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Research Article

The Performance of Radiographic Criteria for Bone Malignancy When Applied to Computed Tomography and Magnetic Resonance Imaging

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ABSTRACT

Background: The conventional radiologic features that differentiate benign from malignant bone lesions were originally described using radiography (x-ray [XR]). When evaluating sectional imaging studies such as magnetic resonance imaging (MRI) and computed tomography (CT), one may apply these principles to identify malignant bone lesions. The aim of this study was to evaluate the performances of these radiographic features for detecting malignity when applied to CT and MRI.

Materials and Methods: This retrospective study was approved by our institutional ethical board. Thirty-nine patients with histopathologic proof of a high-grade bone malignancy and preoperative imaging data obtained with a minimum of two different modalities were included in the study. Four radiologists reviewed the images and scored the lesions for distinctness of margins, presence and type of periosteal reaction, matrix mineralization, and presence of soft tissue mass. The average score for each modality was then tested for accuracy with regard to the histopathology.

Results: When lesion margins were considered, XR was the best modality to detect a high-grade malignancy. MRI, especially post-contrast T1-weighted sequence, was the least helpful in this regard. There was no significant difference between CT and XR and between CT and MRI. When the periosteal reaction was considered, XR was the best modality to detect the malignant type of periosteal reaction. In this regard, MRI and CT were misleading; either by not detecting or undergrading periosteal reaction. MRI was the best modality to detect soft tissue mass.

Conclusion: Conventional imaging criteria for bone malignancy can be misleading when applied to MRI or CT. When cross-sectional imaging features contradict those from XR, the latter should be the guide for clinical management.

RESUME

Contexte : Les caractéristiques radiologiques conventionnelles permettant de distinguer les lésions osseuses bénignes des lésions malignes ont été à l'origine décrites à l'aide de la radiographie (rayons X: RX). Dans l'évaluation des études d'imagerie sectionnelle comme l'imagerie par résonance magnétique (IRM) et la tomodensitométrie (TDM), on tend parfois à appliquer ces principes pour identifier les lésions osseuses malignes. Cette étude vise à évaluer le rendement de ces caractéristiques radiographiques pour la détection de la malignité lorsqu'on les applique à l'IRM et à la TDM.

Matériel et méthodologie : Cette étude rétrospective a été approuvée par notre comité d'éthique de la recherche. Trente-neuf patients présentant des preuves histopathologiques de malignité osseuse élevée et des données d'imagerie préopératoire obtenues par au moins deux modalités différentes ont été inclus dans l'étude. Quatre radiologistes ont examiné les images et noté les lésions selon la netteté des marges, la présence et le type de réaction périostale, la minéralisation de la matrice et la présence de masses dans les tissus mous. La note moyenne pour chaque modalité a ensuite été évaluée pour sa précision en comparaison de l'histopathologie.

Résultats : Lorsque les marges de la lésion sont prises en compte, la RX était la meilleure modalité pour détecter une malignité élevée. L'IRM, et plus particulièrement la séquence pondérée T1 post-contraste, était la moins utile à cet égard. Il n'y avait pas de différences significatives entre la TDM et la RX, non plus qu'entre la TDM et l'IRM. Lorsque

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la réaction périostale est considérée, la RX était la meilleure modalité pour détecter la réaction périostale de type malin. À cet égard, la TDM et l'IRM étaient trompeuses, que ce soit en ne détectant pas la réaction périostale ou en la sous-évaluant. L'IRM était la meilleure modalité pour détecter les masses dans les tissus mous.

Conclusion : Les critères d'imagerie conventionnels pour la malignité osseuse peuvent être trompeurs si on les applique à l'IRM ou à la TDM. Lorsque les caractéristiques des images de coupe transversale contredisent celles de la RX, ces dernières devraient être utilisées comme guide pour la gestion clinique.

Keywords: Bone tumors; radiography; cross-sectional imaging; radiographic criteria

Introduction

The most important clues to the nature of a bone lesion are the patient's age and the location of the lesion. Following these are the imaging findings. Conventional imaging features to differentiate benign from malignant lesions originally were described using radiography (X-ray [XR]). These are mainly lesion margins, periosteal reaction, matrix mineralization, and cortical destruction [1–5].

Cross-sectional imaging has been used with increasing frequency in the initial workup of bone lesions. We observed a tendency to apply XR criteria of malignancy when interpreting cross-sectional imaging studies in our practice, often with misleading results.

Our aim of this study was to document if XR criteria can be applied to cross-sectional imaging studies such as magnetic resonance imaging (MRI) and computed tomography (CT).

