 (3.8)	2 (3.8)
Excision and bone graft	–	1 (1.9)
Resection and prosthetic replacement	2 (3.8)	–

coma diagnosed on plain radiography as a new lytic lesion 20 months after curettage and cementation. A repeat procedure was performed and she remains clear of recurrence for over 5 years. The second case was a recurrence of a chondrosarcoma after curettage and cementation of a proximal tibial chondrosarcoma. Recurrence was detected 13 months after the primary surgery with an MRI indicated by persistent pain. This patient had a further recurrence 11 months after the second procedure and underwent further surgery. She remains free of tumour for over 3 years. Finally, a distal femoral replacement was required for a case of a recurrent chondrosarcoma initially treated by curettage and cementation but complicated by a postoperative fracture. The fracture was treated outside of this unit with a plate and screw construct, which progressed to failure with co-existence of recurrent tumour. Following the distal femoral replacement, the patient remains clear of recurrence for 3 years.

DISCUSSION

Low-grade chondral lesions are diagnosed by a combination of clinical history and examination, combined with radiological imaging. Often a histological assessment is also required. Typically, enchondromata and low-grade chondrosarcomas have similar appearances on plain radiographs, both demonstrating stippled calcification, endosteal scalloping and cortical expansion. The density of calcification is associated with the grade of a lesion, with lower grade lesions tending to be denser (*27*). Endosteal scalloping of greater than two-thirds the cortical thickness occurs more frequently in chondrosarcoma (*26*). Both lesions can lead to a pathological fracture and this may be the first presentation of the tumour. As seen in our data this occurred in three cases (5.7%), and is similar to other quoted figures (*3*). These cases had a histological diagnosis of an enchondroma and included two proximal humeral lesions and a distal radial lesion. Computed tomography and magnetic resonance scans are useful for defining the lesion's extent and adjacent soft tissue involvement. The MRI characteristics of low-grade chondral lesions are of low signal intensity on T1-weighted images, high signal intensity on T2-weighted images, punctate signal voids of matrix calcification, internal septation and lobular margins (*6*). The high signal intensity in higher-grade lesions is less specific in appearance and lacks homogeneity (*27*). A maximum tumour length greater than 5 cm, cortical destruction and soft tissue extension are all significant indicators of a malignant cartilage tumour on MRI (*27*). A bone scan is useful for identifying multiple lesions as in Ollier's disease, otherwise both enchondroma and chondrosarcoma demonstrate increased radionuclide uptake (*14*). In this study, the MRI features of endosteal scalloping (Fig. 2), cortical expansion, soft tissue extension (Fig. 2) and the tumour size were used to differentiate between low and high-grade chondral tumours. Of the 53 cases that were diagnosed as a low-grade lesion on MRI, confirmation was observed at histological assessment in all cases (kappa score = 1.0).

The reliability of biopsy in the diagnosis of low-grade chondral lesions is questionable. Disadvantages of biopsy include sampling errors, delay in treatment, increased risk of local recurrence from seeding, morbidity and cost (*21,32*). Sampling error may occur when a truly representative sample is not obtained by the biopsy procedure and therefore, there is failure to identify the true grade of the lesion. A more recent study has shown improved accuracy rates for differentiating between the grades of chondrosarcomata using needle biopsy. They demonstrated a 94% accuracy rate for diagnostic biopsy in distinguishing between low and high-grade chondrosarcoma (*17*). However, a needle biopsy exactly graded chondrosarcoma lesions in only 86% of cases. This stresses the importance of a combined clinical and radiographical diagnosis for planning surgical treatment and in fact underpins the surgical protocol undertaken in our institution. Using the radiological parameters listed in this study, the differentiation between a low and high-grade lesion was correctly achieved in all cases and surgery carried out accordingly.

The distinction between low-grade chondral lesions and more aggressive high-grade lesions is important as the treatment differs considerably. High-grade chondrosarcoma is typically treated by wide excision (*5*) and often a resection is performed in combination with massive prosthetic replacement. Treatment with adjuvant chemotherapy or radiotherapy does not seem to alter the outcome for these lesions (*7,19*). Several studies have demonstrated that an adequate surgical margin is associated with a lower risk of recurrence and better long-term survival (*10,12,19*). Furthermore, recurrence has been associated with a decrease in overall survival (*19,30,37*).

The treatment of intramedullary low-grade chondral lesions is however more controversial. Enchondromata are benign lesions, which do not metastasize and rarely undergo malignant transformation (*22*). Such transformation typically occurs in multiple enchondromatosis (Ollier's disease) and therefore the presence of this condition should be a clinical prompt for the potential of malignant change (*5*). Treatment options for an enchondroma include simple observation, biopsy, and curettage with or without adjuvant therapy and bone grafting. Treatment of smaller asymptomatic lesions is usually non-surgical, with serial clinical and radiographic evaluation. For symptomatic lesions or for the presence of atypical radiological signs, surgery is preferred. The treatment of low-grade chondrosarcoma also varies from intralesional curettage (*2,13,20*) to wide excision (*12*). Wide excision versus intralesional curettage has been shown to be associated with lower local recurrence rates in some studies (*12,34*). Other studies have demonstrated that intralesional excision with adjuvant therapy can be performed with favourable oncological outcomes (*2,20,33*). Furthermore, such surgery is associated with better bone and joint preservation and overcomes the need for complex limb reconstruction, as may be required with wide excision. Recurrence rates ranged from 0.04 to 0.09% over ten years in one study (*2*).

Adjuvant therapy may be in the form of bone cement or cryosurgery. Two groups studied the effects of intralesional excision combined with cryosurgery in the form of liquid nitrogen (*29,36*) and another cryosurgery followed by cementation (*1*). All studies had good outcomes with very low recurrence rates. Even without the use of cryosurgery, but with curettage and cementation alone the outcomes are still very favourable, with a reported recurrence rate of 5% and excellent functional results (*13,33*). Reconstruction of bone with cement after intralesional excision provides stability and facilitates the post-operative radiological assessment for recurrence. Autogenous or allogenic bone graft is an alternative to cement. In some cases, further stabilisation may be required in the form of internal fixation. The overall recurrence rate in this study for all treatment modalities was 7.5%. One patient had two episodes of recurrence during the study period, each was considered separately for statistical purposes.

In this study the treatment of low-grade chondral lesions was varied. Some lesions were treated by intralesional excision alone (22.6%), but the majority were treated by intralesional excision and cementation (49.1%). Resection and prosthetic replacement was required in 2 cases. This is unusual for low-grade lesions, but these cases were

complicated by underlying pathology necessitating more complex surgery. In the enchondroma group, one case required a proximal humeral replacement as a fracture occurred at the site of the primary curettage and cementation (Fig. 1). The second patient required resection of a proximal tibial lesion followed by a total knee replacement for the presence of advanced osteoarthritis (Fig. 2).

CONCLUSIONS

This study has demonstrated that in a multidisciplinary setting and using certain radiological parameters including endosteal scalloping, cortical expansion, extra-osseous extension and tumour size on MR imaging, the distinction between low and high-grade chondral lesions can be safely determined without the need for pre-operative biopsy. The multidisciplinary team should include a bone tumour surgeon, and specialist musculoskeletal oncological radiologists and histopathologists. We recommend that a biopsy is only required when there exists any atypical radiological findings to suggest a high-grade lesion.

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