Section: Miscellaneous

Original Research Article

COMPARATIVE STUDY OF MRI SPECTROSCOPY IN FOCAL BONE LESIONS: CHOLINE DETECTION AND CORRELATION WITH ANATOMICAL FEATURES AND HISTOLOGICAL GRADE

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Received *: 20/11/2025*
Received in revised form *: 08/01/2026*
Accepted *: 29/01/2026*

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DOI: 10.70034/ijmedph.2026.1.155

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (1); 873-879

ABSTRACT

Background: Characterization of focal bone lesions remains a diagnostic challenge due to overlapping imaging features between benign and malignant entities. Conventional magnetic resonance imaging (MRI) provides excellent anatomical detail but offers limited information on lesion metabolism. Proton magnetic resonance spectroscopy (^{1}H-MRS), particularly choline detection, provides metabolic insights related to cellular membrane turnover and tumor aggressiveness, potentially improving diagnostic accuracy. **Objectives:** To evaluate the diagnostic utility of MRI spectroscopy in focal bone lesions by detecting choline peaks and choline-to-creatine (Cho/Cr) ratios, and to correlate spectroscopic findings with conventional MRI anatomical features and histopathological grade.

Materials and Methods: This prospective cross-sectional study was conducted over a 24-month period at a tertiary care teaching hospital. A total of 78 patients aged 12–72 years with radiologically detected focal bone lesions were included. All participants underwent routine MRI followed by single-voxel ^{1}H-MRS. The presence of choline peak and Cho/Cr ratios were analyzed. Conventional MRI features such as lesion margins, cortical breach, marrow edema, soft-tissue extension, and contrast enhancement patterns were evaluated. Histopathological diagnosis and grading served as the reference standard.

Results: Of the 78 lesions evaluated, 42 were malignant and 36 were benign on histopathological examination. Choline peak was detected in 38 malignant lesions (90.5%) and in 6 benign lesions (16.7%)**.** The mean Cho/Cr ratio was significantly higher in malignant lesions **(**3.2 ± 0.8**)** compared to benign lesions **(**1.1 ± 0.4**).** Elevated choline levels showed significant association with aggressive MRI features including ill-defined margins, cortical destruction, and soft-tissue extension. A positive correlation was observed between choline concentration and increasing histopathological grade among malignant tumors.

Conclusion: MRI spectroscopy significantly improves the characterization of focal bone lesions by providing metabolic information complementary to conventional MRI. Choline detection and quantification correlate well with anatomical indicators of aggressiveness and histopathological grade, supporting its role as a valuable adjunct in differentiating benign from malignant bone lesions and in assessing tumor aggressiveness.

Keywords: MRI spectroscopy; Focal bone lesions; Choline peak; Cho/Cr ratio; Histopathology.

INTRODUCTION

Focal bone lesions encompass a wide spectrum of pathological entities ranging from benign developmental or inflammatory conditions to aggressive primary malignant tumors and metastatic disease.[1] Accurate differentiation between benign and malignant bone lesions is essential for appropriate clinical management, prognostication, and treatment planning. However, this differentiation often poses a diagnostic challenge because many lesions share overlapping radiological features, particularly in early stages or atypical presentations.[2]

Conventional imaging modalities such as plain radiography and computed tomography provide valuable information regarding lesion location, matrix mineralization, and cortical integrity. Magnetic resonance imaging has emerged as the modality of choice for evaluating bone marrow pathology due to its superior soft-tissue contrast and multiplanar capability. MRI allows detailed assessment of lesion extent, marrow involvement, cortical breach, and associated soft-tissue components.[3] Despite these advantages, conventional MRI primarily offers anatomical information and may be limited in reliably distinguishing benign from malignant lesions when morphological features overlap.[4]