Materials and Methods

Patients

This retrospective study was approved by the ethical board of our institution. We reviewed the data from 84 patients with the diagnosis of a high-grade malignant bone tumor from March 2009 to January 2015. Imaging, pathologic, and clinical data were obtained from the picture archiving and communication system and computerized medical records of our center. The inclusion criteria were histopathologic proof of a high-grade malignancy and imaging data of tumor site obtained with at least two different modalities. The exclusion criteria were the lack of preoperative imaging and non-diagnostic studies.

Of 39 patients who met the inclusion criteria, XR was available in 34 patients, CT was available in 25 patients, and MRI was available in 34 patients. The availability of multiple modalities is shown in Table 1. In 34 MRI studies, 21 studies were obtained using a 1.5-T scanner and 13 using a 3.0-T scanner.

Imaging Technique

MRI and CT studies were mostly performed at our institution using 1.5 and 3.0 T units (Philips, Eindhoven, the Netherlands) for MRI and 64-detector scanner (Aquilion 64; Toshiba Medical Systems, Tokyo, Japan) for CT.

MRI studies obtained using two different scanners were performed using similar parameters. Because of the variation of slices required for each patient/anatomy, a range is given in Table 2 for each parameter, instead of a single value.

Similarly, because of the variations in patient weight, size, and tissue thickness, CT parameters varied between patients/studies are shown in Table 3.

Image Evaluation

The data from 39 patients who met the inclusion criteria were evaluated by four radiologists from our department for the following imaging features: lesion margins, periosteal reaction/type, matrix mineralization, and presence of soft tissue mass on XR, CT, and T1-weighted (T1W), T2-weighted (T2W), fat-suppressed T2-weighted (FS-T2W/STIR) and post-contrast T1-weighted sequences (pc-T1W) of MRI. The scoring system and parameters are shown in Table 4. Lesion margin and periosteal reaction scores were evaluated independently, but matrix mineralization and presence of soft tissue mass were evaluated by consensus.

Data and Statistical Analysis

The scores from four radiologists for lesion margins and periosteal reaction parameters were averaged. The differences between imaging modalities for scores of lesion margin and periosteal reaction were tested using paired sample t-test and Wilcoxon signed-rank test. In addition, ''Cohen's d'' effect size was calculated to evaluate the strength of effect. The agreement of matrix mineralization between imaging modalities and histology was analyzed with Cohen's Kappa coefficient. An exact McNemar's test was used to analyze the difference for detecting soft tissue mass between imaging modalities. All statistical tests were performed using IBM SPSS Statistics for Windows, version 23 (IBM Corp., Armonk, NY).

Table 1
Availability of Multiple Modalities

Two Modalities		Three Modalities	
XR–CT	20	XR–CT–MRI	15
XR–MRI	29		
CT–MRI	20		

CT, computed tomography; MRI, magnetic resonance imaging; XR, conventional radiography.

Table 2
MRI Parameters

Sequence Name	Section Thickness (mm)	Distance (mm)	TR (ms)	TE (ms)	TI (ms)	FOV (mm)
T1W	3–5	3–6	500–700	10–20	–	180–430
T2W	3–5	3–6	3,000–4,000	80–120	–	180–430
FS-T2W/STIR	3–5	3–6	9,000–15,000	60–100	210	180–430
pc-T1W	3–5	3–6	500–700	10–20	–	180–430

FOV, field of view; FS-T2W/STIR, fat-suppressed T2-weighted sequence; mm, millimeter; ms, millisecond; pc-T1W, post-contrast T1-weighted sequence; T1W, T1-weighted sequence; T2W, T2-weighted sequence.

Results

Patients

Thirty-nine patients who were diagnosed with a high-grade malignant bone tumor and met the study criteria were investigated. There were 14 females and 25 males. The mean age was 11.6 years with a range between 2.4–25.3 years. The malignant bone tumors investigated were osteosarcoma, Ewing sarcoma, Langerhans cell histiocytosis, neuroblastoma, non-Hodgkin lymphoma, Wilm's tumor, and malignant giant cell tumor.

