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ORIGINAL STUDY

Fracture risk in unicameral bone cyst. Is magnetic resonance imaging a better predictor than plain radiography ?

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The classical indication for treating a simple bone cyst is usually the risk of fracture, which can be predicted based on three parameters : the bone cyst index, the bone cyst diameter, and the minimal cortical thickness. A retrospective review was carried out based on imaging of 35 simple bone cysts (30 humeral and 5 femoral). The three parameters were measured on standard radiographs, and on T1-weighted and T2-weighted MRI. The measurements were performed by two independent reviewers, and twice by the same reviewer. Kappa values and binary logistic regression were used to assess the ability of the parameters to predict the fracture risk. Inter- and intra-observer agreement was measured. T1-weighted MRI was found to have the best inter- and intra-observer repeatability. The bone cyst index was found to be the best predictor for the risk of fracture.

Keywords : magnetic resonance imaging ; radiograph ; simple bone cyst ; bone cyst index.

INTRODUCTION

Simple bone cyst (SBC) is a benign lytic bone lesion that affects children and young patients (*4*). It is usually located in the metaphysis of long bones, and most frequently in the proximal femur and proximal humerus. The aetiology remains unclear. Diagnosis is often made by plain radiography, although magnetic resonance imaging (MRI) can be helpful for the differential diagnosis with an aneurysmal bone cyst. Treatment is advocated when the SBC has weakened the bone so that there is a risk of pathological fracture, which is the most frequent complication. However, predicting which SBC is likely to fracture is difficult, although previous studies have described several parameters.

The bone cyst index (BCI) described by Kaelin and MacEwen (*6*) is often used as an easy method to assess the mechanical resistance of the cyst wall. The BCI is obtained by dividing the cyst area by the diameter of the diaphysis squared. Kaelin and

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MacEwen did not find a significant difference between the BCI measured on the anteroposterior and lateral radiographic views (6). They found that SBC's with a BCI of more than 4 for the humerus and more than 3.5 for the femur were at high risk for fracture. Recently, the BCI has been found to be invalid as an accurate predictor of a future fracture due to low intra-observer and inter-observer reliability (9). Moreover, it has been shown there was a significant difference between the value for the BCI measured on the anteroposterior and lateral views (9). A second predictor for fracture is the bone cyst diameter (BCD), as reported by Ahn and Park (1) ; this is expressed as the percentage of bone occupied by the cyst in the transverse plane. SBC is considered to be at a high risk for fracture when the BCD reaches more than 85% in both the anteroposterior and lateral radiographs. A third predictor of fracturing is the minimal cortical thickness (MCT), with a MCT inferior to 2 mm being an indicator of a high fracture risk (6).

Three objectives were followed in this study. The first was to evaluate the ability of the three parameters (BCI, BCD, MCT) to predict the risk of fracture from standard radiographs and T1-weighted and T2-weighted MRI. The second objective was to assess the repeatability of these three parameters. The last objective was to compare BCI on both the anteroposterior and lateral views on standard radiographs.

MATERIALS AND METHODS

Thirty-five SBCs were retrospectively analyzed, including 30 located in the humerus and 5 in the femur. The mean age of the study population was 11.9 years (range : 3.6-26.3 years) ; 63% of the patients were boys.

Radiography and MRI acquisition

All patients underwent standard radiography and MRI examinations with a mean delay of three weeks between the two examinations. Both anteroposterior and lateral radiographic views were taken. T1-weighted and T2-weighted-MRI scans were acquired using a 1.5-T MR imaging unit (Gyroscan NT Intera T15 ; Philips Medical Systems, Best, the Netherlands), with the following parameters : spacing between slices, 4 mm (T1-T2), reconstruction matrix, 512 × 512 (T1-T2), section thickness, 4.0 mm (T1-T2), repetition time, 440.5 ms (T1) and 3665.5 ms (T2), echo time, 18.0 ms (T1) and 110.0 ms (T2). These parameters are routinely used for analysis of bone cysts in our institutions. The sequences were saved from the PACS system of the institution (Kodak Carestream PACS, Eastman Kodak Company 2006) in dicom format.