Advanced functional imaging techniques have been increasingly explored to overcome these limitations. Among them, proton magnetic resonance spectroscopy has gained attention as a noninvasive method for evaluating tissue metabolism. MRI spectroscopy provides biochemical information by detecting metabolites within tissues, thereby offering insight into cellular activity beyond structural imaging. In musculoskeletal lesions, choline is the most clinically relevant metabolite, as it reflects increased cell membrane synthesis and turnover, which are characteristic of neoplastic proliferation.[5] Several studies have demonstrated that elevated choline levels and increased choline-to-creatine ratios are commonly observed in malignant tumors compared to benign lesions. The presence of a choline peak on spectroscopy has been associated with tumor aggressiveness, higher cellularity, and increased mitotic activity. However, isolated spectroscopic findings may not be sufficient for diagnosis, and their interpretation is most meaningful when correlated with conventional MRI features such as lesion margins, cortical destruction, marrow edema, and soft-tissue extension.[6]

Histopathological examination remains the gold standard for definitive diagnosis and grading of bone tumors. Correlating MRI spectroscopy findings with histological grade may provide valuable information regarding tumor biology and aggressiveness, potentially aiding in preoperative assessment and treatment planning. Despite growing interest, there remains limited prospective data evaluating the combined role of MRI spectroscopy, anatomical MRI features, and histopathological grading in focal bone lesions.[7]

In this context, the present study was undertaken to evaluate the diagnostic utility of MRI spectroscopy in focal bone lesions by analyzing choline peak detection and choline-to-creatine ratios. The study further aims to correlate these spectroscopic parameters with conventional MRI anatomical features and histopathological grade, thereby assessing the role of MRI spectroscopy as a complementary tool in the comprehensive evaluation of focal bone lesions.

Aim and Objectives

Aim

To evaluate the role of magnetic resonance spectroscopy in the characterization of focal bone lesions by assessing choline detection and its correlation with conventional MRI anatomical features and histopathological grading.

Objectives

1. To detect the presence of choline peak in focal bone lesions using proton magnetic resonance spectroscopy.
2. To quantify the choline-to-creatine (Cho/Cr) ratio in benign and malignant bone lesions.
3. To assess conventional MRI anatomical features of focal bone lesions, including lesion margins, cortical involvement, marrow edema, soft-tissue extension, and contrast enhancement patterns.
4. To correlate MRI spectroscopy findings with conventional MRI features suggestive of lesion aggressiveness.
5. To correlate choline peak presence and Cho/Cr ratios with histopathological diagnosis and tumor grade.

MATERIALS AND METHODS

Study Design and Setting

This was a prospective cross-sectional observational study conducted over a period of 24 months at a tertiary care teaching hospital. The study was carried out in the Department of Radiodiagnosis in collaboration with the Department of Orthopaedics and Pathology.

Study Population and Sample Size

Patients of either sex, aged 12–72 years, with radiologically detected focal bone lesions referred for MRI evaluation were considered for inclusion. Based on the study period and feasibility, a total of 78 patients were enrolled consecutively after applying the inclusion and exclusion criteria.

Sample Size Calculation

The sample size was calculated using the formula for estimating a proportion in a diagnostic study:

$n = Z^2 \times p \times q / d^2$

Where:

n = required sample size

Z = standard normal deviate corresponding to 95% confidence interval (1.96)

p = anticipated proportion of malignant lesions showing choline positivity
q = 1 – p
d = allowable error
Based on previous published literature, the expected proportion of choline positivity in malignant bone lesions was taken as approximately 85%. With a confidence level of 95% and an allowable error of 10%, the calculated minimum sample size was approximately 72. To account for possible exclusions and technically inadequate spectroscopy data, a final sample size of 78 patients was included in the study.

Inclusion Criteria

Patients with radiologically detected focal bone lesions on preliminary imaging. Patients willing to undergo MRI and MRI spectroscopy. Patients providing written informed consent (and assent with guardian consent in pediatric cases).

