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A Feasibility Study of Quantitative Molecular Characterization of Musculoskeletal Lesions by Proton MR Spectroscopy at 3 T

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Abstract

OBJECTIVE—The purpose of this study is to establish the feasibility and potential value of measuring the concentration of choline-containing compounds by proton MR spectroscopy (MRS) in musculoskeletal lesions at 3 T.

SUBJECTS AND METHODS—Thirty-three subjects with 34 musculoskeletal lesions (four histologically proven malignant, 13 histologically proven benign or proven benign by follow-up analysis, and 17 posttreatment fibrosis with documented stability for 6–36 months) underwent single-voxel 3-T MRS studies. In each case, both water-suppressed and water-unsuppressed scans were obtained. The quality of the scans was recorded as excellent, adequate, or nondiagnostic, and the choline concentration was measured using water as the internal reference. The choline concentrations of benign and malignant lesions were compared using the Mann-Whitney test.

RESULTS—Spectral quality was excellent in 26 cases, adequate in four cases, and non-diagnostic in four cases. For malignant lesions (three sarcomas), the choline concentrations were 1.5, 2.9, and 3.8 mmol/kg, respectively. For five benign lesions (two neurofibromas, two schwannomas, and one enchondroma), the choline concentrations were 0.11, 0.28, 0.13, 0.8, and 1.2 mmol/kg, respectively. For seven benign lesions (two hematomas, two bone cysts, one lipoma, one giant cell tumor, and one pigmented villonodular synovitis), the spectra showed negligible choline content. For three posttreatment fibrosis cases, the choline concentration range was 0.2–0.4 mmol/kg. For the remaining 12 posttreatment fibrosis cases, the spectra showed negligible choline content. Average choline concentrations were different for malignant and benign lesions (2.7 vs 0.5 mmol/kg; $p = 0.01$).

CONCLUSION—The measurement of choline concentration within musculoskeletal lesions by MRS is feasible using an internal water-referencing method at 3 T and has potential for characterizing lesions for malignancy.

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WEB

This is a Web exclusive article.

Keywords

bone mass; MRI; MR spectroscopy; musculoskeletal neoplasm; soft-tissue mass

Although MRI is widely used in the assessment of musculoskeletal lesions, it is often deficient in its ability to correctly characterize these lesions for malignancy [1,2]. Proton MR spectroscopy (MRS) is a promising non-invasive method for the identification of molecular markers that may be used to characterize musculoskeletal malignancies [3–9]. To date, there has been limited exploration of the utility of proton MRS for the characterization of musculoskeletal lesions, with six published studies all showing that choline-containing compounds are detected in malignant bone and soft-tissue abnormalities, which suggests that the metabolite choline may serve as a marker for malignancy in the musculoskeletal system. However, these studies have focused on a qualitative assessment of the choline content (i.e., detection of the choline peak) [4,5] or a relative measure of choline content as the ratio of the choline signal to another metabolite's signal [6–9]. Relative measures are limited because they vary with a number of factors, including pulse sequence efficiency, magnetic field strength and homogeneity, the type of coil used, the distance between the region of interest and the coil, and the size of the lesion involved. Also, other metabolites to which choline is commonly compared, such as creatine [8], are known to vary widely and are therefore not a suitable reference measure [10]. Finally, because choline has also been found within benign lesions [4,5,7,8], it is preferable to have an absolute measure of the choline content within lesions for more accurate discrimination of benign and malignant entities.

The purpose of this study was to establish the feasibility of proton MRS for determining the choline concentration within musculoskeletal lesions using an internal water-referencing method and to evaluate its utility for distinguishing benign and malignant lesions according to their choline concentrations.

Subjects and Methods

Overall Study Design

Thirty-three subjects with bone and soft-tissue abnormalities referred for routine MRI underwent 34 proton 3-T MRS studies with single-voxel technique designed to measure choline concentration using water as an internal reference compound. Results of MRS were compared with histologic analysis results (obtained as part of a standard workup) and clinical outcome to determine the accuracy with which MRS predicts malignancy. This study was performed with institutional review board approval. Informed consent was obtained from each subject before performance of the study.