Evaluation of radiographs and MRI

The three parameters (BCI, BCD, and MCT) were measured on both anteroposterior and lateral radiographs, and on T1-weighted-MRI and T2-weighted-MRI. The BCI was determined using the method described by Kaelin and MacEwen (6). The area was measured with open-source software (ImageJ 1.40 g ; http://rsbweb.nih.gov/ij/). BCI was determined by the ratio of the area to the square of the diaphyseal diameter, which was measured in its tubular part. BCD was calculated according to the method described by Ahn and Park (1) as the largest width of the cyst divided by the width of the bone at the same level.

Ability to predict the fracture risk

In order to predict the risk of fracture, we classified the cysts into two groups : 21 SBCs were classified as "at risk for fracture" and 14 SBCs were classified as "not at risk for fracture". A cyst was classified in the fracture risk group if a fracture had occurred in a 6-week period before or after imaging, or if cysts had one of the three following criteria : BCI > 4 for the humerus or > 3.5 for the femur ; > 85% of bone occupation by the cyst in the transverse plane ; MCT <1 mm. Ability to classify the cyst in the correct group was tested for BCI > 4 for the humerus and > 3.5 for the femur, for > 80% and > 85% of bone occupation by the cyst in the transverse plane and for MCT values that were < 1 mm, < 1.5 mm, and < 2 mm. The potential predictors of fracture risk were tested using a logistic regression model.

Repeatability of BCI, BCD and MCT

The three parameters were measured on radiographs and MRI by two independent observers. Each observer was blinded to the results of the other. Images were interpreted twice by the same reviewer after a 1-week minimum time interval. The inter- and intra-observer repeatability of each method was evaluated.

