Application of Magnetic Resonance Imaging and Computerized Tomography as an Adjunct to the Surgical Management of Soft Tissue Sarcomas

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Magnetic resonance imaging (MRI) and computed tomography (CT) scans of 53 evaluable patients with biopsy-proven soft tissue sarcomas were reviewed and compared with operative results to ascertain the accuracy for each imaging modality to predict resectability. Location of soft part sarcomas included: abdominopelvic (3), retroperitoneal (7), extremity (35), and other anatomic sites (8). MRI was observed to have greater accuracy than CT to preoperatively predict resectability (96.2% *vs.* 75.5%, respectively, p = 0.0034) following three-dimensional, multiplanar evaluation. Further, MRI was judged to have superior sensitivity to CT (95.6% *vs.* 73.3%, respectively, p = 0.006) and equivalent specificity (100% *vs.* 87.5%, respectively, p = 0.125). MRI represents a sophisticated diagnostic imaging technique to differentiate normal tissue from soft tissue sarcomas with superior contrast resolution in multiplanar imaging. MRI is considered to be the imaging modality of choice for these tumors with the advantage of not exposing the patient to ionizing irradiation or intravenous contrast agents to delineate contiguous structures.

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SOFT TISSUE SARCOMAS challenge the surgeon to achieve maximal tumor extirpation while incurring minimum risk for the patient. Radiographic planning of tumor resectability requires precise three-dimensional localization of the tumor to achieve *en bloc* resection status.

Modern imaging techniques have revolutionized the capabilities of the clinician to diagnose and design operative therapy for neoplastic disease. Among all medical imaging techniques currently available, computed tomography (CT) and magnetic resonance imaging (MRI) represent "state-of-the-art" sophisticated, noninvasive technology to evaluate tumors and provide information beyond that obtainable with conventional measures. Currently, clinicians have evaluated four generations of CT scanners in just more than a decade. In contrast to first-generation devices, third- and fourth-generation CT imagers require less time and use less radiation to produce images with vastly improved resolution compared with the original scanners. MRI provides multiplane, cross-sectional imaging based on magnetism inherent within certain nuclei of the cellular constituents of the organism. *In vivo* studies to date have essentially been confined to parameters that can be related to the concentration of hydrogen, which is abundant in biologic tissues (especially fat and fluids). In contradistinction to CT scanning, MRI provides the clinician with some well-known advantages: notably, free access to otain cross-sectional views of any tissue plane, the absence of bone artifacts, and the absence of ionizing irradiation.

Several recent reports[1-3] suggest that MRI will provide information currently available from no other imaging technique. In addition, MRI may define tumor margins more exactly than currently available imaging modalities.[4-8] This study compares the radiographic characteristics for biopsy-proven soft tissue sarcomas provided by MRI with that derived from CT scans in the same patient population. The advantage to the surgeon of preoperative knowledge of the extent of tumor, its relationship to bony and neurovascular structures, and other determinants of resectability is obvious and well proven by the widely accepted concept of tumor staging. We evaluated and report the impact of MRI on radiologic planning for resectability of soft tissue sarcomas by determining the sensitivity and specificity of the modality with respect to high-quality CT imaging.

Materials and Methods

Between January 1984 and July 1986, 166 patients with biopsy-proven soft tissue sarcomas of varying anatomic

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TABLE 1. *Soft Tissue Sarcoma: Histologic Types*

	N
Malignant fibrous histiocytoma	16
Liposarcoma	14
Neurofibrosarcoma	9
Leiomyosarcoma	3
Fibrosarcoma	2
Synovial cell carcinoma	2
Undifferentiated	2
Rhabdomyosarcoma	2
Kaposi's sarcoma	1
Embryonal cell sarcoma	1
Epitheliod sarcoma	1
Total	53

sites were evaluated in the Clinics of the University of Florida. Fifty-three evaluable patients were identified in whom preoperative CT scans had been performed before or with the performance of prospective MRI before surgical intervention. Eleven histologic types of soft tissue sarcoma were identifiable (Table 1) of which malignant fibrous histocytoma (N = 16) and liposarcoma (N = 14) were the predominant variants. The patients, 27 men and 26 women, ranged in age from 8 months to 81 years (mean age: 48.3 years). The 53 MRI evaluations performed by the Department of Radiology represented 1.3% of the 3948 MRI examinations performed during this 30-month interval. MRI and CT scans of all evaluable patients were reviewed blindly by a single radiologist (REK) without knowledge of operative findings, anatomic extent of disease, or the histologic type of sarcoma. All radiographic data were reviewed with particular attention to anatomic and operative factors that determine resectability by nonamputative, limited surgical procedures or operations that require an amputative or extensive procedure to achieve an *en bloc* resection. The interpretation of these radiographic images was then compared with the operative findings and histopathology data to ascertain the accuracy of MRI and CT to predict resectability without radical amputation procedures, and the overall influence of these imaging techniques on patient management. Location of soft part sarcomas included: abdominopelvic (3), retroperitoneal (7), extremity (35), and other anatomic sites (8).