Recruitment of Subjects and Subject Population

Thirty-three subjects (15 with 16 untreated musculoskeletal lesions and 18 with previously resected masses undergoing a postoperative follow-up evaluation) were prospectively enrolled in this study between May 2006 and September 2009. To be included in the study, subjects were required to undergo conventional MRI for de novo assessment of lesions or for the evaluation of potential recurrent or residual disease after surgical resection, to have abnormalities larger than $1 \times 1 \times 1 \text{ cm}^3$, and to have no contraindication to MRI. Exclusion criteria included a contraindication to MRI or abnormalities that were smaller than $1 \times 1 \times 1 \text{ cm}^3$. Among the 15 subjects with de novo lesions, the mean age was 44 years (range, 13–94 years), and this group was composed of five males and 10 females with five bone and 11 soft-tissue abnormalities (a total of 16 lesions). Among the 18 subjects with postoperative

abnormalities, the mean age was 52 years (range, 15–79 years), and this group was composed of nine males and nine females with 18 soft-tissue signal abnormalities after resection of a musculoskeletal mass. Lesions were classified as malignant after biopsy confirmation (biopsy was performed as part of the patient's routine clinical care). All benign lesions had either histologic confirmation or stable clinical and imaging appearance over time. Correlation was made to all available records to classify lesions as benign or malignant.

For the 16 de novo lesions, the final diagnoses included three malignant and 13 benign abnormalities. The malignant diagnoses included one bone mass (Ewing sarcoma) and two soft-tissue masses (Ewing sarcoma and high-grade undifferentiated sarcoma); the benign diagnoses included four bone lesions (giant cell tumor, presumed enchondroma that was stable for 3 months, unicameral bone cyst, and degenerative cyst) and nine soft-tissue lesions (presumed neurofibroma that was stable for 10 months, histologically proven neurofibroma with atypical features that was sampled twice and was stable for 10 months, histologically proven giant cell tumor of tendon sheath, presumed lipoma by conventional imaging, histologically proven complex ganglion, histologically proven hematoma, hematoma that resolved at 3 months, histologically proven degenerated cystic schwannoma, and presumed schwannoma with stable clinical and imaging appearance at 6 months).

For the 18 postoperative follow-up scans, one case (original histologic diagnosis was a high-grade soft-tissue sarcoma) showed a biopsy-proven recurrent tumor 8 months after surgery by MRI. For the remaining 17 postoperative cases, stability was documented by imaging and clinical follow-up with no evidence of recurrent or residual tumor at 3–33 months (for three cases at 3 months, for one case at 6 months, for one case at 11 months, for two cases at 12 months, for one case at 13 months, for one case at 16 months, for one case at 18 months, for one case at 20 months, for three cases at 21 months, for one case at 24 months, for one case at 31 months, and for one case at 33 months). For these 18 cases, the original histologic analyses included one chordoma, one myxopapillary ependymoma, one angiomatoid malignant fibrous histiocytoma, two myxoid liposarcomas, one Ewing sarcoma, four intermediate-grade sarcomas, five high-grade sarcomas, two desmoid tumors, and one pigmented villonodular synovitis.

Imaging and MR Spectroscopy Acquisition

The MRS sequence was added to routine MRI that the patients underwent for initial evaluation of an untreated mass or for the evaluation of potential recurrent or residual disease after surgery. MRS was performed before administration of contrast material to avoid possible changes in spectra due to contrast material [11].

All studies were performed on a 3-T MR system (MAGNETOM Trio or MAGNETOM Verio, Siemens Healthcare) using a flexible phased-array body matrix coil. Conventional MRI included conventional axial and coronal T1-weighted images (spin echo; TR/TE, 690/15; field of view [FOV], 20; slice thickness, 6 mm) along with axial fat-suppressed T2-weighted images (spin echo, 2,886/100; FOV, 18; slice thickness, 6 mm) and coronal STIR images (inversion recovery; 2,462/100; inversion time, 200 milliseconds; FOV, 20; slice thickness, 6 mm) of the body part in question. Unenhanced and contrast-enhanced axial T1-weighted images (gradient-recalled echo; 436/4.9; flip angle, 90°; FOV, 18; slice thickness, 6 mm) were obtained before and after the IV administration of gadopentetate dimeglumine (0.1 mmol/kg; Magnevist, Bayer HealthCare) followed by a saline flush.