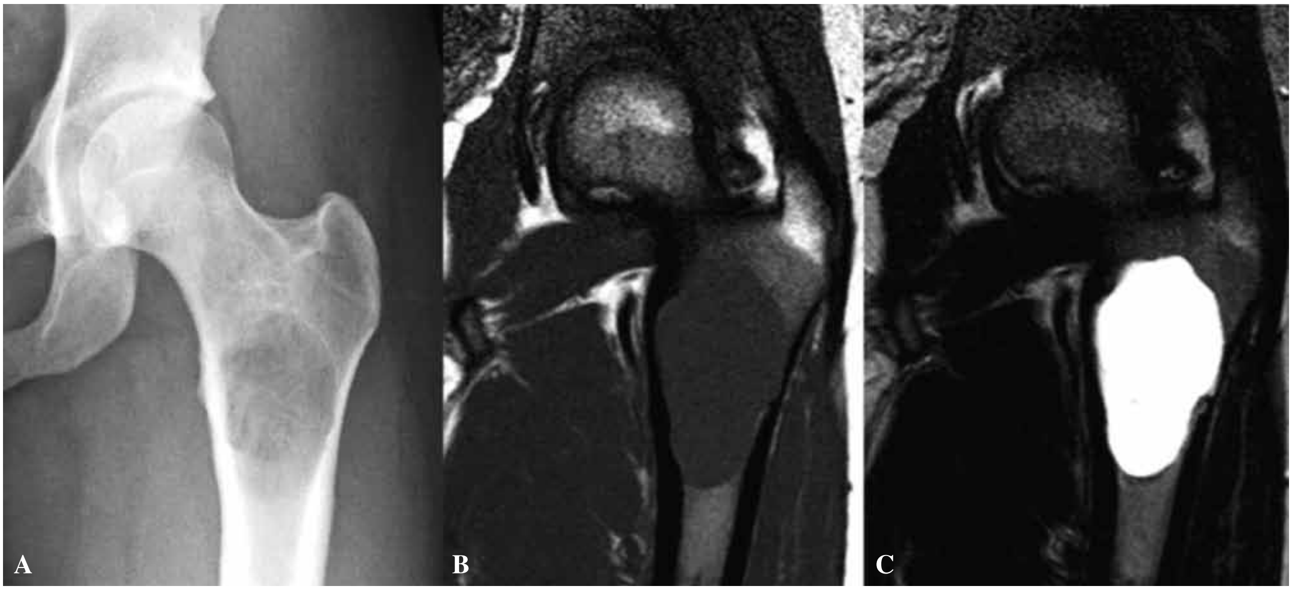

Fig. 1. — A. Standard anteroposterior radiography of a femoral SBC in a 21-year-old woman ; B. T1-weighted MRI coronal slice where the cyst is the most important ; C. T2-weighted MRI coronal slice where the cyst is the most important. The cortex is best visualized on T1-weighted MRI, whereas cyst fluid is best delineated on T2-weighted MRI.

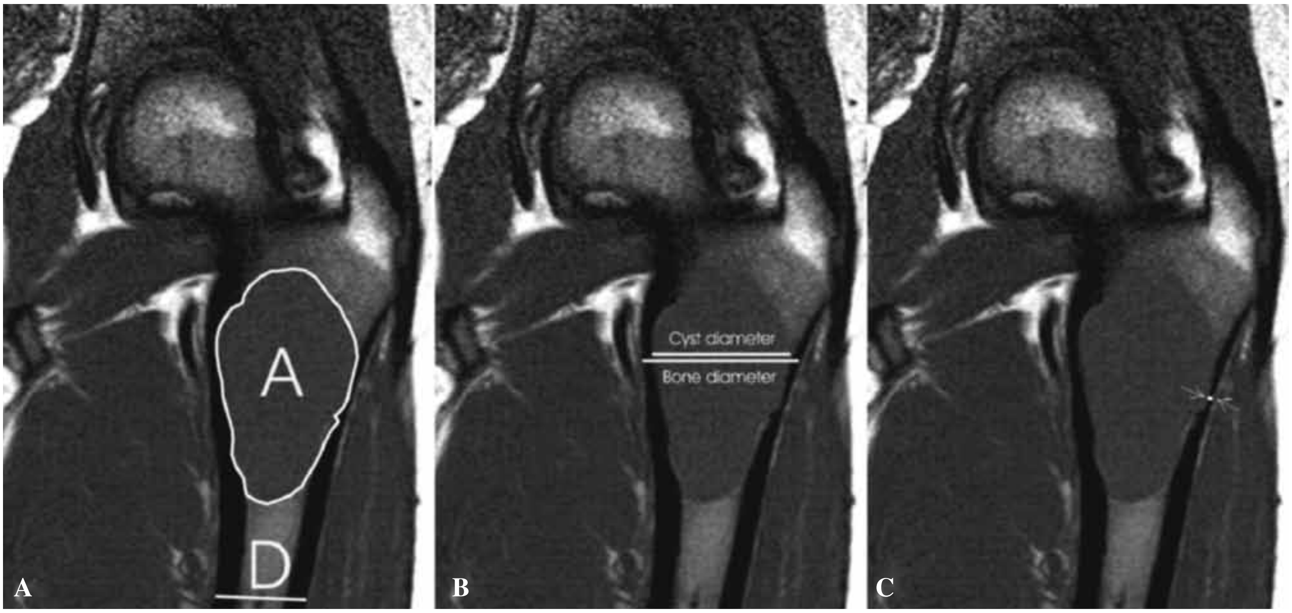

Fig. 2. — Measurement methods. A. BCI = Area/Diameter^2 (A/D^2) ; B. BCD = cyst diameter/ bone diameter ; C. MCT where the cortex is minimal.

Table I. — Mean values of BCI, BCD, MCT measured on standard radiograph, T1-weighted and T2-weighted MRI (Data for observer 1)

	Groups		p value
	Fracture risk (N = 21)	No fracture risk (N = 14)	
Mean bone cyst index (BCI)			
Anteroposterior Radiograph	6.29	3.07	$p < 0.0001$
T2-weighted MRI	5.79	1.55	$p < 0.0001$
T1-weighted MRI	6.40	1.94	$p < 0.0001$
Mean bone cyst diameter (BCD)			
Anteroposterior Radiograph	89%	79%	$p = 0.11$
T2-weighted MRI	86%	49%	$p = 0.001$
T1-weighted MRI	90%	50%	$p < 0.0001$
Mean minimal cortex thickness (MCT) (mm)			
Anteroposterior Radiograph	0.89	1.16	$p = 0.37$
T2-weighted MRI	0.75	1.05	$p = 0.009$
T1-weighted MRI	0.93	1.16	$p = 0.11$

Comparison of BCI measured on anteroposterior and lateral views

The BCI was measured on both anteroposterior and lateral radiographic views to test if a statistical difference existed between the two values.