TABLE 2. *Accuracy of MRI and CT to Predict Resectability for 53 Soft Tissue Sarcomas*

	MRI		
	Correct N (%)	Incorrect N (%)	Total N (%)
CT			
Correct	39 (73.6)	1 (1.9)	40 (75.5)*
Incorrect	12 (22.6)	1 (1.9)	13 (24.5)
Total	51 (96.2)*	2 (3.8)	53 (100)

* MRI *versus* CT, p = 0.0034.

TABLE 3. *Resectability of Sarcoma as Predicted by CT*

	Operative Result		
	Resected N (%)	Unresected N (%)	Total N (%)
Prediction of resectability			
Yes	33 (62.3)	1 (1.9)	34 (64.2)
No	12 (22.6)	7 (13.2)	19 (35.8)
Total	45 (84.9)	8 (15.1)	53 (100)

Sensitivity for each radiologic parameter was calculated as the number of true-positive (TP) studies/number of true-positives (TP) + number of false-negatives (FN). *Specificity* for MRI and CT was determined by the number of true-negatives (TN)/number of true-negatives (TN) + number of false-positives (FP). All data were then collated and expressed as percent sensitivity/specificity to determine efficacy of the particular radiographic procedure compared with the other. Statistical evaluation was determined for each parameter using sign-test analysis. Statistical significance was taken at the 0.05 level.

Computed Tomography

CT images were obtained using a third-generation GE9800 CT Scanner™ (General Electric, Milwaukee, WI), a Siemens (Iselin, NJ) or EMI (Anaheim, CA) 7070 unit. For routine evaluation, section thickness used a 1-cm intersection gap with contiguous section thickness of 5–10 mm. CT images were performed without and with intravenous iodinated contrast (except in dye sensitivities) for all patients. Iodinated contrast (Hypaque™ Meglumine 60%) with its low, but definite, risk was used to enhance imaging of the neurovascular bundle to determine tumor resectability.

Magnetic Resonance Imaging

All MRI examinations were obtained with a 0.15 telsa resistant magnet for T1-weighted and T2-weighted images using a Teslacon™ MR Imager (Technicare, Cleveland, OH). For most cases, coronal (frontal), sagittal, and transaxial images were obtained depending on the site of the sarcoma mass. Patients were examined in varying sequence after they were informed of the benefits and risks of the techniques involved. Before examination, informed consent was obtained according to the guidelines established by research protocol at the University of Florida College of Medicine.

Images evaluated by magnetic resonance determined the signal homogenity and signal intensity (SI) of the sar-

coma relative to surrounding muscle and fat tissues on spin echo (SE) T1-weighted (SE, repetition time (TR) ≃ 500 msec, echo delay time (TE) = 30 msec), T2-weighted (SE, TR ≃ 2000 msec, TE = 90–120 msec), and spin density images (TR = 700–1000 msec, TE = 40–50 msec). This sequence of T1- and T2-weighted images provides good contrast between the tumor and muscle, as well as the tumor and fat on one scanning sequence. The central portion of the sarcoma mass was then estimated after localization in the intramuscular septum, within fascial planes or within subcutaneous fat. Margins of the tumor mass were often depicted as sharply defined, not sharply defined, or infiltrating of contiguous structures/organs.

Results were then tabulated for each imaging method. Thereafter, the specificity and sensitivity and statistical differences between the two modalities were calculated.

Results

For 96.2% (51/53) of the patients evaluated, MRI correctly predicted resectability (or unresectability) (Table 2). CT accurately determined resectability (or unresectability) in 40 patients (75.5%) (p = 0.0034). The group of patients that comprised the difference between these two groups included those who were successfully resected after MRI and yielded different or additional information beyond that obtained by CT, or those who where shown by MRI alone to be unequivocally unresectable.

TABLE 4. *Resectability of Sarcoma as Predicted by MRI*

	Operative Result		
	Resected N (%)	Unresected N (%)	Total N (%)
Predictability of resectability			
Yes	43 (81.1)	0 (0)	43 (81.1)
No	2 (3.8)	8 (15.1)	10 (18.9)
Total	45 (84.9)	8 (15.1)	53 (100)

MRI incorrectly determined resectability in two patients (3.8%) (Table 2). CT was inaccurate with respect to resectability in 13 patients (24.5%). These CT evaluations included evaluable patients in whom CT incorrectly predicted resectability (N = 1) or patients (N = 12) who were determined resectable by contradictory information provided by MRI. One patient (1.9%) was judged to be resectable from data obtained with both imaging modalities but was proven to be unresectable at the time of surgery.

