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# Preoperative Evaluation of Osteosarcoma: Value of Gadopentetate Dimeglumine-Enhanced MR Imaging

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Decisions regarding the surgical approach in osteosarcoma require accurate assessment of tumor extent. In order to determine whether enhancement with gadopentetate dimeglumine could add clinically significant information to that available with unenhanced MR imaging, 21 patients with osteosarcoma underwent preoperative MR imaging. T1- and T2-weighted spin-echo MR images obtained before and after administration of IV gadopentetate dimeglumine were evaluated to determine the conspicuity of marrow and soft-tissue extent of tumor, including tumor involvement of major neurovascular bundles and adjacent joints. MR results were correlated with tumor margins found at surgery. In some instances, use of gadopentetate dimeglumine obscured differentiation of tumor from normal marrow or tumor infiltration into perineurovascular fat, and tumor extension through pseudocapsule could not be differentiated from peritumoral edema after contrast administration. Contrast enhancement did assist in differentiation of intraarticular tumor from effusion; however, synovial invasion could be identified on unenhanced T1-weighted images by loss of synovial fat and cortical disruption.

These results indicate that gadopentetate dimeglumine does not assist in defining tumor margins of osteosarcoma.

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Surgical intervention for osteosarcoma may consist of limb sparing procedures, amputation, or disarticulation. The choice of procedure requires that intramedullary and soft-tissue tumor margins be accurately defined, including tumor infiltration into vital neurovascular structures and joints. In order to determine if gadopentetate dimeglumine-enhanced MR images could assist in the preoperative evaluation of osteosarcoma, we performed pre- and postenhancement imaging preoperatively in 21 patients.

## Subjects and Methods

The study included 21 patients with biopsy-proved primary intramedullary osteosarcoma. There were 11 males and 10 females 13-52 years old (mean age, 21 years). Eleven tumors originated in the distal femur, six in the proximal tibia, and two each in the proximal humerus and proximal femur. No patient had known metastatic disease when the MR images were made.

Four patients were imaged before initiation of preoperative chemotherapy, 13 were at the midpoint of therapy, and four had completed chemotherapy at the time of MR imaging. In all patients, chemotherapy consisted of a 12-week period of high-dose methotrexate, cisplatin, and Adriamycin [1].

MR images were acquired with a 0.3-T hybrid permanent resistive magnet. A surface coil was used for lesions of the knee and shoulder. The field of view varied from 14 to 25 cm, depending on the body part under investigation. Slice thickness and interslice gap were chosen to cover the entire tumor, with 13 images provided for each pulse sequence. Although multiplanar images were obtained in all patients, only axial images were evaluated for this study.

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In order to provide uniformity in image acquisition, a multiple echo, multiple repetition (MEMR) sequence was used both before and after enhancement [2]. T2-weighted images after contrast administration, however, were not used for analysis in the study. This is because gadopentetate dimeglumine-induced T2 shortening is not evident with the dose of contrast material and pulse sequences used for clinical MR scanning. The MEMR sequence allows simultaneous acquisition of spin-echo T1- and T2-weighted images. With a pulse sequence pair of 340/30 and 2200/85 (TR/TE), 13 images were available for each pulse sequence within a single scan acquisition. Two signal averages and 192 imaging levels gave an acquisition time of 17.5 min per scan set. One set was completed immediately before, and one within 20 min after IV administration of 0.1 mmol/kg of gadopentetate dimeglumine. No contrast reactions or complications occurred.

Scans were evaluated simultaneously by two experienced radiologists, and consensus was reached for all readings. Findings on MR images were compared with findings at surgery by evaluating the width of tumor-free margins. Pathologic results were not known at the time of image interpretation. Unenhanced and enhanced images were reviewed to determine intramedullary and soft-tissue tumor signal characteristics (and thus differentiation of tumor from normal surrounding tissue), the presence or absence of an intact tumor capsule or pseudocapsule, the relationship of tumor to major neurovascular structures, and evidence of synovial or intraarticular invasion by tumor.

For analysis of signal characteristics, intramedullary and soft-tissue tumors were independently classified as either homogeneous or inhomogeneous. The predominant signal intensity within the tumor was then determined to be either void, present but lower than that of normal muscle, equal to that of muscle, higher than that of muscle but lower than that of subcutaneous fat, equal to that of fat, or higher than that of subcutaneous fat.