Statistical analysis

The Mann Whitney U test was used to compare mean values of variables (BCI, BCD, MCT) measured by observer 1 in the fracture group and the no-fracture group (Table I), and also to compare values of BCI measured on lateral and anteroposterior views (Table VI).

Kappa values were used to assess the ability of six parameters (BCI, BCD > 80% and > 85%, and MCT < 1 mm, < 1.5 mm and < 2 mm) to predict the fracture risk (Table II). The Kappa value expressed the ability of these parameters to correctly classify the cyst in the appropriate group (risk or no risk of fracture). "Arbitrary" guidelines to characterize Kappa were provided by Fleiss *et al* : over 0.75 as excellent, 0.40 to 0.75 as fair to good, and below 0.40 as poor (*5*).

The Bland and Altman plot and repeatability coefficient (*3*) were used as a measurement of the inter- and intra-observer repeatability for the evaluation of all images. For determination of inter-observer repeatability, only the first measurement of Observer 2 was considered. Intra-observer repeatability was also measured for Observer 2. The Bland and Altman plot (or difference plot) (*3*) was used as a graphical method to compare the two observers (Fig. 3). In this graphical method the differences between the two observers (y axis) were plotted against the averages of the two observers (x axis). The mean difference between the two observers was drawn as a horizontal line and represented the bias between the two observers. Two additional horizontal lines were drawn as the limits of agreement (mean difference ± 1.96 standard deviation). The presentation of the 95% limits of agreement was for visual judgement of how well the measurements of the two observers agreed. The smaller the range between these two limits the better the agreement was. The repeatability coefficient was calculated as 2.77 times the within-subject standard deviation (Table V). The repeatability coefficient was a precision measure which represented the value below which the absolute difference between two repeated test results might be expected to lie with a probability of 95%. By definition, the measurement error was smaller than the repeatability coefficient for 95% of the observations. Therefore, a smaller repeatability coefficient indicated a better repeatability of the method.

We performed a multivariate analysis to identify the predictors of fracture, using a logistic regression model.

