Improved Differentiation of Benign Osteochondromas from Secondary Chondrosarcomas with Standardized Measurement of Cartilage Cap at CT and MR Imaging

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Purpose: To validate a technique for reproducible measurement of the osteochondroma cartilage cap with computed tomography (CT) and magnetic resonance (MR) imaging and to reevaluate the correlation of the thickness of the cartilage cap with pathologic findings to improve noninvasive differentiation of benign osteochondromas from secondary chondrosarcomas.

Materials and Methods: The institutional review board approved the study and waived the need for informed consent. HIPAA compliance was maintained. After validation of the measurement technique, 101 pathologically confirmed osteochondromas were retrospectively reviewed. Patient demographic data, histologic diagnosis, and chondrosarcoma grade were recorded. Two musculoskeletal radiologists used a standardized technique to independently measure the thicknesses of the cartilage caps on CT and MR images; these measurements were compared for interobserver agreement. Agreement between measurements with CT and MR imaging was also evaluated, as were the sensitivity and specificity of both modalities for differentiation of osteochondromas from chondrosarcomas.

Results: Evaluated were 67 benign osteochondromas (from 49 male patients and 18 female patients; mean age, 23.4 years) and 34 secondary chondrosarcomas (from 27 male patients and seven female patients; mean age, 33.2 years). On the basis of the proposed measuring technique, there was 88% interobserver measurement agreement with MR imaging (95% confidence interval [CI]: 80%, 94%) and 93% with CT (95% CI: 84%, 98%). The median difference between measurements of cap thickness at CT and MR imaging was 0 cm (25th and 75th percentiles, –3 mm and 1 mm, respectively). With 2 cm used as a cutoff for distinguishing benign osteochondromas from chondrosarcomas, the sensitivities and specificities were 100% and 98% for MR imaging and 100% and 95% for CT, respectively.

Conclusion: The proposed measuring technique allows accurate and reproducible measurement of cartilage cap thickness with both CT and MR imaging. Cap thickness of 2 cm or greater strongly indicated secondary chondrosarcomas.

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Osteochondroma is the most common benign neoplasm of bone, representing 10%–15% of all primary bone tumors and up to 30% of the benign lesions (1). The prevalence of reported malignant transformation varies from less than 1% for solitary osteochondromas and 2%–5% for hereditary multiple exostosis (1,2). It can be inherently difficult to distinguish a low-grade chondrosarcoma from benign cartilage lesions radiologically and pathologically, even among experienced observers (3).

A major consideration in determining the malignant potential of an osteochondroma is the thickness of its cartilage cap; malignant transformation occurs with cartilage cap thicknesses greater than 1–3 cm (2,4–6). The description and implications of cartilage cap thickness are well referenced in the pathology literature (7,8), but the specific method for measuring cap thickness is not. Relatively small series correlate pathologic findings and cross-sectional imaging for osteochondromas and exostotic chondrosarcoma (9–13). Moreover, these studies did not use a standardized measuring technique for assessing the thickness of large, irregular, convoluted caps.

The purpose of our study was to develop and validate a reproducible imaging technique to accurately measure the thickness of the cartilage cap in osteochondromas. This technique would apply to the usual spectrum of lesions encountered in clinical practice. Measurements were validated by correlation with histologic specimens.

**Materials and Methods**

**Patient Selection and Data Collection**

Institutional review board approval was received for the study. This study was performed with approval of the Mayo Clinic and Armed Forces Institute of Pathology Human Subjects Committee in compliance with the Health Insurance Portability and Accountability Act (HIPAA). Informed consent was not required, and all data collected were HIPAA compliant.

We searched the archives of the Armed Forces Institute of Pathology for pathologically confirmed osteochondromas or secondary chondrosarcomas arising from osteochondromas that had adequate lesion coverage and good-quality magnetic resonance (MR) (T1-weighted and water-sensitive sequences) or computed tomographic (CT) images (obtained with a soft-tissue or bone algorithm). From a total of 142 lesions, 38 were excluded because no CT or MR images were available; three others were excluded because they lacked complete imaging through the lesion. A total of 101 lesions were included: 67 benign osteochondromas and 34 exostotic chondrosarcomas. The pathologic diagnosis was confirmed in all cases by an experienced orthopedic pathologist who had all imaging studies available during histologic review but was blinded to the preliminary pathologic diagnosis.