A tumor capsule or pseudocapsule was considered present and intact when margins of the soft-tissue mass were sharply demarcated. If adjacent muscle showed poorly defined abnormal signal intensity with enhanced T1-weighted or unenhanced T2-weighted imaging, either peritumoral edema or tumor invasion was thought to be present within surrounding soft tissues.

Major neurovascular structures were evaluated as being either free of tumor, abutted by tumor, or encased by tumor. Joints were evaluated for a breach in the normal synovium as evidenced by loss of the normal high signal intensity of synovial fat. Joint distension was also noted and determined to represent either intraarticular tumor or fluid.

## Results

### Tumor Signal Characteristics

**Intramedullary tumor.**—On unenhanced T1-weighted images, the signal intensity of intramedullary tumor was equal to or less than that of muscle in all cases. This pattern was homogeneous in 16 cases and inhomogeneous in five. On T1-weighted images after administration of contrast material, intramedullary tumor enhanced in 11 cases (Fig. 1) and did not change in 10 cases. Four tumors that were homogeneous became inhomogeneous. The signal characteristics of intramedullary tumor on unenhanced T2-weighted images were more variable. Five tumors were of a signal intensity equal to or lower than that of muscle, 10 were higher than muscle and lower than fat, and six were equal to or higher than fat. Four tumors were homogeneous and 17 were inhomogeneous.

**Soft-tissue tumor.**—Five tumors were entirely intraosseous. Of the 16 with a soft-tissue mass, unenhanced T1-weighted images showed 15 with signal intensity equal to that of muscle and one with signal intensity higher than that of muscle but less than that of fat. Eleven of these were homogeneous and five were inhomogeneous. On T1-weighted images obtained after administration of contrast material, the signal intensity of 13 masses increased to become either higher than that of muscle and lower than that of fat (11 cases) or equal to that of fat (two). Three retained their unenhanced signal intensity. Only three tumors remained homogeneous. On unenhanced T2-weighted images, all soft-tissue masses but one showed signal intensity higher than that of muscle (13 equal to or higher than that of fat). Three were homogeneous and 13 were inhomogeneous. Five tumors showed uniform high signal intensity on unenhanced T2-weighted images and a rim of high signal intensity surrounding central intermediate signal intensity on unenhanced T1-weighted images, a pattern of tumor necrosis (Fig. 2).

### Tumor Capsule/Pseudocapsule

In 15 of the 16 tumors with a soft-tissue mass, the soft-tissue component was sharply defined on both unenhanced

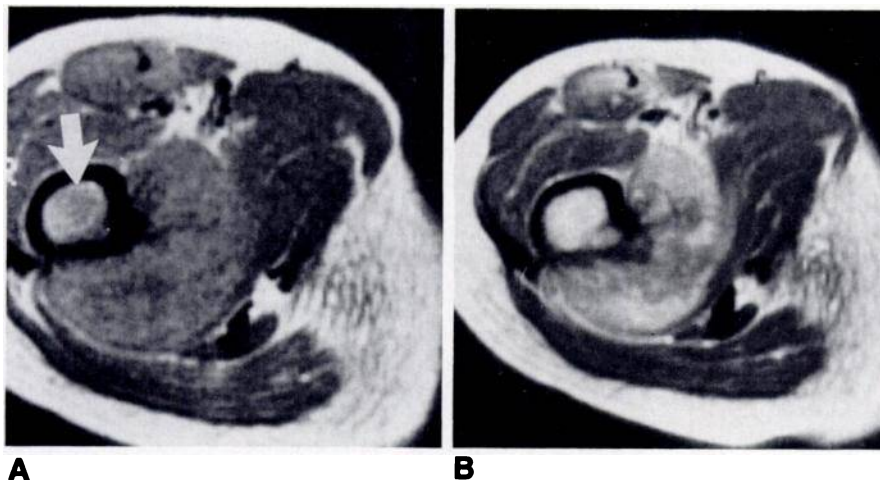


Fig. 1.—Intramedullary tumor enhancement. **A**, Unenhanced T1-weighted MR image of proximal thigh shows intramedullary tumor (arrow) of intermediate signal intensity in right femur. Marrow of left femur and subcutaneous fat were of normal high signal intensity. **B**, Enhanced T1-weighted MR image shows signal intensity of intramedullary tumor in right femur to be equal to that of fat. Differentiation of intramedullary tumor from normal marrow is not possible.