Both imaging techniques gave equivalent information on resectability in 39 patients (73.6%). Of ultimate importance is the group of 13 patients (24.5%) in whom

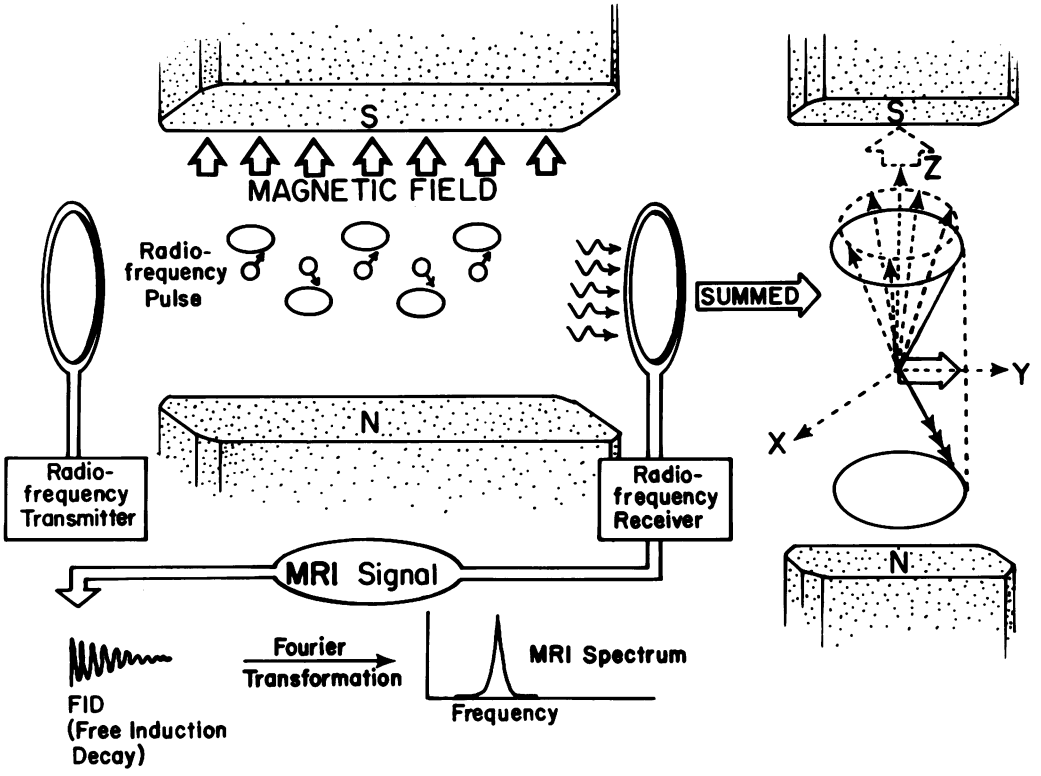
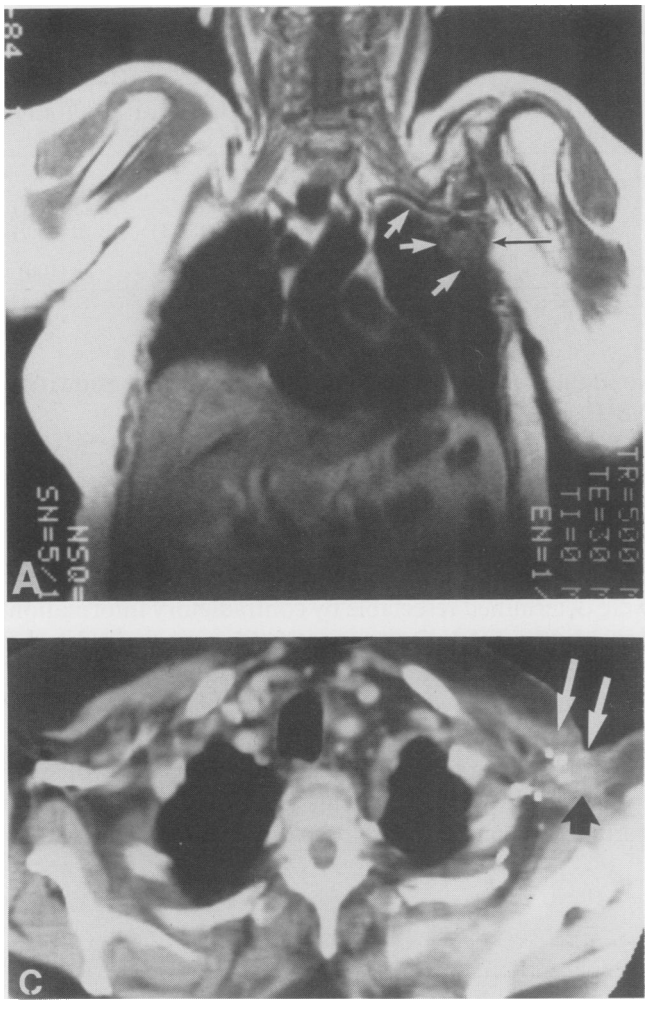