Each patient’s submission record from the Armed Forces Institute of Pathology was reviewed; demographic data (including sex, race, and age) and whether the osteochondroma was solitary or occurred in the setting of hereditary multiple exostosis were recorded. Osteochondroma location, pathologic diagnosis, chondrosarcoma grade according to the Evans classification (16), and thickness of the cartilage cap on the gross pathologic specimen (when available) were recorded.

**Imaging Review**

Guidelines were created for standardization of measurement of the cartilage cap (Fig 1). This required the following: (a) The tienmark of mature mineralization at the cartilage interface with the osteochondroma stalk had to be identified and used as the base for measurement of the cartilage cap; (b) crevasses of cartilage between undulations in the tienmark had to be excluded from measurement by connecting peaks in the tienmark, as illustrated in Figure 1; and (c) cartilage thickness had to be measured perpendicular to the tienmark, with the measurement inclusive of the full thickness of the relatively high-fluid-content cartilage on imaging studies (represented by fluid attenuation at CT and by low-intermediate T1, intermediate proton density, and high signal intensity approaching that of fluid on T2 at MR imaging).

The measurement of cartilage cap thickness obtained from CT and MR images was validated through correlation with cap thicknesses assessed from scaled photographs of bivalved pathologic gross specimens in 32 cases for which pictures were available (26 osteochondromas and six exostotic chondrosarcomas).

After instruction in the measuring technique, the imaging studies for the 101 osteochondromas were reviewed by...
two musculoskeletal radiologists blinded to clinical and histologic information. Reviewer 1 (S.A.B.) had completed 6 months of musculoskeletal fellowship training, and reviewer 2 (M.D.M.) had more than 20 years of musculoskeletal experience. The reviewers independently measured cartilage cap thicknesses from the CT and MR images, and each reviewer was allowed to independently select images for measurement from the sequences and imaging planes available. All MR images included T1- and T2-weighted sequences. Postcontrast T1-weighted fat-suppressed sequences were available in 17 cases, and proton density images were available in 20 cases.

When both CT and MR images were available for the same lesion, the CT images were reviewed first. Interobserver cap measurements were considered concordant if measurement differences were within 3 mm or 15% of the cap thickness, whichever was larger. A third musculoskeletal radiologist (D.J.F.) performed blinded, independent measurement of cartilage caps when the first two reviewers’ measurements were discordant. The final cartilage cap measurement used for pathologic correlation represented consensus agreement.

In addition, exostotic chondrosarcomas were characterized as focal, regional, or diffuse malignant transformation on the basis of consensual visual estimation of the percentage of the circumference of the cartilage cap that was abnormally thickened (focal, <25%; regional, 25%–75%; diffuse, >75%).

### Statistical Analysis

The percentage agreement between cartilage cap measurements from reviewers 1 and 2 were calculated separately for MR imaging and CT. Statistical agreement was determined by calculation of concordance correlation coefficients and 95% confidence intervals (CIs). For lesions with both CT and MR images available, the median differences between cartilage cap measurements for the two modalities were compared. Both 25th and 75th percentiles and Wilcoxon signed rank test values were calculated. Similarly, in evaluating the correlation between cartilage cap measurements obtained with CT and MR imaging and the gross pathologic findings, concordance correlation coefficients with 95% CIs were calculated. The sensitivity, specificity, positive predictive value, and negative predictive value in diagnosing malignant osteochondromas were calculated for MR imaging and CT. Patient age and race, presence of solitary versus hereditary multiple exostosis, and lesion location were evaluated as potential confounding factors. A two-sample t test was used to estimate age differences between the patients with benign lesions and those with chondrosarcomas. The proportionate rates of malignant transformation based on lesion location were calculated with a Fisher exact test. This test was also used to evaluate statistically significant differences based on sex, race, and whether lesions arose from solitary osteochondromas or occurred in a setting of hereditary multiple exostosis. A P value less than .05 was considered to indicate a significant difference.