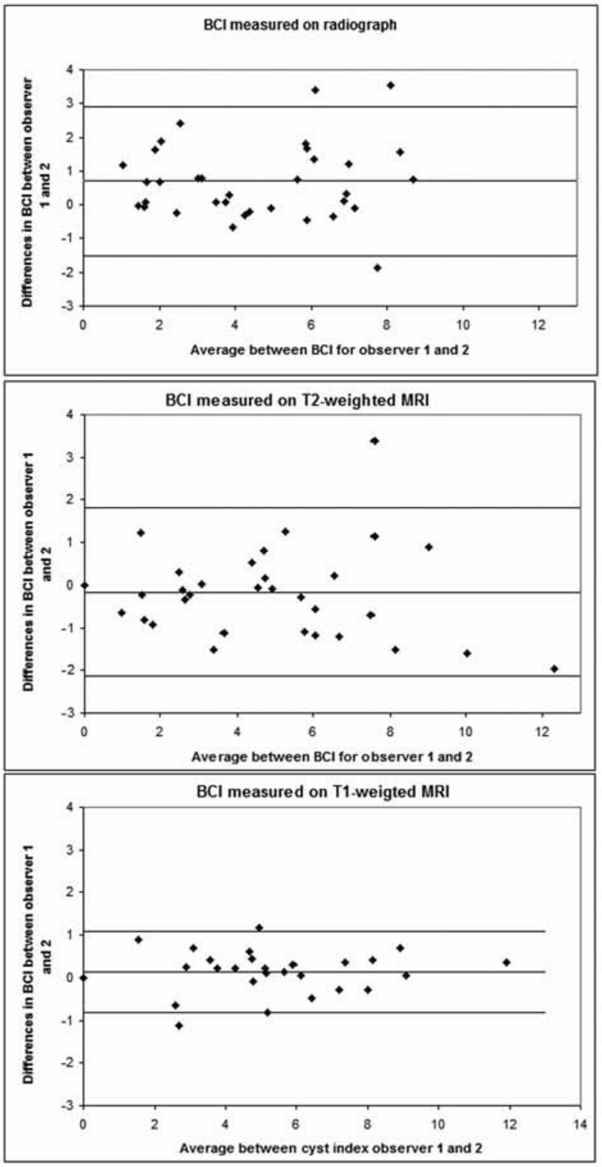

Fig. 3. — Bland and Altman plots for BCI measured on standard radiography (top), on T2-weighted MRI (middle) and on T1-weighted MRI (bottom). The mean difference between the two observers was drawn as a horizontal line and two additional horizontal lines were drawn as the limits of agreement (mean difference ±1.96 standard deviation). The presentation of the 95% limits of agreement was for visual judgement of how well the measurements of the two observers agree. The dispersion was minimal for T1-weighted MRI meaning that the inter-observer agreement was better for T1-weighted MRI.

The potential predictors of fracture risk were tested for inclusion in the model by a progressive selection based on the likelihood ratio tests. Odds adjusted ratios were derived from the final logistic models, like their confidence intervals to 95% and the p-value was presented in the tables (Table III and IV).

For all the analyses, p values < 0.05 were considered significant. Statistical analyses were done with the SPSS 15.0 software.

RESULTS

The mean values of BCI, BCD and MCT are summarized in Table I. A significant difference was found between the two groups (fracture risk and no fracture risk) for BCI. For BCD, a significant difference between groups was found for MRI but not for radiography. For MCT, a significant difference between groups was found only for T2-weighted MRI.

Ability to predict fracture

The ability to correctly classify the cyst in the appropriate group (fracture or no fracture group) was expressed by kappa values for BCI, BCD and MCT (Table II). The best kappa value was found for BCI in T1-weighted MRI, followed by BCI in radiograph and BCI in T2-weighted MRI. Good kappa value was also found for BCD > 80% in T1-weighted MRI, BCD > 85% in T1-weighted MRI, and MCT < 1 mm in T1-weighted MRI (Table II).

Considering the 3 parameters (BCI, BCD and MCT), the regression model identified T1-weighted MRI as the best imaging modality for BCI and BCD whereas it was T2-weighted MRI for MCT (Table III). Odds ratio was high for BCI (good predictor of fracture) but close to 1 for BCD (weak predictor) and inferior to 1 for MCT (bad predictor). Odds ratio was found to be 9.55 for BCI measured on T1-weighted MRI. It means that if BCI value is increased from 1, the risk to be classified in the fracture group is increased from 9.55.

Considering the 3 imaging modalities (anteroposterior radiograph, T2-weighted and T1-weighted MRI) (Table IV), the regression model identified BCI as the best predictor of fracture with good Odds ratio (3.02, 12.1 and 10.18 respectively).

Table II. — Ability of the parameter to classify the cyst in the appropriate group (fracture or no fracture risk) as expressed by the kappa value for BCI, BCD > 80%, BCD > 85%, MCT < 1 mm, MCT < 1.5 mm, MCT < 2 mm. The best kappa values were found for BCI in T1-weighted MRI, followed by BCI in radiograph and BCI in T2-weighted MRI (according to Fleiss *et al*, kappa over 0.75 is regarded as excellent, 0.40 to 0.75 as fair to good, and below 0.40 as poor (5)