FIG. 1. Magnetic resonance imaging (MRI). After pulsed radiofrequency (RF) signal, a population of nuclear magnets (*e.g.*, hydrogen in biologic tissues) is aligned with an applied magnetic field. Net magnetization in the direction of magnetic field results. Should the RF pulse correspond to the frequency of nuclear precession, excitation of the spin-system (resonance) will occur. At resonance, nuclear magnets spin in phase with one another; and a portion of the nuclear magnets are elevated to the excited state with their magnetic moments opposed to the applied magnetic field. Thus, net magnetization is produced in the XY plane to induce an RF signal in the receiving coil. When energy of the excited nuclei is lost, relaxation occurs and the MRI signal is lost. Spin-lattice relaxation (T1) is the return of the magnets to the original alignment with the applied field. T2 (spin-spin) relaxation is the loss of the in-phase spinning of the nuclear magnets. After relaxation processes, the nuclear magnets return to their orientation before excitation, and the MRI signal disappears.



FIGS. 2A–C. MRI of undifferentiated fibrosarcoma of left axilla that occurred 7 years after left modified radical mastectomy and comprehensive chest wall irradiation. (*A*) Coronal MRI T1-weighted image. Arrows delineate sarcoma that encased left subclavian and axillary arteries. Tumor–fat margin is evident with tumor adherence to chest wall. A forequarter amputation was necessary to resect the tumor. (*B*) MRI transaxial view confirms an ill-defined soft tissue mass of the axilla with invasion of the pectoralis major muscle. No artifact is seen. (*C*) Transaxial CT of axilla/chest. The pectoralis major muscle appears retracted. Minimal artifact distortion from metallic clips is evident.

MRI mandated a different operative approach for 12 patients as a consequence of additional data not evident on CT scanning (Table 2). These included patients in whom a different operative procedure was correctly initiated: either a limited *en bloc* resection of the sarcoma with a margin of normal surrounding tissue or more extensive and amputative procedures.

To evaluate sensitivity and specificity for each radiographic modality, preoperative determination of resectability of sarcomas by CT (Table 3) and MRI (Table 4) was necessary. CT correctly predicted resectability (62.3%) less frequently than MRI (81.1%). CT incorrectly predicted operative resection for only one of the 53 patients, whereas, all patients considered unresectable by the radiographic criteria of MRI were confirmed to be unresectable at operation.

$$\text{Sensitivity (true-positives)} = \frac{TP}{TP+FN} \text{ for MRI and CT}$$

were $\frac{43}{43+2}$ and $\frac{33}{33+12}$ = 95.6% and 73.3%, respectively ($p = 0.006$).