### Results

Patient demographic characteristics are summarized in Table 1. For the 67 benign osteochondromas, there was a 2.7:1 male-to-female ratio, which increased to 3.9:1 in the 34 exostotic chondrosarcomas. Patients with chondrosarcomas were nearly a decade older than patients undergoing resection for benign osteochondromas (mean ages, 33.2 years and 23.4 years, respectively). Only three patients with chondrosarcomas were younger than 20 years old, and all had histologically low-grade lesions.

Histologically, the chondrosarcomas were grade I in 68% of patients (n = 23), grade II in 29% (n = 10), and grade III in 3% (n = 1). No correlation between patient age, race, sex, lesion location, or cartilage cap thickness and the grade of chondrosarcoma could be identified (P = .22). The relationship between lesion location and malignancy is shown in Table 2; this table underscores the relationship between anatomic location and the fact that most exostotic chondrosarcomas arose from malignant transformation of central osteochondromas. Malignancy was identified in 71% of pelvic and 35% of spinal lesions compared with 16% of peripheral extremity lesions. Only the rate of malignant transformation...
of pelvic lesions was statistically significant \( P < .005 \).

Correlation of the cartilage cap measurements between imaging studies and the corresponding gross pathologic findings (Fig 2) in 32 cases (26 osteochondromas and six chondrosarcomas) demonstrated measurement variances of 3 mm or less (Figs 3b, 4b).

For the 101 lesions evaluated, interobserver reproducibility of cartilage measurements when applying the described measuring guidelines demonstrated 88% agreement for MR imaging (95% CI: 80%, 94%) and 93% for CT (95% CI: 84%, 98%). The differences in measurements averaged less than 2 mm for MR imaging interpretations (Fig 3a) and less than 3 mm for CT interpretations (Fig 4a). The median difference between measurement of cap thickness in the same lesion when both modalities were available was 0 cm (25th and 75th percentiles, –0.3 cm and 0.1 cm, respectively) (Fig 5).

Two benign scapular osteochondromas had developed overlying bursae and resulted in false-positive thickening of the cartilage cap when measured with CT (Figs 4b, 5). Although both bursae were recognized prospectively by the more experienced interpreters (M.D.M. and D.J.F.) secondary to sacral outpouchings at the periphery, the boundaries could not be accurately differentiated from the cartilage cap at CT; this resulted in discordant measurements of the cartilage caps, measured up to 2.5 cm and 2.7 cm. These two lesions were shown to have cartilage caps of 0.3 cm and 0.4 cm, according to MR imaging (Fig 6) and pathologic analysis.

After exclusion of the two false-positive CT measurements, the thickness of benign cartilaginous caps measured with CT ranged from 0.1 to 1.9 cm. At MR imaging, these measurements ranged from 0.1 to 2.2 cm; only one benign osteochondroma cartilage cap reached or exceeded 2 cm in thickness (Fig 7). Among benign osteochondromas, 7% had cartilage cap thicknesses of 1.5 cm or more, and 18% had thicknesses greater than 1 cm. In contrast, the cartilage thicknesses of chondrosarcomas ranged from 2.0 to 14.0 cm at CT and 2.0 to 17.0 cm at MR imaging; none had caps less than 2.0 cm, and 79% had caps measuring more than 3.0 cm. Further analysis of the morphology of the cartilage thickening in chondrosarcomas showed it to be diffuse in 89% and regional in 11% of cases (Fig 8).

The use of 2 cm as a cutoff for distinguishing benign osteochondromas from secondary chondrosarcomas provided sensitivities, specificities, positive predictive values, and negative predictive values of 100%, 98%, 96%, and 100%, respectively, for MR imaging and 100%, 95%, 93%, and 100%, respectively, for CT.