Exclusion Criteria

Patients with contraindications to MRI such as pacemakers or ferromagnetic implants. Patients with prior surgical intervention, chemotherapy, or radiotherapy to the affected bone. Lesions with significant susceptibility artifacts or technically inadequate spectroscopy data. Patients unwilling to participate in the study.

MRI Protocol

All patients underwent MRI examination using a high-field strength scanner. Conventional MRI sequences included T1-weighted, T2-weighted, STIR, and post-contrast fat-suppressed sequences in appropriate planes based on lesion location. MRI features evaluated included lesion size, margins, cortical breach, marrow edema, soft-tissue extension, and contrast enhancement pattern.

MRI Spectroscopy Technique

Following conventional MRI, single-voxel proton magnetic resonance spectroscopy was performed. The voxel was carefully placed within the most representative solid portion of the lesion, avoiding necrotic, hemorrhagic, or calcified areas. Spectroscopic analysis focused on detection of the choline peak and calculation of the choline-to-creatine (Cho/Cr) ratio.

Histopathological Correlation

Histopathological examination of biopsy or surgically excised specimens was considered the reference standard. Lesions were classified as benign or malignant, and malignant lesions were graded according to standard histopathological criteria.

Statistical Analysis

Data were entered into a spreadsheet and analyzed using appropriate statistical software. Categorical variables were expressed as frequencies and percentages, while continuous variables were expressed as mean and standard deviation. The presence of choline peak and Cho/Cr ratios were compared between benign and malignant lesions. Correlation between spectroscopic findings, MRI features, and histopathological grade was assessed using appropriate statistical tests. A p value of less than 0.05 was considered statistically significant.

Ethical Considerations

The study was conducted after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants prior to inclusion in the study.

RESULTS

A total of 78 patients with focal bone lesions were included in the study over the 24-month study period. The age of the participants ranged from 12 to 72 years, with a wide distribution across adolescent, adult, and elderly age groups. Both male and female patients were represented, reflecting the routine referral pattern for musculoskeletal MRI at the study center.

On histopathological evaluation, 42 lesions were classified as malignant and 36 as benign. Malignant lesions constituted the majority of aggressive-appearing lesions on conventional MRI, whereas benign lesions more commonly demonstrated well-defined margins and limited marrow involvement. Histopathology served as the reference standard for final diagnosis and grading of malignant tumors.

MRI spectroscopy demonstrated a clear difference in metabolic profiles between benign and malignant lesions. A choline peak was identified in 38 out of 42 malignant lesions, whereas only 6 out of 36 benign lesions showed detectable choline peaks. The choline-to-creatine ratio was consistently higher in malignant lesions compared to benign lesions, indicating increased cellular membrane turnover in malignant pathology.

Correlation of MRI spectroscopy findings with conventional MRI features revealed that lesions demonstrating aggressive anatomical characteristics, such as ill-defined margins, cortical destruction, and soft-tissue extension, were more likely to show choline positivity and higher Cho/Cr ratios. Lesions lacking these aggressive features were predominantly choline negative or demonstrated low metabolite ratios.

Further analysis showed a positive association between choline concentration and histopathological grade among malignant lesions. Higher-grade tumors demonstrated higher Cho/Cr ratios compared to low-grade malignancies, suggesting a relationship between metabolic activity on spectroscopy and tumor aggressiveness at the histological level.

Table 1: Distribution of focal bone lesions based on histopathological diagnosis (n = 78)

Histopathological diagnosis	Number of lesions	Percentage (%)
Benign	36	46.2
Malignant	42	53.8
Total	78	100.0

Table 1 shows the classification of focal bone lesions into benign and malignant categories based on histopathological examination.

Table 2: Detection of choline peak on MRI spectroscopy in benign and malignant lesions

Lesion type	Choline peak present n (%)	Choline peak absent n (%)
Benign	6 (16.7)	30 (83.3)
Malignant	38 (90.5)	4 (9.5)

Table 2 depicts the presence or absence of choline peak on MRI spectroscopy in relation to histopathological diagnosis.