Spectroscopy was performed using a single-voxel point-resolved spectroscopy sequence (PRESS) (2,000/135) before administration of IV contrast material. For measurement of choline concentration, the MRS PRESS sequence was applied in each lesion twice, once

with water suppression (128 averages) and once without water suppression (16 averages). No lipid suppression was applied. Initial automatic shimming was followed by manual shimming to optimize the field homogeneity. Scan time was 4 minutes for the water-suppressed scans and less than 1 minute for the scans obtained without water suppression.

The spectral data were obtained from an 8-cm³ voxel (2 × 2 × 2 cm) localized to the most suspicious area of the lesion in question by a musculoskeletal radiologist. If the lesion was smaller than 8 cm³, voxel size was decreased to the largest possible size to include the lesion or a minimum of 1 cm³. For de novo lesions, the voxel was placed in an area deemed to be solid rather than fluid-containing; if no solid portion of the mass was clearly visible, the voxel was placed in the center of the lesion. For postsurgical cases, the voxel was localized to the surgical site in an area of increased T2 signal or suspicious masslike abnormality when present, or over the surgical bed if no significant T2 signal was identified. Regarding voxel placement, inclusion of adjacent bone cortex and muscle was carefully avoided.

MR Spectroscopy Data Processing

The spectra were analyzed by a physicist who recorded whether each spectrum was of diagnostic quality. The quality of the spectra was assessed on the basis of visibility of discrete metabolite peaks, with clear separation of the peaks and the absence of artifacts. An assignment of choline was made according to the visibility of the discrete choline peak at 3.2 ppm and the absence of artifacts. The quality of the spectra was rated as excellent (i.e., well-resolved choline, water and lipid peaks, and clean choline peak with no major baseline distortions), adequate (i.e., resolved choline, water and lipid peaks, and baseline distortion correctable), or nondiagnostic (i.e., choline peak cannot be visualized because of low signal-to-noise ratio or the presence of artifacts).

Spectroscopy data were analyzed using the advanced method for accurate robust efficient spectral fitting [12] in the Java (Sun Microsystems)–based MR User's Interface package (The MRUI Project) [13], which fits the time-domain spectroscopy data as a model of exponentially decaying oscillators using a nonlinear least-squares algorithm. Spectra were processed with a zero-order phase correction based on the water peak. The presence or absence of a discrete choline peak within each spectrum was recorded. When present, the resonance amplitude of the choline signal at 3.2 ppm was quantified along with the amplitude of the nonsuppressed water signal at 4.7 ppm. Choline concentrations, in units of millimoles per kilogram, were estimated using the nonsuppressed water peak as an internal reference compound, a method described elsewhere for lesions of the breast and brain [14–16] and adapted for use in normal skeletal muscle [17]. The choline (*Cho*) concentrations were calculated using the following equation:

$$Cho = \frac{S_{Cho}}{S_{H_2O}} \times \frac{n_{H_2O}}{n_{Cho} \times MW_{H_2O}} \times \frac{fT_1(H_2O)}{fT_1(Cho)} \times \frac{fT_2(H_2O)}{fT_2(Cho)} \times CF_{Lipid}, \quad (1)$$

where S_{Cho} is the area of choline peak at 3.2 ppm, S_{H_2O} is the area of the nonsuppressed water signal, $n_{H_2O} = 2$, $n_{Cho} = 9$ (from 3 CH₃ groups), $MW = 18.0153 \times 10^{-6}$ kg/mmol, $fT_1 = 1 - \exp(-TR/T_1)$, $fT_2 = \exp(-TE/T_2)$, and CF_{Lipid} represents a correction factor that accounts for the volume fraction that is occupied by lipids within each voxel and is equal to $S_{H_2O}/(S_{H_2O} + S_{Lipid})$ measured from the nonsuppressed spectrum. Relaxation time effects were corrected for by use of previously determined in vivo T1 and T2 relaxation times at 3 T in normal muscle (for choline, 1,372 and 134 milliseconds, respectively, and for water, 1,478 and 40 milliseconds, respectively). If a choline signal could not be visualized, it was assumed that the concentration was less than 0.1 mmol/kg.