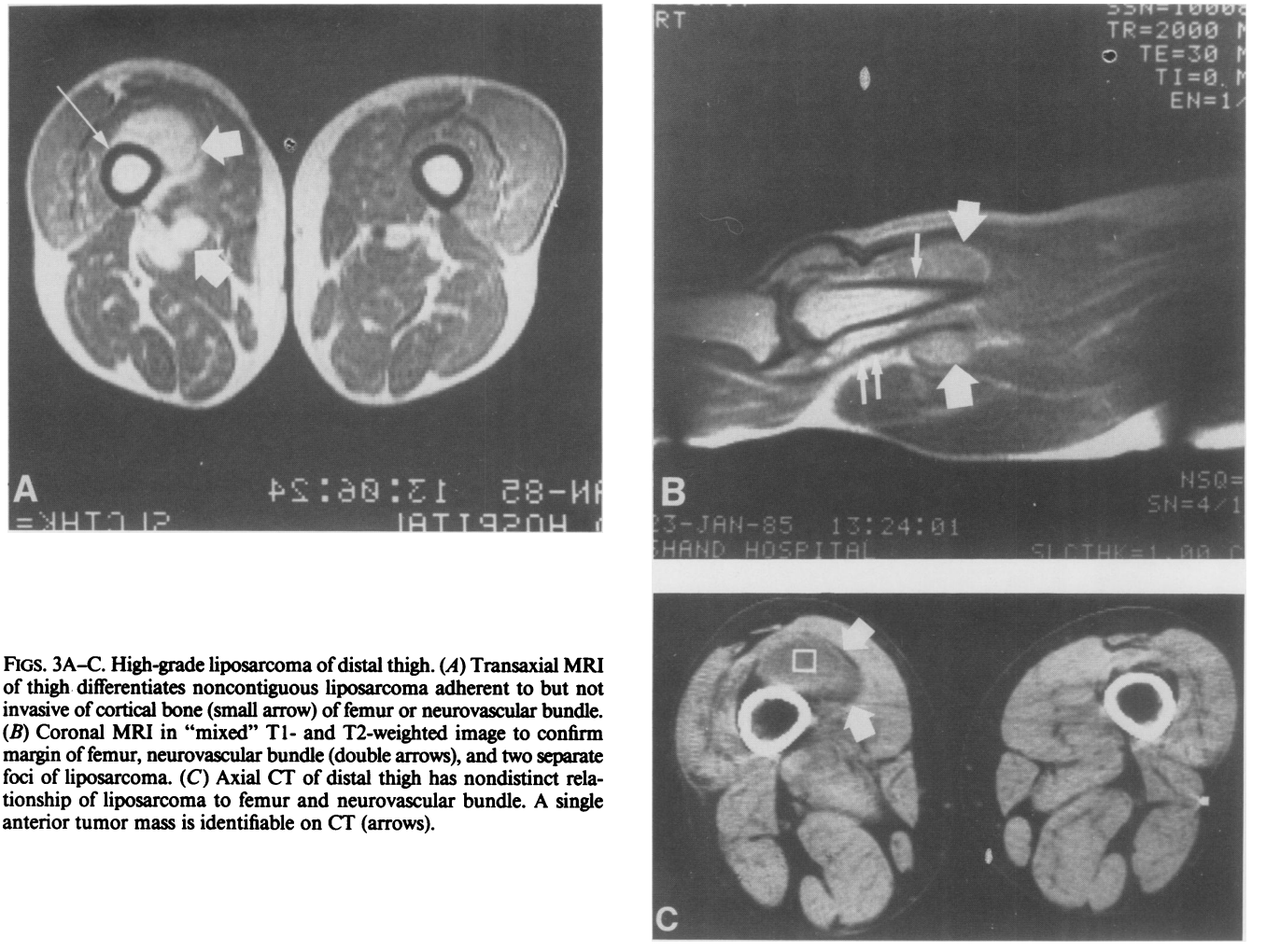
$$\text{Specificity (true-negatives)} = \frac{TN}{TN+FP} \text{ for MRI and CT}$$

were $\frac{8}{8+0}$ and $\frac{7}{7+1}$ = 100% and 87.5%, respectively ($p = 0.125$).

Thirty-five of the 53 patients (66.0%) were managed by *en bloc* resection. Nine patients (17.0%) were treated by extensive amputative procedures (hemipelvectomy, forequarter), one patient was treated by retroperitoneal resection (1.9%), and eight patients (15.1%) proved unresectable.

Discussion

CT imaging is dependent on a single parameter, electron density, whereas MRI can characterize four distinct parameters simultaneously (Fig. 1). These MRI parameters include: (1) spin (proton) density the number of nuclear signals per unit volume; (2) spin-lattice (T1) relaxation time, interval for the nuclear magnets to return to their original alignment with the externally applied mag-



FIGS. 3A–C. High-grade liposarcoma of distal thigh. (*A*) Transaxial MRI of thigh differentiates noncontiguous liposarcoma adherent to but not invasive of cortical bone (small arrow) of femur or neurovascular bundle. (*B*) Coronal MRI in "mixed" T1- and T2-weighted image to confirm margin of femur, neurovascular bundle (double arrows), and two separate foci of liposarcoma. (*C*) Axial CT of distal thigh has nondistinct relationship of liposarcoma to femur and neurovascular bundle. A single anterior tumor mass is identifiable on CT (arrows).