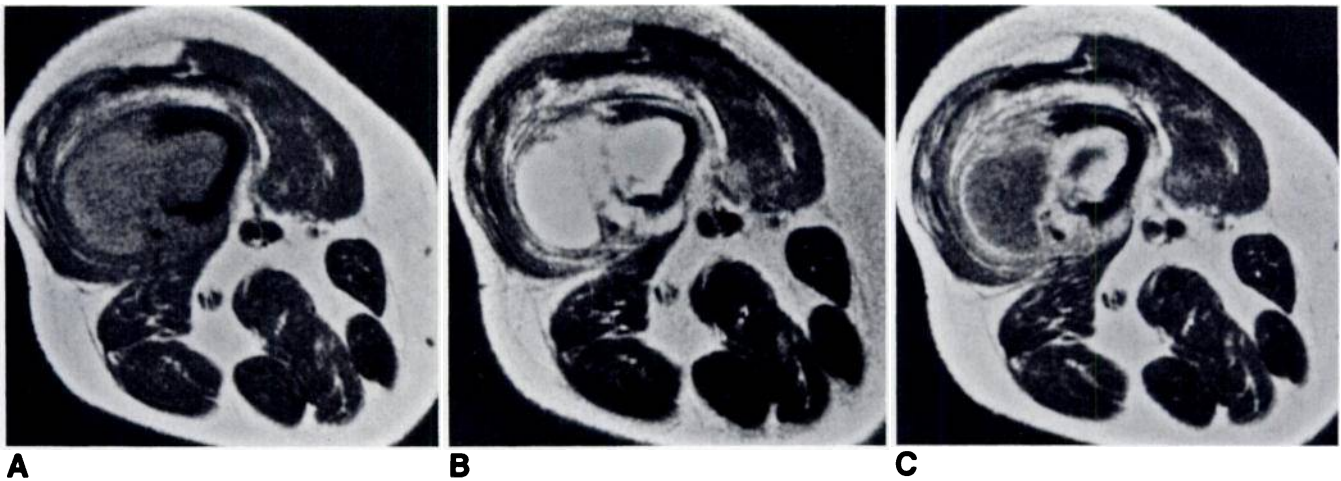


T2-weighted images and enhanced T1-weighted images, indicating the presence of a tumor capsule or pseudocapsule. In one patient, soft-tissue margins were poorly defined on both enhanced and unenhanced images. Unenhanced T2-weighted images in six of the 15 tumors with a capsule or pseudocapsule revealed poorly defined streaks of high signal intensity within adjacent muscle. In all six, there was gadopentetate dimeglumine enhancement in the same location (Fig. 3), and in four, this enhancement was greater than the enhancement of the predominant soft-tissue mass itself. Of these four, surgical margins revealed that this enhancement

represented peritumoral edema in two cases and tumor infiltration in two cases.

#### Neurovascular Involvement

The major neurovascular structures were clearly free of tumor in 15 patients. Comparison of unenhanced T1- and T2-weighted images revealed tumor abutting the major bundles in five patients. On enhanced T1-weighted images, differentiation of tumor from normal fat surrounding the neurovascular bundle was less evident (Fig. 4). In one patient, a major