Statistical Analysis Methods

First, an error term was calculated for each choline concentration measurement where an identifiable choline peak was present in the spectrum. This error term was determined using a fitting error for the estimate of each metabolite integral readily obtained from the spectral analysis, taking into account the frequency range over which the metabolite integral was estimated and the coefficient of variation (SD/mean) previously determined for T1 and T2 relaxation times for choline and water used in Equation 1 [17], the range of which was 2.5–8.2%. A final error for each choline concentration was calculated as the average of all metabolite fitting errors and relaxation time errors.

Second, comparison of malignant and nonmalignant entities was made qualitatively (using the visual presence or absence of a choline peak as a marker of malignancy) and quantitatively (using the choline concentration). The presence of a choline peak was compared for benign and malignant entities utilizing the Fisher's exact test. Choline concentration values between malignant and nonmalignant lesions were compared using a two-sample Wilcoxon's rank-sum (Mann-Whitney) test (statistical significance was set at $p < 0.05$).

Results

Tables 1 and 2 describe the lesion characteristics and patient population. Diagnostic quality spectra were obtained for 30 studies. For one malignant case (recurrent tumor in the thigh at 8 months after surgery) and three benign cases (stable postoperative appearance of pigmented villonodular synovitis of the wrist, stable postoperative appearance of leiomyosarcoma of the calf, and a de novo case of giant cell tumor of tendon sheath of the wrist), the studies were nondiagnostic as a result of poor signal-to-noise ratio in the spectrum, with the expected choline peak location visually indistinguishable from noise and baseline. Most studies were performed in the lower extremity or pelvis, with a higher proportion of nondiagnostic studies in the upper extremities (two of six cases) than in the lower extremities (one of 20 cases).

Regarding the de novo cases, a discrete choline peak was detected in three of three malignant lesions and in five of 12 benign lesions ($p = 0.2$). The choline concentrations within the malignant lesions were 1.5, 2.9, and 3.8 mmol/kg, respectively, and the choline concentrations in the benign abnormalities where choline was detected (neurofibroma, degenerated cystic schwannoma, stable neurofibroma with atypical features, schwannoma stable at 6-month follow-up, and enchondroma) were 0.11, 0.13, 0.28, 0.8, and 1.2 mmol/kg, respectively. For the remaining benign lesions, the choline content was negligible. The mean ($\pm$ SD) choline concentration for malignant lesions was 2.7 ± 1.2 mmol/kg, whereas that for benign lesions was 0.5 ± 0.5 mmol/kg ($p = 0.011$). It should be noted that, in addition to choline, the metabolite creatine was also found in one of the de novo cases (the high-grade undifferentiated sarcoma), though the significance of this pattern is unclear. Figures 1 and 2 show spectra obtained from patients with malignant and benign masses.

Regarding the postoperative evaluations, a discrete choline peak was detected in three of 15 cases (original histologic diagnoses of chordoma, high-grade sarcoma, and desmoid tumor), with choline concentrations of 0.2, 0.2, and 0.4 mmol/kg, respectively. For the remaining postoperative cases, the choline content was negligible.

Discussion

To our knowledge, the feasibility and utility of choline metabolite quantification by proton 3-T MRS for the de novo and postsurgical evaluation of musculoskeletal lesions has not

been previously reported. This study establishes the feasibility of measuring the absolute choline concentration by 3-T MRS with a water-referencing method, extends previous work done with qualitative 1.5-T MRS [3–5] and relative quantitative MRS measures of choline content at 1.5 T [6,9] and 3 T [7,8], and further supports the hypothesis that MRS may be useful as a noninvasive tool for characterizing musculoskeletal lesions.

Several studies have shown that choline can be reliably detected in malignant bone and soft-tissue tumors [3–9] and is therefore thought to be a marker of malignancy. Choline is a precursor of acetylcholine and a component of the phospholipid metabolism of cell membranes. The discrete choline peak visible at 3.2 ppm contains contributions from glycerophosphocholine, phosphocholine, and choline, all compounds that are involved in the synthesis and degradation of cell membranes. Their concentration may be affected in disorders that influence membrane turnover. Therefore, increased choline concentration likely reflects increased membrane synthesis along with cellular proliferation, both of which are features of malignancy. In a report by Hsieh et al. [9], choline levels declined with a decrease in tumor size and dynamic contrast enhancement after chemotherapy in two patients with malignancies, further suggesting that choline levels correlate with malignant activity.