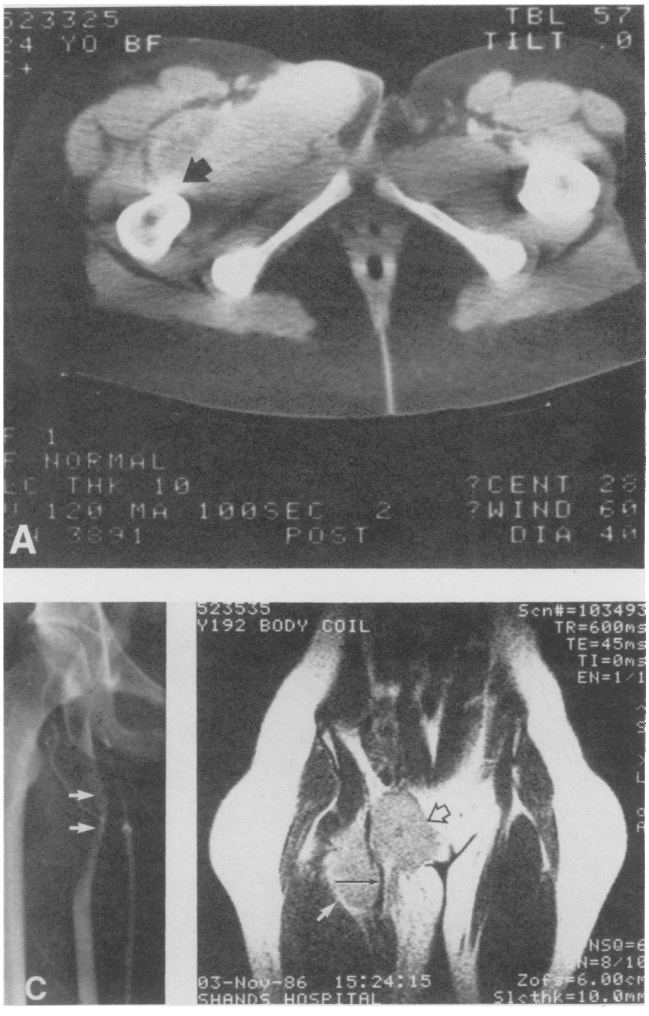
netic field; (3) spin-spin (T2) relaxation time, the interval for nuclear magnetics to lose phase coherence; and (4) chemical shift of the excited molecules in different environments as a variation in the observed resonance frequency of nuclear magnets. These relaxation times (T1 and T2) characterize the distinct types of nuclear interactions in a molecular environment.[9] It is because of these relationships that MRI techniques offer potentially greater pathophysiologic specificity than does CT or other conventional imaging modalities.

The first application to the study of human tumors with MRI was by Damadian and colleagues.[10,11] These investigators initially proposed that innate characteristics of tissue assessed by MRI (spin-lattice and spin-spin relaxation times [T1 and T2], could differentiate benign and malignant tissues *in vitro.* The clinical applications of these theoretical concepts were further enhanced when Lauterbur[12] produced images by spatially encoding MRI signals.

Thus, MRI was a clinical application of nuclear magnetic resonance spectroscopy, a method based on principles derived from quantum mechanics beyond the scope of this report.[13] In brief, weak radiofrequency signals are emitted by protons from water molecules that have been "energized" in a strong external electromagnetic field. With externally controlled variation of time, sequence, and the frequency of applied radiofrequency pulses from the magnet, signal imaging can be optimized. As initially theorized by Damadian[10] in 1971, two lines of evidence suggest that proton signals from the water in cancerous tissue is distinct from radiofrequency emissions of normal tissue. Thereafter, these emitted signals are reconstructed into transaxial, sagittal, and coronal images that allow accurate *in vivo* depiction of pathologic processes.

Recently, numerous authors have reported the usefulness of MRI in evaluating soft tissue tumors of various locations.[14–17] Previous publications described the usefulness of CT in managing soft tissue tumors.[18,19] As yet, only a few reports compare the two imaging modalities in depicting soft tissue tumors.[20,21]

Enneking and associates[22] reported that anatomic location, confinement to an anatomic compartment, pres-



FIGS. 4A–C. Undifferentiated spindle cell sarcoma of anterior thigh, groin, and anterior abdominal wall. (*A*) Axial CT of mass in inguinal space has artifact distortion of proximal femur obscuring tumor margins and contiguous vessels. (*B*) Axial MRI of same level as Figure 4A with mixed T1- and T2-weighted images. Arrows confirm tumor invades contiguous muscles of proximal thigh and abdominal wall. (*C*) Composite view of venography and coronal MRI. Venogram *via* right dorsal foot confirms medial displacement of superficial femoral vein (arrows). *Right.* Arrows delineate mixed T1- and T2-weighted image of neoplasm to depict venous displacement and encasement without use of contrast dyes.

