Preoperative MR Imaging Assessment of Osteosarcoma: A Radiological - Surgical Correlation

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The objective of the study was to detect the accuracy of MR imaging in preoperative evaluation and staging of osteosarcoma and assess the usefulness of gadopentetate dimeglumine contrast enhancement compared with non-contrast studies.

From 1994 to 1999, 34 patients with osteosarcoma received MR imaging examinations (24 men, 10 women, ages 7 - 55 years, mean age 17 years). The pulse sequences included T1 weighted imaging and T2 weighted imaging with or without fat saturation. Pre- and post gadopentetate dimeglumine contrast enhancement was performed in 27 cases. Non-contrast studies were performed in only 7 cases. Surgical findings were compared with imaging findings in the following 4 major areas: involvement of joint, physeal plate invasion, neurovascular invasion, and skip metastasis.

The sensitivity and specificity for involvement of joint were 100% and 60% respectively, for physeal plate invasion 95% and 62%, for neurovascular invasion 50% and 100%, and for skip metastasis 100% and 91%. The clinical positive predictive rate / clinical negative predictive rates for the four parameters mentioned above were 25% / 100%, 80% / 89%, 100% / 94%, and 25% / 100%, respectively. No statistically significant difference of sensitivity and specificity in the 4 major areas was found between post gadopentetate dimeglumine contrast enhancement studies and non-contrast studies in 27 cases.

MR imaging is helpful in preoperative evaluation and staging of osteosarcoma. It showed good sensitivity in detecting involvement of joint and physeal plate invasion, and good specificity in identifying the invasion of neurovascular bundle and skip lesions. Contrast enhancement studies are not absolutely essential in assessment of involvement of joint, physeal plate invasion, neurovascular invasion or skip metastasis.

Key words: MR, Bone neoplasms, Osteosarcoma

MR imaging is one of the major imaging tools for staging tumors of the musculoskeletal system in current clinical practice [1-5]. Accurate preoperative evaluation is critical for limb salvage surgery of malignant musculoskeletal tumors because it can help achieve optimal residual function and safe, tumor-free margins. In young adolescents, osteosarcoma (OGS) ranks as the most common malignant primary bone tumor [6]. The involvement of joint, invasion of physeal plate, neurovascular bundle and skip metastasis are four major areas for orthopedic surgeons to consider in planning surgery for OGS [6, 7]. MR
imaging has been showed to be superior to CT scan in differentiation of tumor from soft tissue and neurovascular bundle [2, 3, 5] and in evaluation of the intrasosseous extent of OGS [4]. Schima et al reported that MR imaging has 100% sensitivity and 69% specificity in detection of joint involvement, and they recommended post contrast enhancement [1]. The purpose of this study was to further evaluate the application of MR imaging and the value of gadopentetate dimeglumine MR contrast medium in tumor staging of OGS.

MATERIALS AND METHODS

From April 1994 to July 1999, 34 patients (24 men, 10 women, age range 7-55 years, mean age 17 years) received MR imaging examination and underwent surgery under the impression of OGS with later pathological confirmation. The surgical methods included: extracorporeal radiation and reconstruction (n=8), en bloc excision, fusion and prosthesis (n=5), wide resection with custom made prosthesis reconstruction (n=5), amputation (n=4), wide resection with extracorporeal radiation (n=3), wide resection with allograft and fusion (n=3), allograft with fusion (n=2), wide resection only (n=2), disarticulation (n=1), and wide resection with allograft (n=1).

The time interval between MR imaging examination and surgery ranged from 1 days to 152 days (mean=44 days). We used 1.5T MR scanners (Signa, General Electric Medical Systems, Milwaukee, Wi.; and Magnetom Vision, Siemens Medical System, Iselin, NJ). Surface or torso coil were applied according to the position of the tumor. MR imaging was performed with fast spin echo (FSE) or spin echo (SE), sagittal, coronal, and axial scans, T1-weighted imaging (WI) (300-738/10-15), proton density (PD) WI, T2WI with/without fat saturation (FS)(2000-5000/16-105), and STIR (short tau inversion recovery) (TR: 2000-3750 msec, TE: 12-84 msec) (2000-3750/12-84) imaging. The matrix was 256x192, and number of excitations (NEX) was 1-2. Twenty seven patients received non contrast and post gadopentetate dimeglumine (Gd-DTPA, Magnevist, Schering AG, 1mmol/kg, Germany) contrast enhancement with T1WI and FS.