Kappa value of the parameter		p value
Cyst index (BCI) > 3.5 for femur or > 4 for humerus		
Anteroposterior Radiograph	0.75	p < 0.0001
T2-weighted MRI	0.71	p < 0.0001
T1-weighted MRI	0.78	p < 0.0001
Diameter (BCD) > 80%		
Anteroposterior Radiograph	0.46	p = 0.002
T2-weighted MRI	0.58	p = 0.001
T1-weighted MRI	0.69	p < 0.0001
Diameter (BCD) > 85%		
Anteroposterior Radiograph	0.49	p = 0.005
T2-weighted MRI	0.48	p = 0.004
T1-weighted MRI	0.63	p = 0.001
Minimal cortex (MCT) < 1 mm		
Anteroposterior Radiograph	0.29	p = 0.101
T2-weighted MRI	0.41	p = 0.14
T1-weighted MRI	0.59	p = 0.001
Minimal cortex (MCT) < 1.5 mm		
Anteroposterior Radiograph	0.05	p = 0.732
T2-weighted MRI	0.09	p = 0.197
T1-weighted MRI	-0.13	p = 0.252
Minimal cortex (MCT) < 2 mm		
Anteroposterior Radiograph	0.02	p = 0.854
T2-weighted MRI	0.09	p = 0.197
T1-weighted MRI	0	

Table III. — Odds adjusted ratios derived from the final logistic models, with the confidence intervals to 95% and the p value (mean data from observer 1 and 2). The best imaging modality was T1-weighted MRI for BCI and BCD and was T2-weighted MRI for MCT. Odds ratio was high for BCI (good predictor) but close to 1 for BCD (weak predictor) and inferior to 1 for MCT (bad predictor)

	Odds Ratio	95% confidence interval	p value
Bone Cyst Index (BCI)			
T1-weighted MRI	9.55	1.41 ; 64.51	p = 0.021
Bone Cyst Diameter (BCD)			
T1-weighted MRI	1.17	1.01 ; 1.35	p = 0.035
Minimal Cortex Thickness (MCT)			
T2-weighted MRI	0.007	0.00 ; 0.49	p = 0.022

Table IV. — Odds adjusted ratios derived from the final logistic models, with the confidence intervals to 95% and the p value (mean data from observer 1 and 2). For the 3 imaging modalities, the best fracture predictor was BCI

	Odds Ratio	95% confidence interval	p value
Anteroposterior radiograph			
Bone Cyst Index (BCI)	3.02	1.50 ; 6.11	p = 0.002
T2-weighted MRI			
Bone Cyst Index (BCI)	12.10	1.13 ; 129.24	p = 0.039
T1-weighted MRI			
Bone Cyst Index (BCI)	10.18	1.50 ; 68.93	p = 0.017

Table V. — Repeatability coefficient of BCI, BCD and MCT for standard radiograph, T1-weighted MRI and T2-weighted MRI. By definition, the measurement error is smaller than the repeatability coefficient for 95% of the observations. Smaller repeatability coefficients were found for T1-weighted MRI meaning better repeatability of this method, with the exception of the intra-observer BCI repeatability. Standard radiography was the least repeatable method

	Repeatability coefficient		
	Standard Radiography	T2-weighted MRI	T1-Weighted MRI
Cyst Index (BCI)			
interobserver	2.55	1.98	0.97
intraobserver	1.78	1.08	1.18
Cyst Diameter (BCD) (%)			
interobserver	20.15%	9.91%	9.52%
intraobserver	12.86%	8.62%	7.01%
Minimal Cortex (MCT) (mm)			
interobserver	0.79	0.77	0.55
intraobserver	0.59	0.62	0.33

Repeatability of BCI, BCD, MCT on radiographs, T1-weighted and T2-weighted MRI images (Table V)

T1-weighted MRI was the method with the best repeatability for BCI, BCD, and MCT, with the exception of the intra-observer BCI repeatability. Standard radiography was the least repeatable method.

Comparison of anteroposterior and lateral radiographic views (Table VI)

No significant difference was observed between the mean BCI measured on anteroposterior and lateral radiographs.