However, our 3-T measurements of elevated choline concentration within malignant and benign entities in this report lend credence to the notion that a reliable quantitative measure of choline content is needed for added specificity in the distinction of benign and malignant disease in the musculoskeletal system. The detection of choline signals in some benign lesions is not an unexpected finding, given that benign lesions may also be metabolically active and that choline is present in normal tissues (such as muscle). Nevertheless, no detectable choline peak was observed in the majority of benign abnormalities, and, overall, there was a significant difference in the choline concentration between benign and malignant lesions, though in one benign case, the choline concentration of 1.2 mmol/kg approached a level observed in malignancy in other organ systems [18,19]. Our data suggest that a threshold value of up to 1.4 mmol/kg to define malignancy would theoretically produce a technique of very high specificity for distinguishing benign from malignant musculoskeletal abnormalities.

In one of the malignant cases in this series, an elevated creatine peak was also observed, though its significance is unclear. Qi et al. [8] reported detectable creatine levels in numerous benign and malignant entities and used the choline-to-creatine peak integral ratio to differentiate between benign and malignant disease. The presence and significance of detectable levels of creatine in musculoskeletal tumors has not been otherwise reported [4–7,9], and it remains unclear whether the presence of creatine is the result of voxel placement, potential outer-voxel contributions from normal skeletal muscle, or a detectable component of malignant proliferation.

With respect to the postoperative assessment of resected tumors for the determination of residual or recurrent disease, conventional MRI is routinely used to detect locally recurrent tumors and to differentiate them from expected postoperative findings [20–23]. However, it can be challenging to identify recurrent tumor in the surgical bed, because variable regions of high signal intensity are often seen on fluid-sensitive sequences. Only in the setting of a mature postsurgical scar can one confidently exclude recurrent tumor [21]. In addition, increased T2-weighted signal is found within reconstructive myocutaneous flaps for 6–12 months or longer, also creating potential difficulty in diagnosing recurrent or residual tumor in the operative bed. There has been limited recent work with regard to the utility of proton MRS in the postoperative setting [7] showing that, for seven postoperative patients without evidence of recurrent or residual tumor by follow-up, proton MRS showed two spectral

patterns. For the postsurgical patients who had undergone myocutaneous flap reconstruction, single-voxel MRS in the surgical bed revealed the typical spectrum of muscle. For patients who had not undergone flap reconstruction, only lipid and water signals were observed, and there was no discrete choline signal to suggest residual or recurrent tumor. In our sample of postoperative patients, no myocutaneous flap reconstructions were performed. Our measurements of choline concentration within the surgical bed showed negligible (13 of 15 cases) or very low choline concentrations (only up to 0.4 mmol/kg) in patients without evidence of residual or recurrent disease. It remains to be seen how the concentrations may evolve over time, how they may predict eventual recurrence of disease, and whether they will be helpful in monitoring patients with myocutaneous flap reconstruction.

A number of different quantitation methods are available for estimating metabolite concentrations from MRS data [24]. Of these methods, the water-referencing method is attractive for single-voxel spectroscopy in that the water signal is recorded from the same region of interest as the choline signal, which removes a number of systematic errors associated with possible B_0 or B_1 inhomogeneity. Also, the additional scan time required to record the water signal is minimal. However, the method does have the potential for error, with one of the more likely sources being variable water content within the lesion. In the current implementation, concentration values were calculated assuming 100% water content (Equation 1). Other potential sources of error include partial volume of the spectroscopy voxel with tissue outside the lesion and fatty infiltration into the region of interest. Because perilesional choline levels are probably lower than those within the lesion itself, partial volume effects may lead to underestimation of lesion choline content. Fatty infiltration (either microscopic or macroscopic) will also dilute the choline concentration, because choline is expected to be present only in the aqueous phase. This infiltration was corrected for in the current study by estimating the fat content of the localized volume on the basis of the relative amplitudes of the water and lipid signals measured from the nonsuppressed spectrum. Choline concentrations will also be in error if the water or metabolite relaxation times change. In the future, the method could be refined to also include estimation of relaxation times and water content, or alteration of acquisition conditions (such as longer TR or shorter TE times) to minimize the influence of relaxation times on the final result.