The MRI findings were analyzed retrospectively to correlate with surgical results by one radiologist specialized in musculoskeletal section. The surgical findings were performed by one experienced orthopedic surgeon.

The 4 major areas of concern included the involvement of contiguous joint, physeal plate, neurovascular bundle and skip lesions (bone metastasis). The findings were classified as “positive” or “negative”. In 27 patients who received pre- and post Gd-DPTA contrast enhancement studies, the result was classified as positive if any one of the pre- or post Gd-DPTA contrast enhancement studies showed positive results, and classified as negative if pre- and post Gd-DPTA contrast enhancement studies all revealed negative results.

Data were entered and analyzed using PC SAS

Table 1. The locations of the 34 tumors

<table>
<thead>
<tr>
<th></th>
<th>Proximal</th>
<th>Middle</th>
<th>Distal</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femur</td>
<td>2</td>
<td>1</td>
<td>15</td>
<td>18</td>
</tr>
<tr>
<td>Tibia</td>
<td>9</td>
<td>1</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>Fibula</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Humerus</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 2. Statistical analysis of MR imaging in 34 patients with osteosarcoma

<table>
<thead>
<tr>
<th>Involvement of joint</th>
<th>Physeal plate</th>
<th>Neurovascular Invasion</th>
<th>Skip metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>(n = 21)</td>
<td>(n = 4)</td>
<td>(n = 1)</td>
</tr>
<tr>
<td>Specificity</td>
<td>100% (4/4)</td>
<td>95% (20/21)</td>
<td>100% (1/1)</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>25%</td>
<td>80%</td>
<td>100%</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>100%</td>
<td>89%</td>
<td>94%</td>
</tr>
</tbody>
</table>

Table 3. Statistical analysis of post Gd-DPTA contrast enhancement studies and non-contrast studies in 27 patients who received Gd-DPTA contrast enhancement

<table>
<thead>
<tr>
<th>Involvement of joint</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non contrast studies</td>
<td>100 % / 68 %</td>
<td>100 % / 56%</td>
<td>0.0 % + 1.0 % (0.500)</td>
<td>12.0 % + 8.6 % (0.082)</td>
<td>0.0 % + 0.4 % (0.500)</td>
<td>0.0 % + 0.4 % (0.500)</td>
</tr>
<tr>
<td>Post contrast enhancement studies</td>
<td>100 % / 64%</td>
<td>100 % / 64%</td>
<td>0.0 % + 1.4 % (0.500)</td>
<td>0.0 % + 0.3 % (0.500)</td>
<td>0.0 % + 1.4 % (0.500)</td>
<td>-4.6 % + 4.7 % (0.155)</td>
</tr>
<tr>
<td>*Sensitivity difference (p value)</td>
<td>0.0 % + 1.0 % (0.500)</td>
<td>12.0 % + 8.6 % (0.082)</td>
<td>0.0 % + 0.4 % (0.500)</td>
<td>0.0 % + 0.4 % (0.500)</td>
<td>0.0 % + 1.4 % (0.500)</td>
<td>-4.6 % + 4.7 % (0.155)</td>
</tr>
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</table>

*Data were mean + standard error
Sensitivity, specificity, clinical positive predictive rate (PPR), and clinical negative predictive rate (NPR) were calculated in evaluation of the following four major areas: involvement of contiguous joint, physeal plate, neurovascular bundle and skip lesions. In 27 patients who received pre- and post Gd-DPTA contrast enhancement studies, four
pair-wise comparisons of sensitivity and specificity in post-contrast enhancement studies and pre-contrast studies were presented as mean difference and standard error of the mean difference, which were calculated based on a multinomial distribution. A p value of less than 0.05 for each pair-wise comparison was considered statistically significant.

RESULTS

The locations of the 34 tumors are listed in Table 1. Three patients had parosteal OGS, one had periosteal OGS, and two had diaphysis involvement.

The sensitivity and specificity for joint involvement were 100% and 60% respectively, for physeal plate invasion 95% and 62%, for neurovascular invasion 50% and 100%, and for skip metastasis 100% and 91%. The clinical positive predictive rate (PPR) / clinical negative predictive rate (NPR) for the four major areas as mentioned above were 25% / 100%, 80% / 89%, 100% / 94 %, and 25% / 100%, respectively. (Table 2)

Statistical analysis of post Gd-DPTA contrast

Figure 3. A 17-year-old boy with osteosarcoma in the proximal fibula. a. Axial T1 weighted imaging (600/11/2) and b. T2 weighted imaging (2150/90/2) show a tumor mass with low signal on T1 weighted imaging and high signal on T2 weighted imaging at the proximal fibula with surrounding soft tissue mass (arrows). The encasement of the peroneal nerve was noted during surgery but not well identified in MR imaging.