DISCUSSION

Magnetic resonance imaging (MRI) is considered the modality of choice for evaluation of benign musculoskeletal lesions because it is highly sensitive to changes in the signal intensity of bone marrow and adjacent soft tissues (*2*). MRI is helpful in the differential diagnosis between SBC and aneurysmal bone cyst (*8*). Double density fluid level, septation, and low signal on T1 images and high signal on T2 images strongly suggest the bone cyst in question is an aneurysmal bone cyst, rather than an SBC. This may be helpful before surgery for the child who has a cystic lesion for which radiographic features do not allow a clear differentiation of SBC from aneurysmal bone cyst (*8*).

Table VI. — Comparison of anteroposterior and lateral views for BCI. No statistically significant difference was found between the BCI values measured on the two views

Radiograph			
	AP view	lateral view	p value
Mean cyst index (BCI)			
Observer 1	4.88	4.99	$p = 0.724$
Observer 2 (1st measurement)	4.21	4.14	$p = 0.246$
Observer 2 (2nd measurement)	4.58	4.40	$p = 0.112$

However diagnosis remains difficult as SBCs frequently appear complicated on MRI, with heterogeneous fluid signals and regions of nodular and thick peripheral enhancement related to previous pathologic fracture and early healing (*7*).

When an SBC is discovered, the ability to assess the risk of it causing future pathology, such as fractures, would be useful. The primary objective of this study was to determine which parameter and method were the most accurate for predicting the risk of fractures at the site of an SBC.

When we compared the two groups (fracture risk or no fracture risk ; Table I), no significant difference was found in the analysis of MCT. The mean value of MCT in the "no fracture risk" group was also less than 2 mm in some parts of the cyst. There was an overestimation of the BCI and BCD with standard radiography compared with MRI. The cyst area and diameter measurements were also more accurate on MRI. This can be explained by the fact that it is easier to delineate the boundaries of the cyst with MRI and the healed part of the SBC is better visualized. In T1-weighted MRI, the cortex is easily visualized, permitting precise measurement of BCI and BCD.

Ability to predict fracture

The best parameter to correctly classify the cyst in the appropriate group (fracture or no fracture) was found for BCI in T1-weighted MRI (best kappa value), followed by BCI in radiography and BCI in T2-weighted MRI (Table II). For the other following parameters : BCD > 80%, BCD > 85% and MCT < 1 mm (Table II), the kappa value was also better for T1-weighted MRI but it was poorer than for BCI. It can be explained by the ability of T1-weighted MRI to show the bone cortex. T2-weighted MRI has given very poor visualisation of the bony cortex, rendering the measures more difficult.

For the last two parameters : MCT < 1.5 mm and MCT < 2 mm, the kappa value was very poor, meaning that these parameters are not able to correctly classify the cyst in the adequate group.

Considering the 3 parameters (BCI, BCD and MCT), the regression model identified only BCI measured on T1-weighted MRI as a good fracture predictor (Table III). Considering the 3 imaging modalities (anteroposterior radiograph, T2-weighted and T1-weighted MRI), the regression model identified BCI as a good fracture predictor for the 3 modalities (Table IV).

Repeatability of BCI, BCD, MCT

The repeatability coefficient (Table V) was smaller for T1-weighted MRI, which means that the error of measurement was smaller for this modality. On T1-weighted MRI, the cyst fluid and cortical bone were correctly visualized. On T2-weighted MRI, the cortex was poorly visualized, whereas the fluid could be identified accurately.

Comparison of anteroposterior and lateral radiographic views

The last objective was to compare both anteroposterior and lateral views on standard radiography (Table VI). Unlike in the report by Vasconcellos *et al* (*9*), the mean BCI was not significantly different on anteroposterior and lateral radiographs. Our finding was consistent with data from Kaelin and MacEwen (*6*).

This study has several limitations, including the relatively small number of SBC's and its retrospective design. Nevertheless, these limitations were also identified in previous studies of the fracture risk related with SBC (*1,6*).

In conclusion, T1-weighted MRI has the best inter- and intra-observer repeatability whereas standard radiography is the worst method for assessing the risk of pathological fracture related to SBC. Among the available predictors, BCI measured on T1-weighted MRI is the best predictor of fracture.

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