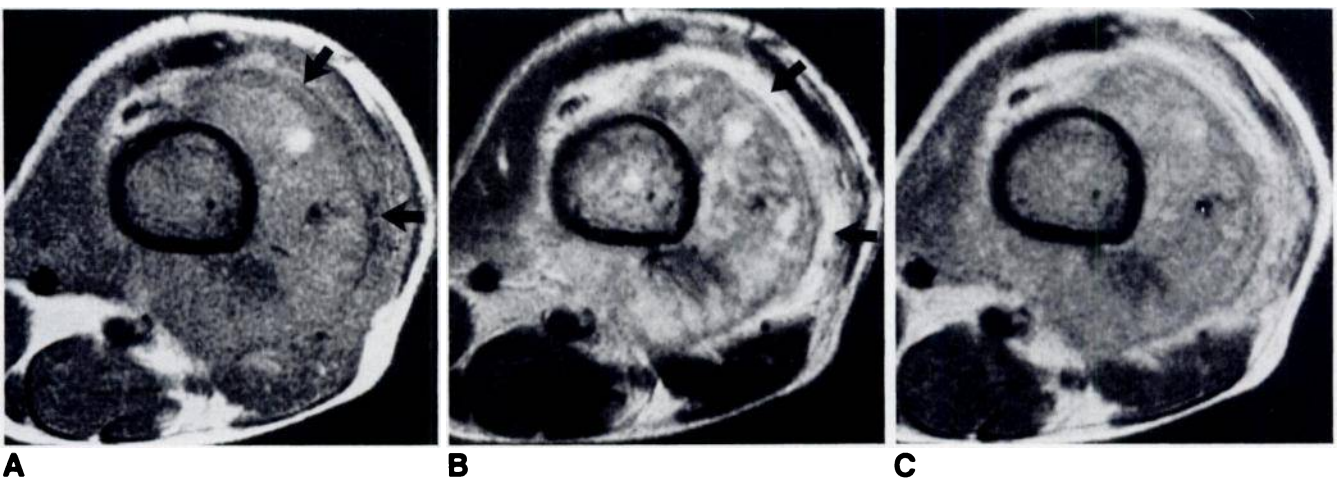


**Fig. 2.—Tumor necrosis.**

**A,** Unenhanced T1-weighted MR image of distal thigh shows marrow tumor and contiguous soft-tissue mass of homogeneous intermediate signal intensity.

**B,** Unenhanced T2-weighted MR image shows both intramedullary tumor and soft-tissue mass are of uniform high signal intensity.

**C,** Enhanced T1-weighted image shows persistent low signal intensity, indicating tumor necrosis. Had this represented tumor mineralization, it would not have had high signal intensity on T2-weighted image.



**Fig. 3.—Tumor capsule.**

**A,** Unenhanced T1-weighted MR image of distal thigh shows margin (arrows) of soft-tissue mass is well defined by pseudocapsule.

**B,** Unenhanced T2-weighted MR image shows low-signal-intensity pseudocapsule separating soft-tissue mass from surrounding muscles. High-signal-intensity peritumoral edema with poorly defined margins is seen laterally (arrows).

**C,** Enhanced T1-weighted MR image shows enhancement of both soft-tissue mass and peritumoral edema. In this patient, edema shows greater enhancement.

neurovascular bundle was obliterated by tumor. This was evident on all images.

#### Intraarticular Tumor

Adjacent joints were free of tumor in 16 patients. This was apparent on unenhanced T1-weighted images, and was evidenced as continuity of a thin band of normal synovial fat and lack of intraarticular mass. Unenhanced images in five patients revealed abnormal signal intensity interrupting synovium (synovial invasion) and joint distension. On T1-weighted images, intraarticular tumor was of intermediate signal intensity, while joint fluid was of very low signal intensity (Fig. 5). Intraarticular tumor became higher signal intensity on unenhanced T2-weighted and enhanced T1-weighted images. Joint fluid became very high signal intensity on T2-weighted images, but

retained its low signal intensity on enhanced T1-weighted images. Normal synovium enhanced uniformly with gadopentetate dimeglumine.

#### Discussion

Preoperative imaging of osteosarcoma generally includes radiographs, scintigrams, and CT scans or MR images [3]. Cross-sectional imaging is used to determine marrow and soft-tissue extent of tumor, including the relationship of tumor to major neurovascular structures and adjacent joints. This information, together with clinical and histological studies, is essential for tumor staging and determining the most appropriate type of surgical treatment (limb-sparing procedure, amputation, or disarticulation).