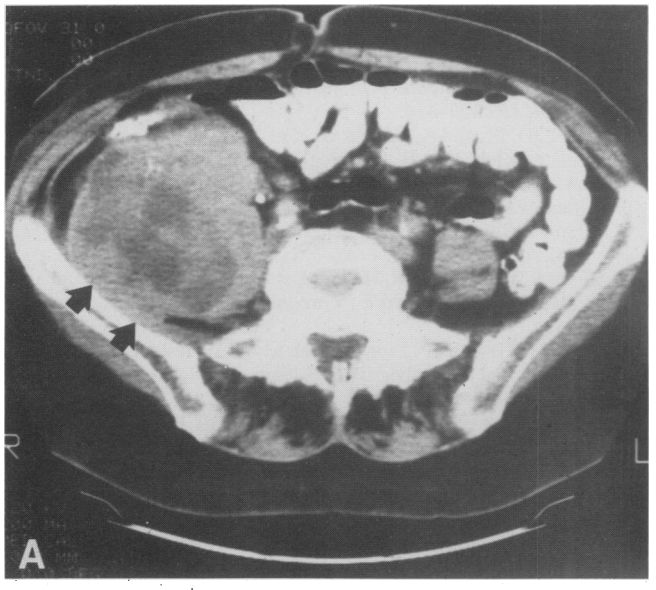
ence or absence of metastatic disease, and histologic grade are the factors that determine success in management of sarcomas. Modern surgical techniques, including reconstructive surgery, combined with radiotherapy and chemotherapy, have led to advances in the treatment of sarcomas, but accurate preoperative staging is essential.[22,23]

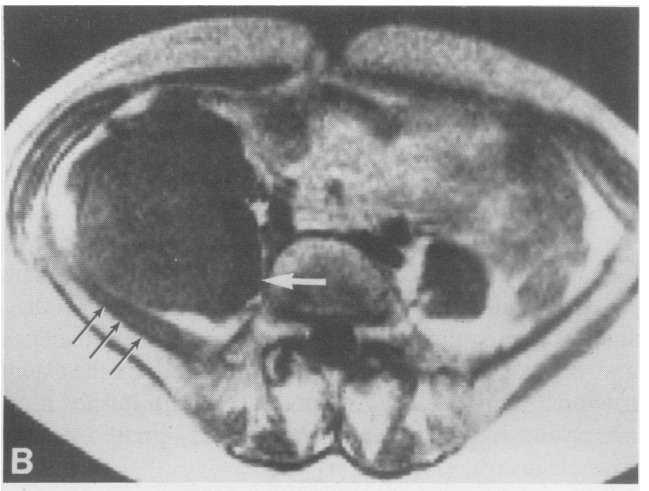
Our current study confirms that MRI offered a more precise depiction of soft tissue sarcomas than CT. MRI had better soft tissue contrast resolution that provided greater sensitivity in tumor detection. Better contrast between normal and pathologic tissues facilitated equivalent specificity of MRI to CT. In addition, direct coronal and sagittal imaging obtained with MRI provided three-dimensional images that allowed superior estimation of configuration, extent, and margins of tumors. Three-dimensional imaging enhanced estimation of the anatomy with relationship of the tumor to contiguous vascular and important nonvascular structures. Clearly, these advantages offered by MRI enabled better operative planning than information obtained with CT alone.

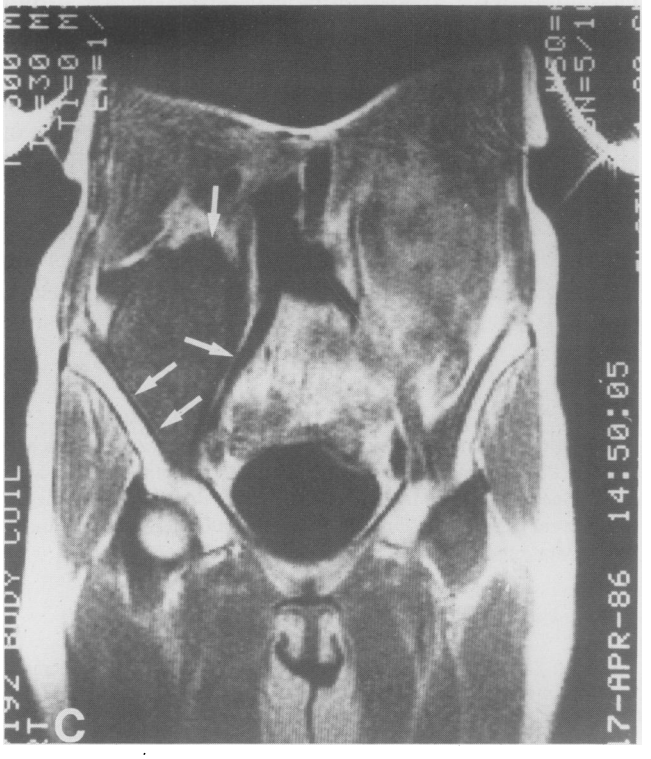
MRI is performed without exposing the patient to ionizing radiation. No intravenous contrast agents are required to delineate vascular structures. MRI was considered to provide more accurate information about the relationship of tumors to adjacent neurovascular sructures than CT scans obtained with the use of intravenous contrast. Thus, estimation of resectability and operative planning was better facilitated with MRI.

Artifact visualization from metallic vascular clips was not problematic on MRI, whereas such aberrations frequently prevented imaging of certain areas with CT scans. Dense bone also gave artifact on CT that never appeared on MRI.