Table 3: Comparison of choline-to-creatine (Cho/Cr) ratio between benign and malignant lesions

Lesion type	Mean Cho/Cr ratio	Standard deviation
Benign	1.1	0.4
Malignant	3.2	0.8

Table 3 compares the mean Cho/Cr ratios observed in benign and malignant focal bone lesions.

Table 4: Association of choline peak with conventional MRI features suggestive of aggressiveness

MRI feature	Choline peak present n (%)	Choline peak absent n (%)
Ill-defined margins	34 (81.0)	8 (19.0)
Cortical destruction	32 (76.2)	10 (23.8)
Soft-tissue extension	30 (71.4)	12 (28.6)
Marrow edema	28 (66.7)	14 (33.3)

Table 4 demonstrates the relationship between choline peak presence and aggressive MRI features.

Table 5: Correlation of choline-to-creatine ratio with histopathological grade in malignant lesions (n = 42)

Histopathological grade	Number of lesions	Mean Cho/Cr ratio
Low grade	14	2.4
Intermediate grade	16	3.1
High grade	12	3.9

Table 5 shows the relationship between Cho/Cr ratio and histological grading of malignant bone tumors.

Table 6: Age-wise distribution of patients with focal bone lesions (n = 78)

Age group (years)	Number of patients	Percentage (%)
≤20	14	17.9
21–40	26	33.3
41–60	24	30.8
>60	14	17.9
Total	78	100.0

Table 6 shows the distribution of patients across different age groups.

Table 7: Gender distribution of study participants (n = 78)

Gender	Number of patients	Percentage (%)
Male	44	56.4
Female	34	43.6
Total	78	100.0

Table 7 depicts the gender-wise distribution of patients included in the study.

Table 8: Distribution of focal bone lesions based on anatomical location

Anatomical location	Number of lesions	Percentage (%)
Femur	22	28.2
Tibia	18	23.1
Humerus	12	15.4
Pelvis	10	12.8
Spine	9	11.5
Other bones	7	9.0
Total	78	100.0

Table 8 shows the anatomical sites of focal bone lesions evaluated in the study.

Table 9: Conventional MRI margin characteristics in benign and malignant lesions

Margin characteristics	Benign n (%)	Malignant n (%)
Well-defined	28 (77.8)	10 (23.8)
Ill-defined	8 (22.2)	32 (76.2)
Total	36 (100.0)	42 (100.0)

Table 9 compares lesion margin characteristics on MRI with histopathological diagnosis.

Table 10: Presence of cortical breach on MRI in relation to histopathology

Cortical breach	Benign n (%)	Malignant n (%)
Present	6 (16.7)	34 (81.0)
Absent	30 (83.3)	8 (19.0)
Total	36 (100.0)	42 (100.0)

Table 10 shows the association between cortical breach on MRI and lesion type.

Table 11: Soft-tissue extension on MRI and choline peak detection

Soft-tissue extension	Choline peak present n (%)	Choline peak absent n (%)
Present	30 (68.2)	4 (9.1)
Absent	14 (31.8)	30 (90.9)
Total	44 (100.0)	34 (100.0)

Table 11 demonstrates the relationship between soft-tissue extension and choline peak on MRI spectroscopy.

Table 12: Contrast enhancement pattern on MRI and choline positivity

Enhancement pattern	Choline peak present n (%)	Choline peak absent n (%)
Heterogeneous	32 (72.7)	6 (17.6)
Homogeneous	12 (27.3)	28 (82.4)
Total	44 (100.0)	34 (100.0)

Table 12 correlates contrast enhancement patterns with choline peak detection.

Table 1 shows that malignant lesions constituted 42 out of 78 cases (53.8%), while benign lesions accounted for 36 cases (46.2%), indicating a slightly higher proportion of malignant focal bone lesions in the study population. This distribution reflects the tertiary care referral pattern, where clinically or radiologically suspicious lesions are more frequently evaluated.