On unenhanced T1-weighted MR images, determination of

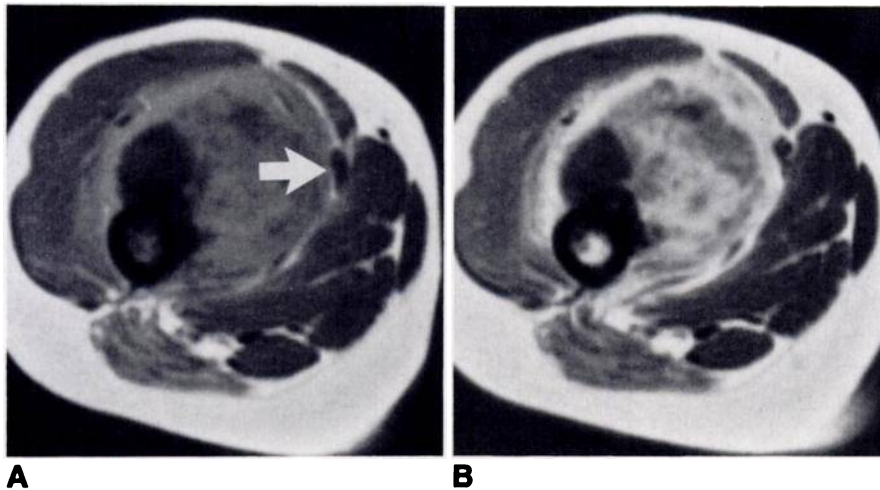


Fig. 4.—Neurovascular bundle.

**A**, Unenhanced T1-weighted MR image through proximal thigh shows soft-tissue mass abuts signal void of superficial femoral vessels. High-signal-intensity fat, however, separates tumor from vascular structures (arrow).

**B**, Enhanced T1-weighted image. Because both soft-tissue mass and peritumoral edema enhance, normal fat surrounding neurovascular structures is no longer evident.

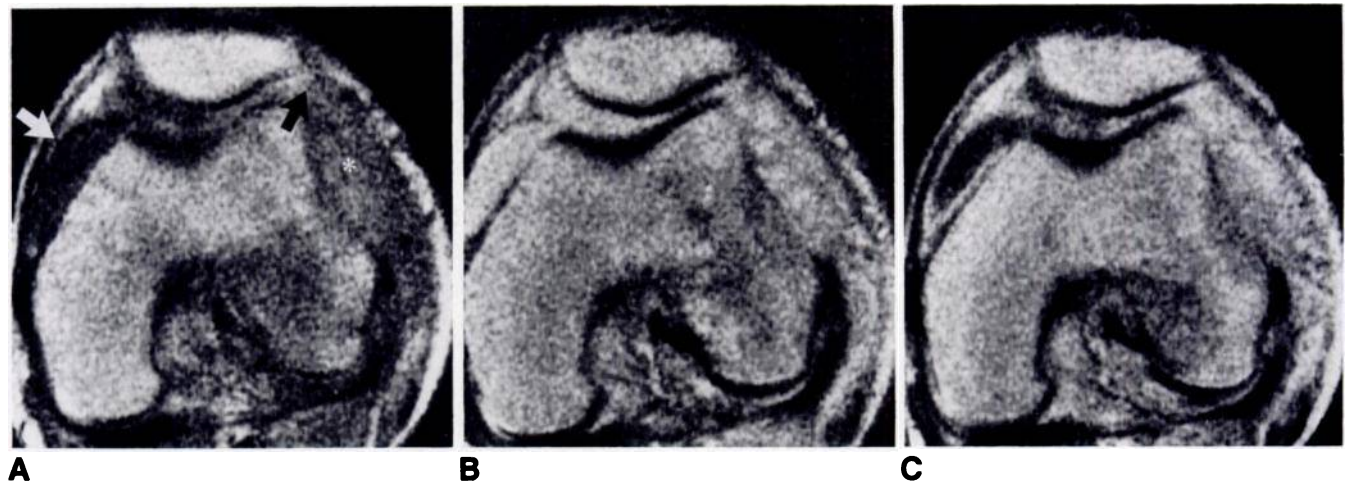


Fig. 5.—Normal synovial enhancement and joint invasion.

**A**, Unenhanced T1-weighted MR image through knee shows soft-tissue mass in region of lateral recess of knee joint (asterisk). Invasion of fat has occurred adjacent to patella (black arrow). Medially, very low signal joint fluid is present. An intact synovium is evident as a thin band of fat signal intensity (white arrow).