Lesion Margins

There were significant differences between XR scores and all sequences of MRI except T2W scores with the XR received higher scores. When MRI sequences were compared, T1W, T2W, and FS-T2W/STIR sequences received higher scores than pc-T1W sequence. There were no significant differences between T1W and T2W, or T1W and FS-T2W/STIR, but there was a significant difference between T2W and FS-T2W/STIR with T2W receiving higher scores ($P < .05$). When CT was compared with other modalities, there were no significant differences between CT and XR and between CT and MRI except for pc-T1W, CT received higher scores than pc-T1W ($P < .01$; Table 5)

Periosteal Reaction

Periosteal reaction types were evaluated in ordinal scales. The higher scores reflected the more malignant types of periosteal reaction. We compared average periosteal reaction scores—from four radiologists' evaluation—between T1W, T2W, XR, and CT imaging. XR received significantly higher scores than T1W and T2W ($P < .001$ and $P < .05$, respectively). There were no significant differences between T1W and T2W and between CT and XR. When CT scores were compared with MRI sequences, CT received higher scores than T1W ($P < .01$), but there is no significant difference between CT and T2W scores (Table 6).

Table 3
CT Parameters

mA	kV	FOV (mm)	Slice Thickness (mm)
50–150	120	270–400	0.5–5

CT, computed tomography; FOV, field of view; mA, milliampere; kV, kilovolt.

Table 4
Evaluated Imaging Criteria and Their Scoring Methods

Lesion margin identification (for T1W, T2W, FS-T2W/STIR, pc-T1W sequence of MRI, CT, and XR)	1 = Lesion margins can be clearly identified from adjacent normal tissue 2 = Lesion margins can be somewhat clearly identified from adjacent normal tissue 3 = Lesion margins can be identified with difficulty from adjacent normal tissue 4 = Lesion margins can be barely identified from adjacent normal tissue 5 = Lesion margins cannot be identified.
Periosteal reaction (for T1W and T2W sequences of MRI, CT, and XR)	0 = No periosteal reaction 1 = Uniform periosteal reaction 2 = Periosteal reaction exists but cannot be assessed 3 = Malignant type of periosteal reaction (interrupted, sunburst, hair-on-end, Codman's triangle, and so on)
Matrix mineralization (for MRI, CT, and XR)	0 = No matrix mineralization or cannot be assessed 1 = Chondroid matrix 2 = Osteoid matrix
Soft tissue mass (for MRI, CT, and XR)	0 = Soft tissue mass existent 1 = Soft tissue mass nonexistent

CT, computed tomography; FS-T2W/STIR, fat-suppressed T2-weighted sequence; MRI, magnetic resonance imaging; pc-T1W, post-contrast T1-weighted sequence; T1W, T1-weighted sequence; T2W, T2-weighted sequence; XR, X-ray.

Matrix Mineralization

Matrix mineralization types were evaluated categorically as osteoid, chondroid, and no matrix mineralization. Cohen's Kappa was run to determine assessment between histologic matrix mineralization type and detected matrix mineralization type by XR, CT, and MRI. All radiologic modalities were in statistically significant agreement with the histologic matrix mineralization type. The strongest agreement was seen with the CT ($\kappa = 0.749$), then XR and MRI, respectively (Table 7).

Soft Tissue Mass

Detection of soft tissue mass was evaluated in paired samples for each combination of imaging modalities. When MRI and XR compared, XR has detected soft tissue mass in 14 patients, while MRI has detected in 25 patients in a total of 29 patients. An exact McNemar's test determined that the difference in the proportion of soft tissue mass detection between XR and MRI was

Table 5
Analysis of Lesion Margin Scores for MRI Sequences, XR, and CT

Pairs	Mean Difference	SE	t(df) or Z	P	Confidence Interval	Effect Size ("d" or "r")
T1W–T2W	0.15	0.25	1.59 (19)	.562	−0.38 to 0.68	0.49
T1W–FS-T2W/STIR	0.01	0.19	0.05 (29)	.956	−0.41 to 0.39	0.20
T1W–pc-T1W	0.50	0.21	2.32 (33)	.027*	0.06 to 0.93	0.97
T2W–FS-T2W/STIR	0.39	0.17	2.19 (16)	.044*	0.01 to 0.77	0.51
T2W–pc-T1W	1.33	0.18	$Z = 3.30$	.001*	1.00 to 1.66	$r = 0.73$
FS-T2W/STIR–pc-T1W	0.50	0.12	$Z = 2.66$	.008*	0.33 to 0.66	$r = 0.48$
XR–T1W	0.81	0.22	3.60 (28)	<.001*	0.36 to 1.27	1.24
XR–T2W	0.40	0.21	1.84 (14)	.086	−0.06 to 0.86	0.16
XR–FS-T2W/STIR	0.67	0.24	2.80 (26)	.009*	0.18 to 1.17	1.25
XR–pc-T1W	0.33	0.22	$Z = 3.55$	<.001*	0.83 to 1.83	$r = 0.65$
XR–average MRI	0.88	0.19	$Z = 3.36$	<.001*	0.45 to 1.27	$r = 0.62$
XR–CT	0.16	0.18	$Z = 0.91$	.362	−0.33 to 0.66	$r = 0.20$
CT–T1W	0.18	0.32	0.55 (19)	.584	−0.50 to 0.87	1.12
CT–T2W	0.14	0.34	0.41 (13)	.684	−0.60 to 0.88	0.78
CT–FS-T2W/STIR	0.47	0.24	2.00 (15)	.064	−0.03 to 0.99	0.36
CT–pc-T1W	0.81	0.24	3.35 (19)	.003*	0.30 to 1.32	1.00
CT–average MRI	0.45	0.22	2.02 (19)	.570	−0.01 to 0.91	0.44