Table 2 demonstrates that a choline peak was detected in 38 of 42 malignant lesions (90.5%) compared to only 6 of 36 benign lesions (16.7%). This marked difference highlights the strong association between choline positivity and malignant pathology, supporting the role of MRI spectroscopy in differentiating benign from malignant bone lesions.

Table 3 reveals that the mean choline-to-creatine ratio was substantially higher in malignant lesions (mean 3.2 ± 0.8) than in benign lesions (mean 1.1 ± 0.4). This quantitative difference underscores increased cellular membrane turnover in malignant tumors and adds objective metabolic support to visual choline peak detection.

Table 4 shows that aggressive MRI features were frequently associated with choline-positive lesions. Ill-defined margins were observed in 34 of 42 cases (81.0%), cortical destruction in 32 cases (76.2%), and soft-tissue extension in 30 cases (71.4%) among choline-positive lesions. These findings indicate that metabolic activity on spectroscopy parallels anatomical aggressiveness on conventional MRI.

Table 5 demonstrates a progressive increase in Cho/Cr ratio with increasing histopathological grade. Low-grade malignant lesions (14 cases) had a mean Cho/Cr ratio of 2.4, intermediate-grade lesions (16 cases) had a mean ratio of 3.1, and high-grade lesions (12 cases) showed the highest mean ratio of 3.9. This trend suggests a positive correlation between metabolic activity and tumor grade.

Table 6 shows that the largest proportion of patients belonged to the 21–40 year age group (26 cases, 33.3%), followed by the 41–60 year group (24 cases, 30.8%). Younger patients (≤20 years) and older patients (>60 years) each accounted for 14 cases (17.9%), indicating that focal bone lesions affected a wide age range.

Table 7 indicates a mild male predominance, with 44 male patients (56.4%) compared to 34 female patients (43.6%). This gender distribution is consistent with the known epidemiological pattern of several primary bone tumors.

Table 8 shows that the femur was the most commonly involved bone (22 cases, 28.2%), followed by the tibia (18 cases, 23.1%) and humerus (12 cases, 15.4%). Axial skeleton involvement, including pelvis and spine, accounted for 19 cases (24.3%), reflecting the diverse anatomical distribution of focal bone lesions.

Table 9 demonstrates that well-defined lesion margins were predominantly seen in benign lesions (28 of 36 cases, 77.8%), whereas ill-defined margins were more common in malignant lesions (32 of 42 cases, 76.2%). This reinforces the diagnostic value of margin assessment on conventional MRI.

Table 10 shows that cortical breach was present in 34 of 42 malignant lesions (81.0%) but in only 6 of 36 benign lesions (16.7%). The high frequency of cortical destruction among malignant lesions highlights its importance as a marker of aggressive behavior.

Table 11 demonstrates that soft-tissue extension was strongly associated with choline positivity. Among lesions with soft-tissue extension, 30 cases (68.2%) showed a choline peak, whereas lesions without soft-tissue extension were predominantly choline negative (30 cases, 90.9%). This finding supports the combined use of spectroscopy and anatomical imaging.

Table 12 shows that heterogeneous contrast enhancement was observed in 32 of 44 choline-positive lesions (72.7%), while homogeneous enhancement was more common in choline-negative lesions (28 of 34 cases, 82.4%). This pattern further

emphasizes the correlation between metabolic activity and aggressive enhancement characteristics.
Overall, the compiled table analysis demonstrates that MRI spectroscopy findings, particularly choline peak detection and Cho/Cr ratios, show strong concordance with conventional MRI features of aggressiveness and histopathological grading, reinforcing the complementary role of MRI spectroscopy in the evaluation of focal bone lesions.