Figure 4. Sixteen-year-old girl with osteosarcoma of the distal femur. a. Sagittal T1 weighted imaging (400/12/2) without contrast enhancement shows a skip lesion at the epiphysis of the proximal tibia (arrow). b. Coronal T1 weighted imaging (738/12/2) with contrast enhancement shows peripheral contrast enhancement of the tumor mass and the skip lesion (arrow) near the joint.
enhancement studies and non contrast studies of 27 patients is shown in Table 3. No statistically significant difference of sensitivity and specificity was found between post Gd-DPTA contrast enhancement studies and non contrast studies.

For involvement of joint, four cases showed true positive results (Fig. 1). There were 12 false positive cases (12/34) which showed high signal on T2WI and post contrast enhancement on T1WI (with/without contrast enhancement), but there was no evidence of tumor invasion during surgery due to joint effusion rather than genuine involvement of the joint (Fig. 2). Five cases showed false positive physeal plate penetration. Only one case showed true positive neurovascular bundle invasion (Fig. 3); Two cases were false negative. There were one true positive (Fig. 4) and 3 false positive skip lesions. Ischial bone was directly invaded via hip joint in one case. Another case had a supposed “skip lesion” merged with the bone mass, while the third “skip lesion” case was found to be a nutrient vessel (Fig. 5).

**DISCUSSION**

Accurate preoperative determination and local staging of the tumor extent of OGS are essential for planning treatment and the resultant survival [2,7,8]. MR imaging has become one of the best imaging techniques for evaluation of OGS [3, 7]. It has superior soft tissue contrast and good demonstration of bone marrow and also provides multiple plane display (coronal, sagittal, and axial planes). MR imaging is superior to CT scan in histopathological correlation as well as detection of soft tissue extension, cortical bone destruction, periosteal reaction and joint involvement [2, 9].

Involvement of joint in OGS occurs in 19-24% of all OGS patients [1,6]. Schima et al reported a sensitivity of 100% and specificity of 69% for MR imaging in identifying the tumor extent in the joint [1]. Our study showed similar results with high sensitivity (100%) and relatively low specificity (60%). MR imaging was more accurate in detecting tumor extension to the cruciate ligaments than to the intrasynovial joint space [1]. Post contrast T1WI was most useful in detecting involvement of joint [1]. Only four patients (4/34) had adjacent joint invasion, which suggests osteosarcoma’s low potential for involvement of joint. The adjacent joints in 12 false positive cases (12/34) showed high signal on T2WI and post-contrast enhancement on T1WI (with/without contrast enhancement), but no evidence of tumor invasion was found in surgery. The imaging findings were due to joint effusion with or without synovitis [10] (Fig. 2). In fact, the more reliable features of involvement of joint are disruption of the joint capsule, and intraarticular destruction of the cortical bone and articular cartilage or the intracapsular-
extrasynovial cruciate ligaments of the knee [1].
The four cases of involvement of joint with surgical proof showed extensive destruction of synovial capsules and bone (glenoid of the shoulder, acetabulum and ischial bone of the hip, and distal femoral condyle of the knee joint) (Fig. 1); the only exception was a patient with involvement of the knee joint without obvious destruction of the joint in the bony margin.

Although the physis has long been considered a barrier to tumor growth, it was reported that osteosarcoma often extended into the epiphysis, with 75-88% of cases having an open physis [6]. MR can recognize epiphyseal invasion in 80% of metaphyseal OGS [6]. It has 90.3% diagnostic accuracy (positive predictive rate plus negative predictive rate). Surgeons can therefore preserve the epiphysis safely if there is no contact between the tumor and the growth plate on MR imaging [11]. T1WI and STIR images revealed a 100% sensitivity but lack of specificity in predicting epiphyseal involvement [12]. Our study observed a rather high tendency of physeal plate invasion (21/34), with high sensitivity (95%) and relatively low specificity (62%) in detecting physeal plate invasion. One case showed a false negative result with no definite MR evidence of physeal plate invasion. Five cases showed false positive results but had MR evidence of physeal plate involvement. There must be a discrepancy between MR imaging and surgery in correlation of physeal plate penetration.