**Discussion**

To our knowledge, this is the largest cross-sectional imaging study evaluating cartilage cap thickness with pathologic correlation. Although the relationship between cartilage cap thickness and malignancy has been well described, a reliable and reproducible measuring technique to assess this thickness has not been adopted. As has been previously demonstrated for MR imaging (14,17), in this study MR imaging and CT showed excellent validity for noninvasive evaluation of cartilage cap thickness compared with pathologic findings. Cartilage cap thickness is easily measured when lesions are small and cap thickness is uniform. However, it becomes considerably more difficult when caps are convoluted and irregular. Accordingly, we proposed the method depicted in Figure 1 after extrapolation of histologic patterns of cartilage cap growth.

Cartilage in osteochondromas grows perpendicular to the base from a zone...
The differentiation of benign osteochondromas from secondary chondrosarcomas depends on patient age. Among exostotic chondrosarcomas, 74% had cartilage caps greater than 4 cm. In this group—the 18% of benign osteochondromas and 21% of chondrosarcomas with cartilage cap thicknesses in this intermediate range of 1–3 cm—the measuring technique becomes more critical for correctly differentiating benign osteochondromas from secondary chondrosarcomas. Applying the 1- or 1.5-cm cutoff currently used for recommending resection on the basis of concern for malignant transformation would result in a higher rate of removal of benign osteochondromas and the resultant associated morbidity. Because exostotic chondrosarcomas are slow-growing, overwhelmingly low-grade, and of low metastatic potential, imaging surveillance of osteochondromas with cartilage caps approaching 2 cm represents a reasonable and safe alternative.

We found that the use of standardized measurement guidelines permitted highly reproducible measurement of cartilage caps, with similar results from both a relative novice and a highly experienced musculoskeletal radiologist. This standardization also constricted the thickness range that distinguished benign osteochondromas from secondary chondrosarcomas. A relatively sharp delineation of benign osteochondromas from chondrosarcomas occurred at a 2-cm cartilage cap thickness (Fig 6). With a 2-cm cutoff, 100% of chondrosarcomas were correctly identified with both MR imaging and CT thickness criteria, and the percentage of benign osteochondromas that would have undergone resection solely for concerns of malignant transformation could have been reduced to fewer than 2% on the basis of MR imaging criteria. Although the initial tendency was to be conservative in excluding apparent focal deeper crevasses of cartilage (as was predicted by the behavior of cartilage growth), this exclusion was shown not to affect the ability to accurately recognize pathologic thickening of the cartilage cap. No chondrosarcomas demonstrated less than 25% cartilage cap involvement, and in most cases (89%) the cartilage cap thickening was diffuse.
A particular subset of osteochondromas occurs at sites of friction or impingement of a lesion with adjacent bone or soft-tissue structures, leading to the development of an overlying bursa. Although bursae may form at any location, they are most often associated with the osteochondromas arising from the ventral surface of the scapula or lesions about the hip (20–25). Bursae may be associated with up to 1.5% of osteochondromas (19). Given the relative similarity of bursal fluid to the high-fluid-content cartilage signal intensity with most MR sequences and attenuation

Figure 3: Concordance of interobserver measurements and radiologic-pathologic measurements of cartilage cap thickness at MR imaging. (a) Interobserver comparisons of cartilage cap measurement at MR imaging showed differences averaging less than 2 mm and 88% agreement (concordance correlation coefficient, 0.990; 95% CI: 0.985, 0.994). (b) MR imaging accurately reflected cartilage cap thickness on gross specimens (concordance correlation coefficient, 0.990; 95% CI: 0.981, 0.995).

Figure 4: Concordance of interobserver measurements from CT imaging. (a) Interobserver comparisons of cartilage cap measurements at CT showed differences averaging less than 3 mm and 93% agreement (95% CI: 84%, 98%). (b) CT imaging accurately reflected cartilage cap thickness on gross specimens, except in the setting of bursa formation (black circle) (concordance correlation coefficient, 0.976; 95% CI: 0.940, 0.990).
Differentiation of Benign Osteochondromas from Secondary Chondrosarcomas

Bernard et al

At CT, bursae can confound accurate measurement of cartilage cap thickness (20). In this study, lesions with bursae represented the only two false-positive cartilage cap measurements. For most osteochondromas in this study, cartilage cap measurements with MR imaging relied heavily on fluid-sensitive sequences; depiction of cartilage caps was excellent with proton density or gradient echo sequences when available. While postcontrast MR images were available in only 16 cases, contrast enhancement provided little additional information compared with unenhanced images.