CT, computed tomography; d, Cohen's d; FS-T2W/STIR, fat-suppressed T2-weighted sequence; MRI, magnetic resonance imaging; pc-T1W, post-contrast T1-weighted sequence; SE, standard error; t, statistic of t-test; Z, standardized statistic of Wilcoxon's signed-rank test; r, effect size of Wilcoxon's signed-rank test.
* Statistically significant results.

statistically significant, $P < .001$. There was no significant difference between MRI and CT and between XR and CT ($P = 1.0$ and $P = .05$, respectively).

Discussion

The conventional imaging features such as lesion margins, cortical destruction, presence and type of periosteal reaction, and matrix mineralization to differentiate benign from malignant bone lesions were originally described using radiography [1, 2]. Our results suggest that the radiographic criteria for bone malignancy may be misleading when applied to MRI or CT (Figure 1). It has always been stated that radiography is the mainstay of bone tumor imaging and should not be omitted from the initial work-up. Besides that, the sectional imaging modalities, especially MRI, can give valuable information about soft tissue invasion of tumors, local staging, pre- and post-operative evaluation, and response to therapy. Nasciemto et al (2014) reviewed these features of MRI that can help to narrow the differential diagnosis or can make a specific diagnosis of bone tumors [6]. What our study may add to this knowledge is that one should refrain from using radiographic criteria when interpreting sectional images and should make clinical management decisions relying on radiographic data when these contradict with sectional imaging data.

In a patient population with a high-grade malignancy, our findings suggest that sectional imaging data, when interpreted using radiographic criteria, result in underestimation of tumor malignity. Interestingly, in a series of cases with non-malignant bone lesions, Hayes et al (1992) reported that where sectional imaging findings alone suggested a high-grade malignancy, radiographs correctly pointed at the diagnosis [7]. They also arrived at the conclusion that radiographs should always be given priority in clinical management decisions.

The distinctness of lesion margins is a major feature when differentiating benign from malignant bone lesions [1–5]. The reason for underestimation of tumor grade by sectional imaging when compared with XR when lesion margins are concerned may be better lesion delineation on individual slices instead of overlapping tissue characteristics provided by planar imaging. This, on the other hand, may be an advantage for XR when evaluating periosteal reaction by showing the

Table 6
Analysis of Periosteal Reaction Scores for MRI Sequences, XR, and CT

Periosteal Reaction Pairs	N	W	Z	P	Confidence Interval	r (Effect Size)
T1W–T2W	33	18.00	1.69	.970	−1.66 to 0.33	0.29
XR–T1W	29	0.00	3.54	<.001*	−2.00 to −0.66	0.65
XR–T2W	20	9.00	2.28	.023*	−2.00 to −0.33	0.50
CT–T1W	28	14.50	2.67	.007*	−1.00 to −0.66	0.50
CT–T2W	19	5.00	1.61	.100	−2.50 to 0.50	0.36
XR–CT	20	6.50	0.27	.780	−1.33 to 1.00	0.05

CT, computed tomography; MRI, magnetic resonance imaging; N, number of analyzed pairs; W, statistic of Wilcoxon signed-rank test; Z, standardized statistic; T1W, T1-weighted sequence; T2W, T2-weighted sequence; XR, X-ray.
* Statistically significant results.

Table 7
Agreement Between HMM and the Matrix Mineralization Detected by XR, CT, and MRI

Comparison	Cohen's Kappa	Standard Error	P
XR–HMM	0.508	0.120	<.001
CT–HMM	0.749	0.118	<.001
MRI–HMM	0.306	0.130	.007

HMM, histologic matrix mineralization.