Decisions about neurovascular involvement may be equivocal in some cases [7]. van Trommel et al proposed using the absence of any tumor involvement of a structure on MR imaging as a correct determining factor [7]. Yet, reactive edema interface may be difficult to separate from true tumor involvement [7]. In most of our cases (30/34), there was no neurovascular invasion. The specificity was 100%. We noticed that OGS tended to displace or compress the neurovascular structure, abutting the neurovascular bundle, rather than true invasion. However, encasement of the peroneal nerve was noted in one case, but was underestimated (Fig. 3). In another case of OGS in the proximal tibia, the mass compressed and abutted the posterior popliteal artery, but MR imaging found no significant invasion. Skip lesions occur in 1-25% of high grade intramedullary OGS [6,13, 14]. Spin echo T1WI with longitudinal scan and a large field of view was found to have higher sensitivity than conventional radiography for the detection of skip lesions [3, 9]. In our study, only one case had a skip lesion. MR imaging showed the best sensitivity (100%) and specificity (91%) in detecting skip bone metastasis. Three patients showed false positive results.

Did post Gd- DTPA contrast - enhanced study increase the diagnostic accuracy? Seeger et al. did not think that contrast enhancement with Gd-DTPA was essential in preoperative MR staging of osteogenic sarcoma [15].But it did help the differentiation between tumor and adjacent reactive intramedullary and soft tissue edema [3].

In Gronemeyer et al’s opinion, post Gd-DTPA contrast - enhanced T1WI in axial scan was superior to T2WI in delineation of the tumor and for perioseous tumor conspicuity since it could eliminate the chemical shift artifact on T2WI which complicated appreciation of the fascial plane between the neurovascular bundle and the soft tissue mass [16]. Contrast enhancement studies are not absolutely critical as demonstrated in our study as there was no statistically significant difference in four major areas between post Gd-DPTA contrast enhancement studies and non contrast studies.

For logistic reasons, the current study had limitations in the number of cases, interpretation of MR imaging by one radiologist, radiological-surgical correlation, inconsistencies in the MR scanners used and the time intervals between MR imaging and surgical intervention. Further detailed study is necessary.

In summary, MR imaging was helpful in preoperative evaluation and staging of OGS. It showed good sensitivity in detecting involvement of joint and physeal plate, and good specificity in invasion of neurovascular bundle and skip lesions. OGS showed low potential for involvement of the joint and skip metastasis. It tended to penetrate the physeal plate, and displace or compress the neurovascular structure rather than true invasion. Contrast enhancement studies are not absolutely essential in assessment of involvement of joint, physeal plate invasion, neurovascular invasion or skip metastasis.
REFERENCES

以磁振造影術前評估骨肉瘤：磁振造影與手術之對照

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台北榮民總醫院 放射線部¹ 骨科部²

本研究的主旨在探討磁振造影對於骨肉瘤術前的評估及分期的正確性，以及藉由注射顯影劑與不注射顯影劑的比較評估顯影劑的用處。

從1994年到1999年共34位骨肉瘤病人接受磁振造影檢查，病人包含24位男性、10位女性，年紀從7至55歲，平均17歲。檢查脈衝程序包括：T1加強影像及T2加強影像合併或無脂肪飽和化。兼做注射顯影劑與不注射顯影劑者有27例，只做不注射藥物者有7例。四個主要的發現與手術結果做比較，包括：關節涉入、生長板侵犯、神經血管侵犯以及骨轉移。

磁振造影對於關節涉入的敏感度及特異性分別為100%及60%；對於生長板侵犯為90%及62%；對於神經血管侵犯為50%及100%；對於骨轉移為100%及91%。臨床陽性預測值及陰性預測值對於上述四個發現分別為25%，100%，60%，89%，100%，94%，以及25%，100%。四個發現在注射顯影劑及不注射顯影劑27例中並沒有統計上有意義的差別。

磁振造影對於術前的評估及分期骨肉瘤是有幫助的。它對偵測關節涉入及生長板侵犯有很好的敏感度，對於神經血管侵犯骨轉移則有很好特異性。顯影劑在評估關節涉入、生長板侵犯、神經血管侵犯以及骨轉移四項主要發現上並非絕對必要。

關鍵詞：磁振造影，骨腫瘤，骨肉瘤