Figure 5: Concordance of cartilage cap measurement with CT and MR imaging. With the exception of two osteochondromas that developed bursae (arrow), the median difference between measurements obtained with MR imaging and CT was less than 2 mm; no significant difference was seen with Wilcoxon signed rank test.

Figure 6: Images of ventral scapular osteochondroma with bursa in 29-year-old man. (a) Axial CT image obtained with soft-tissue algorithm (window width, 300 HU; window level, 40 HU). (b) T2-weighted (repetition time msec/echo time msec, 4000/96.4) MR image. (c) Postgadolinium T1-weighted (572/15) MR image of a ventral scapular osteochondroma with bursal formation. CT did not help distinguish the bursa from cartilage cap (arrow in a). MR imaging depicted the thin, low-signal-intensity fibrovascular covering (arrowheads in b) separating cartilage cap from adjacent bursa and allowed accurate measurement. Postgadolinium T1-weighted image shows enhancement of the bursa (arrow in c) and the fibrovascular surface of the cartilage (arrowheads in c), making cartilage cap distinction difficult.

Figure 7: Correlation of cartilage cap thickness and pathologic findings. Cap measurements were 2 cm or more (mean thickness, 6.5 cm; n = 34). Sarcomas are shown according to their grade as listed across the top. Benign osteochondromas (○) had cartilage cap thicknesses of less than 2 cm (mean thickness, 0.6 cm; n = 67). The one exception was a benign osteochondroma of the distal tibia in a 21-year-old man, which had a cap thickness of 2.2 cm (arrow).
This remained true even in the setting of bursae because both the bursa and cartilage caps were imaged similarly; both demonstrated peripheral and septal enhancement with internal fluid signal intensity. As a result, the postcontrast MR images performed only as well as CT or unenhanced T1-weighted sequences; these MR images did not permit accurate identification of the cartilage cap boundary. In our experience, cartilage caps can be most reliably differentiated from bursal fluid with cartilage-sensitive fat-suppressed spoiled gradient-echo sequences in which bursal free-water signal is suppressed while the hyaline cartilage signal remains increased (26).

We acknowledge several limitations of the study. As with all reviews based on referral populations, the possibility of selection bias makes it impossible to draw conclusions based on patient demographic characteristics. The racial distribution in this study parallels that of the US population. Also as a result of the nature of our referral population, we could not determine the actual rate of malignant transformation of lesions based on skeletal location. The specimens available to us, however, reflect what has been previously well reported in the literature; an increased rate of malignant degeneration of centrally located and especially pelvic osteochondromas (7,8,12,27). The percentage of benign lesions with cartilage cap thicknesses greater than 1 cm was disproportionately higher in our study population than would have been expected in clinical practice. This is probably a function of inclusion of only surgically resected lesions with pathologic confirmation—the typical benign osteochondromas with very thin cartilage cap did not pose a diagnostic dilemma and was not excised unless symptomatic. In addition, imaging was performed at numerous institutions, and imaging techniques, parameters, and planes therefore varied. However, we believe that this variability strengthened the evaluation of the reproducibility of the measuring technique across the spectrum of imaging parameters and systems available.

In conclusion, this study supports application of a standardized measuring technique for improved distinction of benign osteochondromas from chondrosarcomas, with a cartilage cap thickness of 2 cm or greater as the determinant of chondrosarcomas and as the criteria for recommending resection for malignant concerns. For lesions with cartilage caps measuring greater than 2 cm at CT evaluation, MR imaging or ultrasonography should be considered to exclude bursal formation. Closer surveillance of central lesions, especially pelvic osteochondromas, is warranted as a result of their increased propensity for malignant transformation.

References