**B**, Unenhanced T2-weighted MR image shows tumor and fluid both have high signal intensity.

**C**, Enhanced T1-weighted MR image shows enhancement of both tumor in lateral recess and uninvolved synovium in medial recess. While lack of tumor invasion into medial recess is more striking on enhanced image, this information is available on unenhanced images.

intramedullary tumor extent is rendered possible by the inherent contrast differentiation between the high signal intensity of normal fatty marrow and the intermediate signal intensity of tumor. After administration of contrast material, intramedullary tumor enhanced in 11 of our patients, and the usual contrast differentiation between marrow and tumor was lost. This same phenomenon was observed by Stimac et al. [4] in the evaluation of spinal neoplasms.

The majority of intramedullary and soft-tissue tumors in our study increased in signal intensity after contrast administration. The clinical significance of this phenomenon, however, is questionable. Because contrast enhancement is an indication of vascularity, authors have attempted to characterize tumors according to their enhancement pattern. Stimac et al. [4] found that enhancement with gadopentetate dimeglumine could determine the vascular character of tumors of the spine, but determined that enhancement was not specific for tumor activity. Erlemann et al. [5] studied primary musculoskeletal tumors with dynamic gadopentetate dimeglumine-enhanced MR imaging with a 1.5-T magnet. They determined that dynamic imaging with gradient-echo techniques (flip angle of 90°) after contrast administration allowed differentiation of malignant vs benign lesions with an accuracy of 80% [5]. Others, however, have not been able to duplicate these findings using a 1.0-T magnet and a flip angle of 40° [6]. It was not noted in the study of Erlemann et al. whether differentiation between benign and malignant bone lesions was possible with plain radiography, a much less expensive and more readily available technique.

Sharp tumor margins, indicating the presence of a tumor capsule or pseudocapsule, were present in 15 patients. This was easily identified on both unenhanced T2-weighted and enhanced T1-weighted images. Of substantial clinical concern, however, was the peritumoral high signal intensity seen in adjacent soft tissues on the unenhanced T2-weighted and enhanced T1-weighted images of six patients. Pettersson et al. [7] studied five patients with soft-tissue tumors by using gadopentetate dimeglumine-enhanced MR and found that both richly vascularized tissues and edematous structures enhanced. Hanna et al. [8] found that viable tumor, granulation tissue after biopsy, and peritumoral edema enhanced with gadopentetate dimeglumine. We also found that this streaky pattern of high signal intensity could represent either edema or infiltration of tumor into adjacent tissues. In addition, peritumoral edema may enhance more dramatically than soft-tissue tumor. This is in contradistinction to the findings of Bloem et al. [9], who found that strong enhancement was a reliable indication of tumor.

Definition of the proximity of tumor to major neurovascular structures presents little problem with the combination of unenhanced T1-weighted and T2-weighted MR images. The high-signal-intensity fat surrounding large vessels and nerves is easily identified on T1-weighted images, and tumor increases in signal intensity on T2-weighted images. With gadopentetate dimeglumine, most soft-tissue tumors become

high signal intensity, similar to fat. When tumor is very near the neurovascular bundle, demarcation between tumor and neurovascular bundle fat is either less evident or lost in T1-weighted images after contrast administration.

Normal synovial tissue can be identified on unenhanced images by the high signal intensity of synovial fat on T1-weighted images. Tumor that has invaded synovium, however, shows intermediate signal intensity on T1-weighted images and signal intensity equal to or higher than that of fat on T2-weighted images. Although distinction between joint effusion and intraarticular tumor is more obvious on enhanced T1-weighted images, the presence of tumor is nonetheless evident before contrast enhancement by identification of synovial infiltration and adjacent cortical disruption. In addition, joint fluid is of low signal intensity on the unenhanced T1-weighted images, and tumor is of intermediate signal intensity.

Our preliminary results suggest that enhancement with gadopentetate dimeglumine in preoperative MR imaging of osteosarcoma is not necessary. As compared with unenhanced T1-weighted images, differentiation of tumor from normal fat, including marrow, fat investing neurovascular structures, and fatty synovium is more difficult after injection of contrast material. Although circumstances may arise in which contrast enhancement may be useful, we believe that the routine use of gadopentetate dimeglumine adds unnecessary imaging time, cost, and remote but potential risk. Further investigation with large numbers of patients may provide clinically useful indications for gadopentetate dimeglumine in MR imaging of the musculoskeletal system.

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