MRI is not operator dependent as are some imaging modalities. It also is not dependent on body habitus, whereas CT is adversely affected by morbid obesity. CT provided superior spatial resolution, allowing better distinction between two closely set points. CT provided much shorter scanning time. In particular, MRI often required multiple imaging sequences for three-dimensional views. Specific information about tumor margins and, in limited instances, cell type, can be obtained from the different







FIGS. 5A–C. Large mesenchyoma of right retroperitoneal space and iliac fossa. (*A*) Transaxial CT with intravenous contrast demonstrates necrotic tumor of right iliac fossa. Mass appears to invade iliac bone (arrows). Involvement of iliac vein is indeterminable. (*B*) Axial MRI delineates noninvolved cortical bone (arrow) and patent right iliac venous system. (*C*) Coronal MRI of mesenchyoma depicts uninvolved cortical bone (arrows) and complete visualization of right iliac vein without contrast. The lesion was resected *en bloc*.

spin-echo (SE) sequences. T1-weighted images (TR = 500; TE = 30) provide good anatomic detail and allow differentiation between tumor and fat margins in nonlipomatous tumors (Figs. 2A–C). On this sequence, nonlipomatous sarcomas have a signal intensity ≦ adjacent muscle. Therefore, the tumor is often difficult to visualize within or adjacent to normal muscle, as the T1 values of these sarcomas are similar to normal muscle. However, only T1-weighted images of nonlipomatous tumors are well differentiated from normal fat. Sarcomas with high fat content (Figs. 3A–C) may blend with adjacent fat on T1-weighted images, but may be differentiated from muscle.

T2-weighted images provide excellent tumor–muscle differentiation because of the marked differences in T2-relaxation values. All sarcomas show greater signal intensity than normal muscle on T2-weighted images. However, because T2 values of the tumor may be equivalent to fat, tumor margins may blend with fat on these images. Both sequences, therefore, are needed to provide tumor–muscle and tumor–fat contrast. With the *mixed* (spin-density) T1- and T2-weighted image (Figs. 4A–C) it is common to have both tumor–muscle and tumor–fat contrast on a single imaging sequence. In many case, all three sequences were necessary, and different imaging planes

were used to fully evaluate the anatomic extent of the neoplasm (Figs. 5A–C). Thus, both T1- and T2-weighted images of sarcomas are appropriate to obtain optimal information from MRI. T1-weighted images distinguish tumor–fat margins and best identify relationships to the neurovascular bundle. T2-weighted images provide superior tumor–muscle contrast.

Cost is a significant factor with any modern imaging technique. Although cost is seemingly a disadvantage with MRI, it could prove to be cost effective if other studies, such as angiography, were obviated. The cost efficiency and value of any diagnostic tool is dependent on the extent to which it changes treatment strategy, diminishes morbidity and mortality, and/or improves disease-free and overall survival.

In summary, MRI is a sophisticated diagnostic imaging technique that provides enhanced sensitivity for tumor detection and equivalent specificity in differentiation of normal from malignant tissues by allowing superior soft tissue contrast resolution and multiplanar imaging. Therefore, MRI was chosen to be the imaging method of choice in the diagnosis and operative planning for soft tissue sarcomas. Although CT scanning was judged to be effective in the evaluation of this neoplasm, it required exposure of the patient to intravenous contrast agents and ionizing radiation and was less sensitive and specific than MRI.

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Discussion

Dr. J. Shelton Horsley, III (Richmond, Virginia): I apologize for rising again, but Dr. Bland was kind enough several weeks ago to send me this manuscript.

Several years ago Drs. Neifeld, Walsh, and Lawrence reported a series of 46 patients with soft tissue sarcomas evaluated both clinically and by computed tomography (CT) scans at the Medical College of Virginia. They found that in the retroperitoneum where most of these were located, in 21 patients, CT scan was a great asset. There were 16 patients who had lesions in their extremities. All had CT scans and careful clinical evaluation. In two patients, both in upper extremity lesions, CT scans gave additional information that led to forequarter and chest wall excisions when clinically it did not appear surgical resection would have to be that extensive. However, in the lower extremities, there were two lesions that appeared to involve the femoral artery and vein, but on careful surgical exploration were completely resectable. The limb was salvageable and the margin was adequate without involvement of the neurovascular bundle.

We are also in the process of trying to find the proper place for magnetic resonance imaging (MRI). It gives you some tremendous pictures. However, we use the CT scan in our patients with soft tissue sarcomas to evaluate their lungs. Do they have pulmonary metastases? We have found that the MRI has not been good for lung details. I would like to ask Dr. Bland what his experience has been in this regard?

Again, I believe the bottom line here is careful clinical examination