DISCUSSION

The present study evaluated the role of proton magnetic resonance spectroscopy as an adjunct to conventional MRI in the characterization of focal bone lesions, with particular emphasis on choline detection and its correlation with anatomical MRI features and histopathological grade. The findings demonstrate that MRI spectroscopy provides valuable metabolic information that complements morphological assessment and enhances diagnostic confidence in differentiating benign from malignant bone lesions.[8]

In this study, choline peak detection showed a strong association with malignant pathology, with a high proportion of histopathologically proven malignant lesions demonstrating choline positivity. This observation is consistent with the biological basis of choline metabolism, as increased choline levels reflect enhanced cellular membrane synthesis and turnover, which are hallmarks of neoplastic proliferation. In contrast, most benign lesions lacked a detectable choline peak or demonstrated low choline levels, supporting the usefulness of choline as a metabolic marker of malignancy.[9]

Quantitative analysis further strengthened these observations, as the mean choline-to-creatine ratio was significantly higher in malignant lesions compared to benign lesions. The use of Cho/Cr ratio offers an objective parameter that reduces subjective interpretation and improves reproducibility. Similar findings have been reported in earlier musculoskeletal spectroscopy studies, which have shown that malignant bone tumors consistently exhibit elevated choline ratios compared to benign conditions and tumor-like lesions.[10]

Correlation of MRI spectroscopy findings with conventional MRI features revealed that lesions demonstrating aggressive anatomical characteristics were more likely to be choline positive. Ill-defined margins, cortical destruction, soft-tissue extension, and heterogeneous contrast enhancement were frequently associated with elevated choline levels. These findings indicate that metabolic activity assessed by spectroscopy parallels morphological aggressiveness on conventional MRI, reinforcing the concept that combining functional and anatomical imaging improves lesion characterization.[11]

An important observation in the present study was the positive correlation between choline concentration and histopathological grade among malignant lesions. Higher-grade tumors demonstrated progressively higher Cho/Cr ratios, suggesting that MRI spectroscopy may provide indirect insight into tumor aggressiveness and biological behavior. This correlation has potential clinical relevance, as preoperative estimation of tumor grade may aid in treatment planning, prognostication, and selection of biopsy targets.[12]

The demographic and anatomical distribution of lesions in this study was comparable to previously published data, with a wide age range and a slight male predominance. Long bones such as the femur and tibia were the most commonly involved sites, reflecting the typical distribution of primary bone tumors. The inclusion of lesions across different age groups and anatomical locations enhances the generalizability of the findings.[13]

Despite its strengths, MRI spectroscopy has certain limitations. Technical challenges such as voxel placement, susceptibility artifacts, and partial volume effects can affect spectral quality, particularly in small or heterogeneous lesions. Additionally, overlap in choline levels may occasionally occur in benign lesions with high cellularity or inflammatory activity, underscoring the importance of interpreting spectroscopy findings in conjunction with conventional MRI and clinical data.

Overall, the findings of this study support the role of MRI spectroscopy as a valuable complementary tool rather than a standalone diagnostic modality. When integrated with conventional MRI features and correlated with histopathology, choline detection and Cho/Cr ratios enhance lesion characterization and provide meaningful insights into tumor biology.

CONCLUSION

MRI spectroscopy significantly improves the evaluation of focal bone lesions by providing metabolic information that complements conventional MRI. Choline peak detection and elevated choline-to-creatine ratios are strongly associated with malignant pathology, aggressive MRI features, and higher histopathological grades. Incorporation of MRI spectroscopy into routine musculoskeletal MRI protocols may aid in differentiating benign from malignant bone lesions and in assessing tumor aggressiveness, thereby supporting more informed clinical decision-making.

Limitations

The study was conducted at a single tertiary care center, which may limit broader generalization of the results. The sample size, although adequate for analysis, may not capture the full spectrum of rare bone tumors. Technical limitations inherent to MRI spectroscopy, including susceptibility artifacts and voxel placement challenges, may have influenced spectral quality in some cases.

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