We observed a technical failure rate of four in 32 cases for performing MRS for musculoskeletal abnormalities. In general, lower quality studies and nondiagnostic studies were observed in peripheral rather than central locations in the body, such as the forearm. This result is not surprising because the success of MRS heavily depends on the success of good local shimming of the magnetic field, which is more difficult to achieve in peripheral locations in the body. It may also be true that adequate shimming will be difficult to achieve in specific types of tumors that are as yet unidentified. Also, over the 3-year period of recruitment for this study, errors in acquisition as a result of limited experience with MRS may have contributed to the non-diagnostic rate that was observed.

Finally, in addition to the technical limitations described, our sample size was small, with a heterogeneous group of musculoskeletal abnormalities. Nevertheless, statistically significant results were obtained. In addition, although all malignant cases in this series had histologic confirmation, several benign cases did not have a tissue diagnosis. In the latter cases, clinical and imaging confirmation of benign nature was used, and a histologic diagnosis was not obtained in accordance with clinical practice. Despite these potential sources of error, the current study proves that it is possible to estimate musculoskeletal lesion choline concentrations using the water-referencing method and that these concentration values provide good separation between benign and malignant lesion groups.

In conclusion, this report establishes the feasibility of performing quantitative MRS at 3 T in musculoskeletal abnormalities. The potential utility of choline concentration measurements in characterizing musculoskeletal abnormalities for malignancy in the de novo as well as the postoperative setting is shown. However, the quantification method used to determine the choline concentration within musculoskeletal abnormalities should be optimized in future studies to account for the relative water variability within different abnormalities.

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Fig. 1.

25-year-old woman with Ewing sarcoma of sacrum.

A, Single-voxel proton MR spectroscopy performed within sacral mass, with weak water suppression, shows discrete choline peak (choline concentration, 2.9 mmol/kg).

B, Axial T1-weighted MR image (spin echo; TR/TE, 690/15) shows left sacral mass as low-signal-intensity lesion.

C, Axial fat-suppressed T2-weighted MR image (fast spin echo; 2,886/100) shows mass involving neural foramina and crossing sacroiliac joint. Anteriorly, mass is associated with soft-tissue component. Although mass has malignant features and was categorized as probably malignant by conventional MRI, diagnosis of giant cell tumor was also entertained given some characteristic features, such as crossing of sacroiliac joint. However, elevated choline concentration (2.9 mmol/kg) detected by MR spectroscopy points toward malignancy.

Fig. 2.

64-year-old man with left thigh hematoma. Biopsy showed no evidence of malignant cells, and lesion subsequently decreased in size over time.

A, Single-voxel proton MR spectroscopy obtained within mass, with weak water suppression, shows no evidence of discrete choline peak.

B, Axial fat-suppressed T2-weighted image (fast spin echo; TR/TE, 2,886/100) shows indeterminate mass of slightly heterogeneous T2 signal with hemosiderin ring.

C, Axial T1-weighted image (spin echo; 690/15) shows mass of increased T1 signal suggesting possibility of blood products, but with underlying tumor difficult to exclude.

D, Axial contrast-enhanced T1-weighted image (gradient-refocused echo; 436/4.9) shows questionable contrast enhancement within mass, because it contains increased T1 signal on unenhanced imaging. Differential diagnosis includes hematoma as well as underlying malignant neoplasm. Negligible choline content may help guide diagnosis toward benign cause.

TABLE 1
Summary of MR Spectroscopy Results Observed in Benign and Malignant De Novo