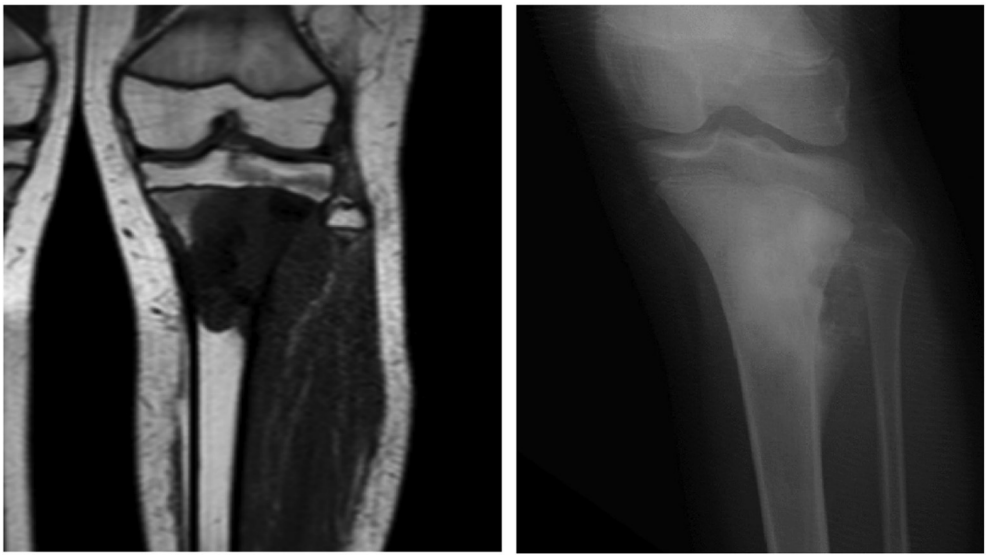


Figure 1. Osteosarcoma of the tibia: a coronal T1WI (left) shows a large hypointense lesion in the proximal tibia whose margins are clearly identified from the adjacent normal bone tissue. Corresponding XR images of same lesion (right) reveal a large lesion with malignant periosteal reaction whose margins are barely identified from adjacent normal bone tissue.

entire picture on one image, while the presence and characteristics of periosteal reaction are difficult to perceive on individual slices, especially on MRI. CT, theoretically, should allow for equal or better characterization of periosteal changes compared with XR, but it was not better than XR in our study. This may have resulted from the limited number of patients on whom an initial CT study was available. In six patients, the only CT study was that of an initial fluorodeoxyglucose positron emission tomography-CT, the resolution of which is usually low for local lesion characterization.

Matrix mineralization is not as helpful in predicting malignancy as lesion margins and periosteal reaction are, but still has diagnostic significance [1, 4]. In our study, CT was the most helpful modality assessing this feature, probably owing to its high spatial resolution and cross-sectional capability.

The presence of soft tissue mass is an important finding indicating malignancy in some bone tumors, especially Ewing's sarcoma and osteosarcoma [6]. In our study, MRI was superior to XR for detecting soft tissue mass. CT was equally helpful in this regard. Since we originally aimed at evaluating the performances of conventional XR criteria, the soft tissue extension was not included as a main criterion of our study.

Our study has several limitations. Our data include only high-grade malignant bone tumors so we were not able to compare the performances of radiologic modalities on benign bone lesions or low-grade bone tumors. The number of patients is relatively small. Our scoring system is subjective, although we aimed at achieving a more objective reading by obtaining average scores and consensus decisions from the evaluations by four radiologists. In six patients, the CT part of a PET-CT study was evaluated, which typically has lower resolution than a regular CT study. The results did not change when these studies were excluded. In addition, patients with no regular CT and a PET-CT with prohibitively low resolution for scoring were excluded initially. The use of multiplanar reconstruction planes may improve the performance of CT when evaluating periosteal reaction or lesion margins. In our study, multiplanar reconstruction was used only in a number of cases when the radiologist thought it was required.

In conclusion, a well-defined bone lesion with little or no significant periosteal reaction on MRI or CT may appear completely different on XR, prompting urgent biopsy or excision rather than follow-up. If a lesion is indistinct or suspicion of malignancy exists in initial XR examination, a multimodality approach with MRI and/or CT can be more helpful by yielding more detailed information about malignancy signs [6]. Nonetheless, clinical management decisions on a newly diagnosed bone lesion should be based on radiographic features when these contradict with those of sectional imaging studies. Cheap and widely available, the XR should remain as the mainstay of initial evaluation of a bone lesion [1–5, 8, 9].

Footnotes

Contributors: All authors contributed to the conception or design of the work, the acquisition, analysis, or interpretation of the data. All authors were involved in drafting and commenting on the paper and have approved the final version.

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Ethical approval: This study was approved by the authors' institutional ethical board.

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