Subject	Location	Size (cm ³)	Diagnosis	MR Spectroscopy Quality	Choline Concentration (mmol/kg), Mean $\pm$ SD
1	Sacrum	5.5 $\times$ 4.8 $\times$ 5.3	Ewing sarcoma	Excellent	2.9 $\pm$ 0.17
2	Thigh soft tissue	6.1 $\times$ 6.0 $\times$ 8.4	Ewing sarcoma	Excellent	3.8 $\pm$ 0.15
3	Calf soft tissue	5.9 $\times$ 5.3 $\times$ 8.8	High-grade undifferentiated sarcoma	Excellent	1.5 $\pm$ 0.06
4	Iliac	2.0 $\times$ 1.0 $\times$ 1.4	Bone cyst	Excellent	< 0.1
5	Femur	7.3 $\times$ 4.3 $\times$ 6.4	Giant cell tumor	Excellent	< 0.1
6	Retroperitoneum	4.1 $\times$ 3.7 $\times$ 4.5	Neurofibroma ^a	Excellent	0.28 $\pm$ 0.01
6	Calf soft tissue	2.5 $\times$ 3.2 $\times$ 5.8	Neurofibroma	Excellent	0.11 $\pm$ 0.004
7	Thigh soft tissue	13.6 $\times$ 6.5 $\times$ 6.0	Degenerated cystic schwannoma	Excellent	0.13 $\pm$ 0.005
8	Chest wall soft tissue	4.3 $\times$ 1 $\times$ 3.4	Lipoma	Excellent	< 0.1
9	Calf soft tissue	1.5 $\times$ 1.0 $\times$ 1.4	Hematoma	Excellent	< 0.1
10	Humerus	3.6 $\times$ 3.5 $\times$ 10.8	Bone cyst	Excellent	< 0.1
11	Upper arm soft tissue	4.8 $\times$ 4.0 $\times$ 5.9	Complex ganglion	Excellent	< 0.1
12	Upper arm soft tissue	1.9 $\times$ 1.9 $\times$ 2.1	Schwannoma	Excellent	0.8 $\pm$ 0.03
13	Femur	2.0 $\times$ 1.3 $\times$ 4.8	Enchondroma	Adequate	1.2 $\pm$ 0.07
14	Thigh soft tissue	4.3 $\times$ 4.7 $\times$ 8.1	Hematoma	Adequate	< 0.1
15	Wrist soft tissue	1.2 $\times$ 1.2 $\times$ 2.6	Giant cell tumor of tendon sheath	Nondiagnostic	—

Note—Dash indicates that the level of choline was not measured.

^aNeurofibroma with atypical features that was sampled twice and stable for 10 months.

TABLE 2

Summary of MR Spectroscopy Results Observed in Postoperative

Subject	Location	Original Histologic Diagnosis	Duration of Follow-Up (mo)	Result of Follow-Up	Spectral Quality	Choline Concentration (mmol/kg), Mean $\pm$ SD
1	Sacrum	Chordoma	33	Stable	Excellent	0.2 $\pm$ 0.01
2	Sacrum	Myxopapillary ependymoma	11	Stable	Excellent	<0.1
3	Knee soft tissue	Angiomatoid malignant fibrous histiocytoma	12	Stable	Excellent	<0.1
4	Calf soft tissue	Myxoid liposarcoma	24	Stable	Excellent	<0.1
5	Thigh soft tissue	High-grade fibrosarcoma	31	Stable	Excellent	<0.1
6	Thigh soft tissue	High-grade liposarcoma	16	Stable	Excellent	<0.1
7	Thigh soft tissue	Intermediate-grade sarcoma	12	Stable	Excellent	<0.1
8	Thigh soft tissue	High-grade sarcoma	13	Stable	Excellent	0.2 $\pm$ 0.01
9	Thigh soft tissue	Intermediate-grade sarcoma	3	Stable	Excellent	<0.1
10	Thigh soft tissue	High-grade sarcoma	18	Metastatic disease distant from surgical bed	Excellent	<0.1
11	Thigh soft tissue	High-grade sarcoma	20	Stable	Excellent	<0.1
12	Pelvis soft tissue	Desmoid	3	Stable	Excellent	<0.1
13	Pelvis soft tissue	Desmoid	8	Stable	Excellent	0.4 $\pm$ 0.02
14	Chest wall soft tissue	Ewing sarcoma	21	Stable	Adequate	<0.1
15	Forearm soft tissue	Intermediate-grade sarcoma	3	Stable	Adequate	<0.1
16	Thigh soft tissue	High-grade sarcoma	6	Recurrence	Nondiagnostic	—
17	Calf soft tissue	Myxoid liposarcoma	21	Stable	Nondiagnostic	—
18	Elbow soft tissue	Pigmented villonodular synovitis	21	Stable	Nondiagnostic	—

Note—Dashes indicate that the level of choline was not measured.